

EFFECT OF PROTEIN-CALORIE INTERVENTIONS ON HUMAN

GROWTH RETARDATION AND MORTALITY RATES

NARRATIVE OF PROBLEM AND PROPOSED RESEARCH

March 1976

*BEST AVAILABLE COPY*

PROJECT STATEMENT

TITLE: Effect of Protein-Calorie Interventions  
on Human Growth, Retardation and Mortality  
Rates

DURATION: Five Years

ESTIMATED TOTAL COST: \$2,288,020.00

Year 1 - \$409,460

Year 2 - \$535,720

Year 3 - \$553,420

Year 4 - \$577,020

Year 5 - \$212,400

RAC requested authorization 3 years

INVESTIGATORS: Ricardo Bressani, Ph.D., Co-Principal  
Investigator  
Robert E. Klein, Ph.D., Co-Principal  
Investigator  
Juan J. Urrutia, M.D.  
Charles Yarborough, Ph.D.

INSTITUTION: Institute of Nutrition of Central America  
and Panama (INCAP), Guatemala City,  
Guatemala, Central America

PROJECT MANAGER: Harold L. Rice, TA/N

## 1. SUMMARY

Protein-calorie malnutrition is a major problem in Central America and in many parts of the underdeveloped world. Until a few years ago, overwhelming emphasis was placed on protein deficiency as the major factor in malnutrition. However, investigations in Guatemala (Lechtig, et al) and India (Gopalan) suggest that caloric deficiencies may also be very important. As a result, more attention has recently been given to caloric deficiency and there is presently considerable debate about the relative importance of protein versus calories.

This is an important debate, both for scientific and practical reasons. Many governments and agencies are currently involved in planning and implementing large scale nutritional interventions in malnourished populations. The relative differences in costs of alternative interventions are large. Caloric supplements are relatively inexpensive as compared to animal protein based supplements. Further, relatively little work has been done on the advantages and disadvantages of alternative delivery programs, and the gains to be expected when inexpensive, medical care systems are combined with nutritional interventions of various types. Data which describes the health effects on the population from interventions are the major expected outputs from this study. Information on the operational aspects of alternative nutritional interventions to achieve specific health and nutritional outcomes will be obtained.

The proposed investigation will test the effectiveness of nutritional interventions involving dietary improvements in protein quality and quantity and increases in caloric quantity as well as combinations of these treatments. New genetic varieties of opaque-2 corn are now available which

provide improvements in protein quality without significantly changing protein quantity. Similarly, improved soybean varieties are available which can provide improvements in both protein quantity and quality.

The effectiveness of the nutritional intervention will be assessed in terms of fetal and postnatal physical growth and morbidity and mortality rates during the first two years of life. The study will be carried out in rural villages with known protein-calorie malnutrition and where high levels of participation can be obtained.

The design of the study is informed by findings from previous protein and calorie nutritional interventions (Mata, Klein) and provides for diet supplements ranging from the normal diet through an optimal diet. The study will provide unambiguous answers to questions about the effectiveness of caloric and protein food supplements, using outcome measures that have policy implications.

## 2. RESEARCH PURPOSE AND EXPECTED RESULTS

### a. Purpose

The principal purpose is to determine, in populations with dietary limitations in energy and in protein quantity and quality, the relative effectiveness of several nutritional interventions which provide improvements in protein quality, quantity and increased calorie intake.

Effectiveness will be measured in terms of the impact of these interventions on fetal and postnatal physical growth and on morbidity and mortality rates in the first two years of life.

### b. Products

A variety of specific outcomes are anticipated. These include:

1. The establishment of the nutritional impact of a range of nutritional supplements in terms of birthweight and infant growth and on morbidity and mortality during the first two years of life. The nutritional interventions include:

- a. Caloric supplements
- b. Protein quality supplements
- c. Protein quantity supplements
- d. Protein quantity and quality supplements
- e. Caloric, protein quality and quantity supplements

2. A test of the hypothesis that, if available in adequate quantities, undernourished populations are capable of consuming an adequate amount of their normal diet to cover their normal protein and calorie requirements.

3. A determination of the acceptability and nutritional impact of new varieties of opaque-2 corn.

4. The solution, based on field trials, of technical and cultural problems associated with the implementation of nutritional supplementation programs.

5. The relative effectiveness of the nutritional interventions as compared to and in conjunction with a high quality, low cost medical care program.

6. Cost comparisons among alternative nutritional interventions and their associated health and nutritional benefits.

It is expected that all the nutritional interventions will result in benefits to the populations being studied.

### 3. SIGNIFICANCE AND RATIONALE

AID as well as other donors have invested millions of dollars in programs designed to develop nutrition interventions that will have a major impact on malnutrition. Until recently, overwhelming emphasis was placed on overcoming protein deficiency.

Thus, AID's agriculture program has supported genetic research to develop varieties with improved protein quality and/or quantity in corn, wheat, and sorghum. AID's nutrition program has underway field studies (near completion) to determine the nutritional impact of fortifying cereal grains such as wheat, rice and corn with essential amino acids and/or protein concentrates.

These studies have been productive. New varieties such as high lysine corn and sorghum have been developed and high protein wheats have been produced. Improved soy/wheat flours have been developed and are available through Food for Peace channels and hopefully will be introduced through commercial channels. The feasibility of adding lysine to wheat flour during milling has been demonstrated and soy fortified corn meal has been found acceptable in the preparation of tortillas.

We have reached the point where decisions must soon be made regarding the utilization of these possible interventions -- interventions that if implemented, will cost tens of millions of dollars.

The dilemma faced by the nutrition planner relates not only to cost but to the potential benefits to be derived from these interventions. FAO/WHO has lowered the protein "requirements" for the target groups (pregnant women, preschool children). Some highly regarded nutritionists

insist that eating more of the basic cereal staple is all that is required to overcome malnutrition, other argue that the "requirements" are unrealistically low, etc.

Attempts to resolve these questions thru field studies indicate that protein and calorie supplementation can give beneficial results. For example, studies at INCAP indicate that child mortality is reduced by 50% in families consuming soy fortified corn. A second series of studies has shown that pregnant women whose diets have been supplemented with as little as 20,000 calories during pregnancy produce fewer low birthweight babies, a significant and surprising improvement since low birthweights are associated with high mortality. These studies, useful as they are, cannot be considered conclusive since the studies have not been carried out under conditions that are comparable and in some cases were designed for other purposes. In addition to our knowledge the nutritional impact of improved crop varieties has never been evaluated in the field.

The present study builds on past experiences. The use of "fincas" should result in better dietary control. A full year has been set aside to evaluate and modify the proposed interventions. The proposed design is statistically sound and, difficult as field studies may be, it is believed that the unique combination of talent, experience and test sites available at INCAP should produce answers to the serious questions raised concerning the relative merits of protein vs. calorie supplementation of deficient diets in LDCs.

#### 4. PLANS TO COORDINATE THE RESEARCH WORK INCLUDING NETWORKS

This is a unique time and place to conduct the proposed investigation. INCAP has pursued basic and applied research in food technology for over

two decades and has perhaps more extensive experience in the field evaluation of nutritional status and the evaluation of field trials in nutrition research than any other Institute. The proposed investigation melds these areas of research activity. In addition, this research is an immediate outgrowth of the AID-supported corn fortification study in Santa Maria Cauque (AID/csd-3357), the INCAP research program in food technology (Bressani et al., 1972, INCAP Publication L-3) and the NICHD supported longitudinal study of malnutrition, physical growth and mental development (Klein, et al., 1973). It is also related directly to efforts of International Agricultural agencies to develop and promote the use of opaque-2 corn. The Center for International Maize and Wheat Improvement (CIMMYT) has expressed great interest in the proposed research and has offered to collaborate with ICTA in Guatemala in the production of adequate amounts of the opaque-2 corn varieties needed for the study. In addition, MASECA, a private corporation based in Monterey, Mexico has offered to collaborate and will produce and donate sufficient amounts of soy-fortified flour for the necessary pretests of this intervention.

The need for two types of consultant support is also foreseen. The first is for an oversight review committee which could assemble in Guatemala once each year to review the project and give advice. In addition, there will be a need for individual consultants on specific problems and technical aspects of the proposed research. Finally, travel of the principal investigators to coordinate with AID, to visit related research projects and to attend scientific meetings will also be necessary.

##### 5. Plans to Facilitate Utilization of Research Results

The results of the proposed research will be of interest both to the general scientific community, in that they extend biological knowledge in the area of human nutrition and its effects, as well as to public health officials insofar as these results bear on their efforts to improve the quality of life of the populations for whom they are responsible. With respect to general scientific interests, the results will be disseminated thru publication in a variety of scientific journals, both in English and Spanish and in this fashion be made available to the scientific community through INCAP symposia.

More important from AID's viewpoint in the area of public health INCAP, the Pan American Health Organization (PAHO) and WHO will serve as conduits for disseminating information. INCAP is administered by PAHO and, through its Division of Applied Nutrition, is in direct contact with the ministries of health of the Central American countries. In addition, through its linkage with the Pan American Health Organization and with the World Health Organization, public health officials throughout the world will quickly be informed through the bulletins of the above mentioned organizations of the results of this investigation. Thus, dissemination of information to public health and planning officials will be accomplished through INCAP's local and international connections with public health ministries.

In addition, through the close collaboration of the investigators with the Division of Applied Nutrition at INCAP, the results of this investigation will play an important role in informing and planning nutrition intervention programs in Central America.

The research plan includes the recording of cost estimates for the nutrition interventions, and comparison of these to benefits associated with the specific interventions. This information will be highly useful to planners and governments who are formulating policy and designing nationwide programs to combat malnutrition. Detailed reporting of cost and benefit information will be made and the reports circulated to AID countries and to governments served by PAHO. Since the project outcomes have important implication for agriculture through the opaque-2 and soybean intervention the close collaboration of the Institute of Agriculture, Science & Technology (ICTA) and CIMMYT will make possible the appropriate distribution of results for use in agricultural policy and crop introduction programs. Also because the interventions will be testing the feasibility of introducing industrially processed tortilla flour fortified with full fat soy to the villagers a linkage to commercial utilization of project information has been arranged.

#### 6. MANAGEMENT CONSIDERATIONS

The project is organized into three closely interlocked phases. The first is the location and the selection of villages having the appropriate characteristics needed for participation in this study. The area expected to meet all the criteria is in a coffee growing region on the Pacific slope where six will be selected from the approximately forty fincas accessible at elevations of between 1500-2000 ft.

The logistics of setting up and managing a complex multi-village field study is no easy task, however, the principal investigators have had a successful experience over the last eight years in doing just this

in Guatemala. In the first phase, during the intervention research a separate village will be used. This village will not be a part of the controlled study of Phase II.

As the activities chart on page 38 shows, there will be a planning review of findings at the end of the first year, prior to beginning of the nutrition interventions in the villages. The purpose of this review is to report on the results of the intervention research, the state of the base line data collection, in selected villages, the progress on logistics, and the updating of budgets and other input needs based on the experience of the first year. If insurmountable problems have been encountered in critical areas affecting the power to interpret clearly the interventions, certain portions of the study may be redesigned.

The management plan includes, in addition to annual written reports, annual oral reporting to AID by the investigators, and annual visits by consultants in the fields of epidemiology, statistics, nutrition and food technology to the project sites.

At the end of the second year an intensive review will be conducted in order to determine whether AID should recommend to RAC that the study proceed for the total life of the project as planned.

## 7. TECHNICAL REVIEW

This review of the published literature is principally concerned with the effect of nutrition on the physical growth, mortality and morbidity rates of young children. Particular attention is paid to the relative importance of proteins versus calories.

Work at INCAP indicates that the relative contribution of calories and proteins to an increase in birthweight depends on the limiting nutrients of the home diet in the population under study. Other factors like physical activity, prevalence of disease and magnitude of the maternal nutritional stores before pregnancy may also be important determinants of the relative contribution of calories and proteins to birthweight. The expected reduction in proportion of low birthweight (LBW under 2.5 kg) babies following a nutritional intervention may therefore depend not only on the estimated range of fetal weight increase but also on the nature and total amount of supplement ingested during pregnancy as well as on the existent proportion of low birthweight babies prior to the intervention. The offspring of women who have low prepregnant weight, poor diet, low level of replacement of the home diet by the supplement, low physical activity during pregnancy and poor health status can be expected to show larger increases in birthweight of offspring when their diet is improved.

Parallel findings are evident from the literature on the effects of food supplementation on physical growth. That is, the expected relative effect of proteins and calories on postnatal growth appears to depend on what the dietary limitations of the study populations are. Thus, in

populations in New Guinea, where proteins were considered limiting, caloric supplementation reportedly affected growth in weight but not in height (Malcolm, 1970). But in India, where calories were considered limiting, caloric supplementation apparently improved growth in weight and height. (Gopalan et al., 1973)

Three types of naturally occurring comparisons suggest that nutrition is related to morbidity and mortality rates. The first comparison is between developed and underdeveloped countries where better maternal nutrition in developed countries is accompanied by lower infant mortality rates. The second comparison arises from secular trends within countries, wherein improving maternal nutrition is accompanied by a fall in infant mortality rates (Keyfitz & Flieger, 1968). A striking example of this kind of comparison was the fall in perinatal mortality in England during World War II, when England's maternal nutrition was improved through rationing (Duncan, Baird & Thomson, 1952). In all these comparisons, however, other factors which would influence infant mortality also vary. Thus, the associations between improved maternal nutrition and decreased infant mortality cannot be reliably claimed to be causal.

Preliminary finds from INCAP studies are encouraging because they suggest that it is possible to address this problem directly. The results of studies carried out in four rural Ladino villages and in Santa Maria Cauque indicate that child mortality decreases as the level of maternal supplementation increases.

The published literature also suggests that nutrition during pregnancy and lactation and morbidity are associated. First, this relationship can be inferred from comparisons of morbidity levels among populations of differing nutritional status. These comparisons show that populations

of poor nutritional status have markedly higher morbidity rates (Gordon, et al., 1963; Marsden, 1964; Banik et al., 1967; Ghai, et al., 1971; Mata, et al., 1971). Secondly, there is some evidence that within a population, poor nutritional status is associated with increased morbidity. Various studies have noted that the frequency of illnesses, notably diarrhea, is markedly higher among those clinically defined as malnourished than among clinically normal children (Scrimshaw, et al., 1966; Salomon, et al., 1966; Salomon, et al., 1968; James, 1972; Salomon, et al., 1971). An extensive review of early literature on this subject appears in Scrimshaw, Taylor and Gordon (1968). Their general conclusion is that seriously malnourished children experience more illness than clinically normal children. Lastly, there is some evidence that nutritional supplementation programs result in decreased morbidity rates (Scrimshaw, et al., 1966; Scrimshaw, et al., 1968a; Baertl, et al., 1970; Wray, 1967; Urrutia, N.D.).

Definitive answers to these questions are urgently needed. By combining the experimental treatments proposed and measuring their impact in terms of the outcome variables described in the context of an experimental design with adequate sample sizes and careful controls and measures for both independent and dependent variables we will be able to provide these answers in terms that are immediately useful to planners and Public Health Officials.

## 8. RESEARCH PROJECT DESIGN AND METHODS

### A. Research Design and Methods

#### . Research Plan

There are three phases of operation in the proposed investigation.

The first phase includes: a) intervention decision research; b) identification

and selection of study villages, c) implementation of medical care and data collection systems, and d) selection of food processing technology required. The second phase covers implementation of the nutritional interventions and measurement of its effects. The last phase includes final analysis and publication of results. This is summarized in Table 1.

### Hypotheses

The structure of the experimental design will permit simultaneous and semi-independent experiments. There are five basic hypotheses:

- 1) Nutritional status can be improved by simply promoting the consumption of more corn and beans;
- 2) Nutritional status can be improved by adding more energy to the existing corn and bean based diet;
- 3) Nutritional status can be improved by increasing the protein quality of the diet by utilizing Opaque-2 corn;
- 4) Nutritional status can be improved by increasing both the protein quantity and quality in the diet by soybean fortification;
- 5) Optimal improvements in nutritional status can be obtained if protein quality and quantity as well as the amount of energy is increased.

Each hypotheses will be tested by comparing an appropriate nutritional intervention to both a negative control, i.e.: a group with no change in diet, and to a positive control, i.e.: a group receiving a maximal nutritional intervention. Thus, the impact of each of the interventions can be bracketed on both ends of its possible range.

As we shall explain below, there will be three levels of comparison: 1) across villages; 2) within a village between pre- and post-intervention periods, and 3) within the same individual mother between successive and differently treated pregnancies.

#### Populations Required

Six separate populations fulfilling the following criteria will be studied:

- 1) Each community should have about 200 families and 50 births per year.
- 2) The main diet staple should be corn. Calories and proteins, both from the point of quantity and quality, should be deficient.
- 3) They should exhibit poor nutritional status as evidenced by:
  - i) A prevalence of low birthweight babies (/ under 2.5 kg) of around 30% and,
  - ii) A prevalence of moderate and severe malnutrition (Gomez grades 2 and 3) of 40% in two and three year-old children.
- 4) A standardized health care system must be available in each community.
- 5) The populations should be staple, with little or no migration.
- 6) The dwellings in each village should be fairly well clustered together and the village must be accessible by road from Guatemala City.

Thus, it is expected that the six populations chosen will be comparable to one another in terms of the five characteristics outlined above. Villages in the "fincas" (large plantations) situated in the department of Suchitepequez 150-200 kms from Guatemala City will be the test sites. These are of the desired population size and characteristics and offer the advantage that wages paid by finca owners include a weekly corn ration. It is also the custom for the "finca" owners to provide a limited amount of land where families may plant corn and beans. This pattern of grain supply and production provides excellent opportunities for controlling the supplemented diets.

#### Research Design

After one year of baseline data collection the six populations will be randomly assigned to each of the following groups as shown in Table 2:

- a) The first, Group A, will receive additional corn and beans;
- b) Group B will receive an energy supplement. The particular form of the supplement will be determined through pretesting during the first year of project. Cooking oil and high calorie cookies are currently being considered.
- c) Group C will benefit from improvements in protein quality (substitution of conventional corn by Opaque-2);
- d) Group D will receive a corn diet fortified by a defatted soy flour providing a diet of high protein quality and increased protein quantity. The decision on the mechanism for delivery of the supplement,

soy pellets added at the village mill, or a precooked commercially produced flour, will be determined during the pretest.

e) Group E will receive all three improvements: protein quality and additional protein and energy through combinations of the above supplements and mechanisms.

f) Group F will serve as a control receiving only medical care and vitamin and mineral supplements as do all groups.

This design allows each group to serve as its own control. In addition, it will be possible to compare each of the interventions against the control group, and each of the treatment groups against each other.

Medical care will be introduced during the first year and we expect that important changes in health status will occur. These will be measured carefully and their presence will be taken into account during the data analyses.

TABLE 1

RESEARCH PLAN

PHASE I Year I	PHASE II Year 2 to 4	PHASE III Year 5
Identification and selection of suitable communities	Nutritional intervention	Medical care turned over to Ministry of Public Health
Commencement of the health care program	Data collection following nutrition intervention	Final analysis and publication of data
Intervention decision research baseline data collection in villages	Preliminary analysis and publication of results	
	Production and quality control of food supplements	

TABLE 2

EXPERIMENTAL DESIGN

Design	Increased Protein Quantity	Increased Energy	Food Given
1	Yes	Yes	Additional corn & beans
2	No	Yes	Energy Supplm. (e.g. cooking vegetable oil, or cookies)
3	No	No	High Quality protein (opaque-2 corn substituted for common variety)
4	Yes	No	High quality and quantity protein supplm. Mixture of corn (85%) and soybean (15% flour)
5	Yes	Yes	High protein quantity & quality plus energy (Oil, Mixture of corn (85%) and soybeans (15%) and cookies)
6	No	No	None

BEST AVAILABLE COPY

TABLE 3

DATA TO BE COLLECTED UNDER THE PRESENT PROPOSAL BY VARIABLE

Variable	Measured By	Field Worker
<b>1. <u>INDEPENDENT VARIABLE:</u></b>		
Food Supplementation	Attendance to the central distribution centers	Supplementation auxiliaries
<b>2. <u>DEPENDENT VARIABLES:</u></b>		
Infant and second year Mortality Rates	Births, Deaths (0-24 months of age)	Census updater; nurse
Nutritional status of newborn and of children less than 3 years of age	Anthropometry	Anthropometrist
Morbidity prevalences	Morbidity survey	Home interviewer
<b>3. <u>PARTIALLY CONFOUNDING VARIABLES OR VARIABLES NEEDED TO ELUCIDATE MECHANISMS:</u></b>		
a) Maternal nutritional status	Home dietary survey; Anthropometry	Home interviewer; anthropometrist
Maternal clinical history	Health clinic records	Nurse
Gestational Age (For interpretation of birthweight)	Physical examination	Nurse
b) Child nutrition	Home dietary surveys	Home interviewer
Child clinical history	Health clinic records	Nurse
c) Socioeconomic data	Income, housing, education	Home interviewer

TABLE 4

KINDS OF DATA TO BE COLLECTED UNDER THE PRESENT PROPOSAL BY INSTRUMENT

Instrument	Variables to be measured	Periodicity	Place	Field Worker
Census and Clinic records:				
- Births and Deaths (0-24 months of age)	Infant Mortality	Daily	Home	Nurse*; home interviewer
- Pregnant mothers	Number of pregnant women	Daily	Medical Unit	Nurse; census updater
Supplementation Attendance Surveys	Receipt of food supplements	Weekly**	Medical Unit	Supplementation auxiliaries
Home Caloric and Protein Intake (Dietary Surveys)	Nutritional Status	Every month from the 13th week of pregnancy to 3 yr. of age	Home	Home interviewer***
Food Quality Control Samples	Protein Calorie PER	Monthly	Home	Home interviewer & Lab Technician
Anthropometry of Mother and Child	Nutritional Status	Every 3 months from the 13th week of pregnancy to 1 yr. post-partum; every 6 mos. in children from birth to 3 yrs. of age	Medical Unit	Anthropometrist ****
Morbidity Survey	Diarrhea Respiratory Ailment Other Infections	Monthly in mothers & children	Home	Home interviewer
Clinical Examination of Pregnant Mothers and Infants	Mother and child health status	Every 3 mos. from the 13th week of pregnancy to birth; every 6 months in children from birth to 3 years of age	Medical Unit	Nurse

Instrument	Variables to be measured	Periodicity	Place	Field Worker
Record of Outpatient Medical Care	Mother & child health status	Daily	Medical Unit	Nurse
Socioeconomic Survey	Sociocultural factors	One a year	Home	Home Interviewer

\*See next page for footnotes

- \* The nurses are principally responsible for providing medical care and most of their activities are confined to the out-patient clinic.
- \*\* Measurements of receipt of the supplement will be determined ultimately. If soy pellets are used, inclusion of the pellets will be checked daily at the village mill. In contrast if a soy fortified flour is used, it will be dispensed, and its receipt checked weekly.
- \*\*\* The home interviewer is specifically trained to collect home dietary survey data, morbidity data, collect periodic food samples and to collect socio-economic data. She also provides the most direct and consistent link between the program and the members of the study population.
- \*\*\*\* The anthropometrists rotate weekly through the 6 villages and take all anthropometric measurements. This reduces measurement to a minimum and allows for careful standardization.

TABLE 5

EXPECTED IMPACT OF THE NUTRITIONAL INTERVENTION ON KEY DEPENDENT VARIABLES

Variable	Estimated By	Expected Impact
Nutritional Status in Children	Percentage of: - Low birthweight babies - Prevalence of 1, 2, and 3 year old children with less than 75% of the normal weight for age	A decrement: - From 30% to 10% - From 40% to 10%
Infant Mortality	Infant deaths per 1000 alive births	A decrement from 160 to 80 per thousand

TABLE 6  
EXPECTED SAMPLE SIZE

<u>Group</u>	<u>Initial Control (12 months)</u>	<u>Partial Treatment (9 months)</u>	<u>Full Treatment (27 months)</u>	<u>Second births to mothers in the initial control</u>
All Groups	50	37	113	33

The types of food intervention to be given are shown in the right hand column of Table 2. The amount of food to be given will be that necessary to reach the recommended allowances; the absolute amounts will be dependent on the normal dietary intakes of these populations.

The rationale as to why the particular foods were chosen is as follows: Group A will receive additional amounts of corn and beans. These are staple foods in rural Guatemala. It has been hypothesized that consumption of the normal diet in adequate amounts would provide the basic protein and calorie requirements but that ingestion of adequate amounts would provide the basic protein and calorie requirements but that ingestion of adequate amounts is limited by economic considerations. Another possibility is that because of their bulk, physiological limitations, particularly in children, limit intake of adequate amounts of the basic diet.

During the first phase, in the intervention decision research activity, the feasibility of this intervention will be tested in a separate but comparable population. If intake cannot be increased, group A will be eliminated from phase II.

Group B will receive calories in the form of cookies made from wheat, corn flour and oil.

It should be mentioned, some governments (i.e. Panama), have implemented distribution of oil in rural areas as a means of alleviating energy dietary limitations. There is a need, therefore, for evaluating the nutritional potential and impact of oil supplementation. However, to reach very young children who may not already be consuming the normal diet, we propose to test the potential for highly palatable cookies prepared from wheat, corn flour and oil. These cookies, while apportioning little in the way of protein, will provide substantial amounts of energy.

To improve the protein quality of the diet of Group C, opaque-2 corn will be substituted for regular corn. The high nutritional quality of opaque-2 corn protein has been known for over 12 years, as determined in experiments with animals and human subjects. As a matter of fact, INCAP was the first institution to show, in young children, that opaque-2 proteins had a biological value of about 90%. The high quality of opaque-2 protein has also been demonstrated in mixed diets, similar to those consumed by the rural Guatemalan population. The varieties of opaque-2 corn expected to be acceptable to the Guatemalan population and feasible to produce by poor farmers provide improvements in protein quality with very little change in protein quantity. The opaque-2 corn to be used will be in Guatemala cooperatively with CIMMYT and ICTA.

The objective of the nutritional intervention for Group D is to provide increases in both protein quantity and quality with minimal changes in dietary calorie levels. The supplement will be a mixture of 85% corn and 15% soybeans. Several alternative techniques for delivery are being considered. These include whole soybeans prepared in the home with

corn, pre-cooked soy in pellet form mixed with corn at village mills and pre-cooked corn-soy blend flour. The decision regarding the form of the intervention for Group D will be made during the intervention decision research phase on the basis of acceptability and precision for control and measurement of the intervention itself. This will result in a product providing about 50% more protein, protein quality similar to Group C, and slightly more calories when compared on opaque-2 corn alone. The nutritional improvement of this approach to the diet has been demonstrated in experimental animal work. This approach is recommended because there is interest in the industrial preparation of a lime-treated corn flour with 15% soybeans. Such a preparation is now available commercially in Costa Rica.

Group E will receive a diet supplement which includes increases in energy, protein quality and quantity. This will be accomplished by combining the intervention described for Groups B and D.

Group F will serve as a control, receiving medical care, vitamins and minerals as do all groups. This will allow for the evaluation of the nutritional intervention across the three year intervention period since improvements in health are expected to be achieved across the three-year period as a function of the medical care program.

Careful records will be maintained on the costs of the various nutritional interventions, including costs of materials, production, quality control, delivery and consumption estimates. Subsequently the nutritional costs will be related to the differential benefits observed for each of the interventions.

### Data Collection Activities and Sample Size

The data to be collected in the proposed investigation and the periodicity of measurements are presented in Tables 3 and 4. To achieve the objectives of this study, food supplementation, physical growth, morbidity and mortality data are necessary. In addition, to rule out alternative explanations and to elucidate the mechanisms which may relate food supplementation to physical growth and mortality, additional data about mothers and children are crucial. These additional data include diet surveys, maternal anthropometry, obstetrical history, clinical course of pregnancy, duration of pregnancy, health of the mother and child, and socioeconomic characteristics of the family.

Careful planning of data collection and data flow is essential. After an initial census of the population, data collection activities will be programmed for all individuals in the study sample. Each week precoded data forms will be brought from Guatemala City. These will bear a label identifying the individuals to be examined and the date of examination. Periodic census updates will be carried out to make sure all study subjects are included for study.

The completed data forms will be checked in the field for clerical errors and sent each week to Guatemala City for punching. These data will be punched immediately, and the values will be inspected. Doubtful information will be immediately recollected. All original data forms will be filed in Guatemala City.

The required sample size is a function of the expected effect. The main dependent variables in this study are mortality, morbidity and nutri-

tional status (as defined by anthropometric data) in children 3 years or younger. Table 5 shows that we expect to lower:

- 1) The prevalence of low birthweight babies from 30 to 10%;
- 2) The prevalence of moderate and severely malnourished 1 to 3 year old children as defined by weight for age less than 75% of the normal (Gomez grades 2 and 3), from 40 to 10%; and
- 3) The infant mortality rate from 160 to 80 per thousand.

The projected sample sizes are shown in Table 6. We have calculated (using arcsin power tables in Cohen, 1972) that given these sample sizes we will be able to demonstrate a nutritional impact of the magnitude presented in Table 5. For all the first variables mentioned, percent low birthweight, an effect will be seen 90% of the time in each group at a 5% significance level. For the second variable, percent growth retardation, the power of the design is 99% in each group. Finally, for the last variable, infant mortality, because the predicted nutritional impact is less than half that predicted for the other outcome variables (e.g. birthweight) the power to detect a significant difference is only 43% within each group, but is 98% if all groups are combined. Thus, in each group, we can provide essentially definitive test of the basic effects.

#### Analytic Plans

We plan two types of control against the selection biases which potentially accompany any feeding experiment. The first control is implicit in the design and consists in having groups which bracket the range of possible effects. Group F, receiving no nutritional intervention

provides a baseline while Group E, receiving all interventions, serves as a "positive control" (i.e. shows the maximum expected effect in these communities).

In this set-up the analytic steps for any outcome measure are as follows:

1) Is Group E higher (better) than Group F? If not, it is highly unlikely that the range of interventions has any effect at all.

2) Each of the supplemented groups will be compared with Groups E and F to determine if there are differences associated with the experimental treatments. Our experience suggests that different supplements may have differential impacts on the outcome variables. Thus, the calorie intervention may be more effective in increasing birthweight (and thus reducing infant mortality) whereas the protein supplements may improve physical growth rates in two year olds and reduce morbidity rates in this group. This type of information is not now available and would be especially useful for nutrition and health planners.

3) Finally, we plan a two-way analysis of variance using the design:

		<u>Energy</u>	
		None	Yes
<u>Protein</u>	None	F	B
	Yes	D	A, E

We do not know in advance whether we will have the power to separately assess the two factors of more energy and more and better protein, which is why we have put an evaluation of main effects as an important prior step. Nevertheless, we do plan to do a full two-way ANOVA (Analysis of Variance) as a final pass.

The second control, a within village control, addresses itself to a problem inherent in all nutrition intervention studies -- differences between experimental groups or villages in this case. To guard against unforeseen or unrecognized differences among villages we plan to collect data in all communities for one year before beginning the three-year intervention period. This will provide baseline data for assessment of initial group comparability, and will allow us to collect two or more observations on some families for a single indicator (e.g. birthweight), one control and one experimental. Thus, within-family or within-mother analyses are possible. These have relatively greater power since within-family variability can be expected to be less than population variability. These within family comparisons proved to be the most powerful in the INCAP study of malnutrition and mental development.

9. OVERALL COST - See Budget page 38.

10. WORK PLAN AND BUDGET

The work ahead has been subdivided into three phases. These are:

Phase 1:

Concurrently with the decision intervention research, potential study villages will be surveyed and selection will be made according to the criteria outlined earlier.

Once the villages have been selected base line data collection for all pertinent variables will begin. Prior to this time, staff will have been recruited, trained and standardized in the use of the data collection forms and the measurement techniques.

Simultaneously with the initiation of the base line data collection, the medical care program will begin. The nurses will have been previously trained in the context of another ongoing medical care project, and thus will be ready to begin when village selection has been accomplished. Quality control of the medical care program is routinely checked by the supervising physician.

The first phase is principally concerned with laying the ground work for measuring the effects of the interventions. Work can begin immediately on the intervention decision research to investigate the nutritional properties of some of the food

supplements. Three areas of research are contemplated:

- 1) Food technology of alternate food supplements;
- 2) Animal evaluation of alternate food supplements;
- 3) Human evaluation of alternate food supplements.

## 1. Food technology of alternate food supplements

### 1.1 Increased energy intake

Energy increments are contemplated in some of the experimental groups. To reach very young children, we propose to distribute high-calorie low-protein cookies ("chapurrada"). Cookies are known to be highly acceptable in Guatemala, particularly with pre-school children. The cookies will contain wheat, corn flour and oil (concentrations ranging from 10 to 20% can be included). Work is needed on developing such a cookie. It should have a standard concentration of oil, a fixed weight and its "food technology" characteristics, especially storage stability over time, should be known. The unit cost will be investigated and appropriate quality control techniques will be devised.

### 1.2 Replacement of common corn by Opaque-2 corn

Opaque-2 constitutes another nutritional intervention (Group C, Table 2). Tortillas of good texture and quality have been successfully made in the laboratory from lime-treated classic opaque-2 corn. No work has been done with two or three other types of opaque-2 corn. The classic opaque-2 corn has a soft starchy kernel, while some of the varieties being developed have a hard endosperm. Because the latter types are more advantageous, investigations regarding the quality of tortillas made from these new varieties need to be done. This information will enable us to select the type of opaque-2 corn most suitable for the study.

### 1.3 Use of corn supplemented with soybean

Two of the test populations (Group D and E, Table 2) will receive a mixture of corn (85%) and whole soybean (15%). Soybeans have been chosen because they provide protein of good quality and in relative large amounts.

corn tortillas made from this mixture must be tested and then acceptance evaluated both in the laboratory and in the field." We need to choose among three options: (a) distributing a mixture of corn and soybeans to be processed at home; (b) distributing a precooked flour made of 85% corn and 15% soybeans; and (c) adding soybean pellets to the corn dough during wet milling. Regardless of the choice, a quality control measurement must be developed.

### 2. Animal evaluation of alternate food supplements

The proposed field experimental design calls for five different treatments, the effectiveness of which should be examined in experimental animals. These studies will provide knowledge as to the nutritional properties of the supplements and their impact on the basic diet of the groups to be studied. In addition, their biological impact will be evaluated in rats and in swine. A weanling rat growth test is contemplated in which the animals will be fed ad libitum the food composites of each of the proposed food interventions. This study will assure us of the nutritional quality of the supplements.

The second test will be carried out in 4-5 week-old swine. These will be fed human food composites. For example, the cookie will be incorporated into the food composite of one group. In another group, common corn will be replaced by opaque-2 corn or by the corn soybean mixture. All these foods will be processed and fed as if being consumed by humans. The experiment will predict likely impacts of the supplements on humans.

### 3. Human evaluation of alternate food supplements

The acceptance, tolerance and physiological intake limitations of the food supplements must be briefly tested (20 days) in humans under field conditions to insure that no problems arise in the preparation and ingestion of the supplements.

Phase 2:

Phase 2 covers the second, third and fourth years of the study and includes the delivery of the nutritional interventions, the measurement of their impact, continued production and quality control of the nutritional supplements and preliminary analysis and publication of results.

The techniques used for delivery and the methods for the control and measurement of the ingestion of the nutritional supplements will be dictated by decisions regarding the exact form of the supplements based on the decision intervention research during Phase 1. However, regardless of the form of the supplements, the most precise measurement possible of receipt and use will be obtained.

Consistent with this concern for the precise measurement of the independent variable is the quality control required on the production of the supplements. Monthly samples will be collected by the home visitor and will be analyzed at the INCAP laboratories.

The measurement of the impact of the food supplements (the dependent variables) is the largest single activity in phase two. The specific activities of each type of staff member are laid out in table 2. In addition, periodic standardization trials are required to insure comparability of data across villages. This is accomplished in the field under the direction of the Field Director.

Because of ethical considerations, efforts will be made to continue medical care after the completion of the project. During the last half of year 4 of the project, alternative forms of providing medical care for the communities will be sought. It is anticipated that the medical care clinics in these villages can be incorporated into the national health care system.

Finally systematic data reduction, analyses and publication of preliminary findings are planned. Many of the findings of Phase 1 and 2 will be of great interest and use to the scientific community.

### Phase 3:

Phase 3 consists of final analyses and publication of results. This activity will take place during the fifth and last year and will follow the General Analytic Plan laid out earlier.

#### C. Facilities and Personnel

INCAP has the necessary major resources for this research. During Phase 1, equipment and construction costs will be incurred. In order to coordinate the daily research activities between the various villages and INCAP, a radio communication system is necessary. In each village, a medical care center must be constructed. In the geographic area of the villages a field station for personnel residence is needed, as well as a warehouse at INCAP. The food technology research efforts will need: a) Wiley mill, b) two analytical balances, and c) bakery technology equipment.

The professional staff to be associated with this study have worked closely together for several years. The complex logistical and scientific considerations which frequently bedevil a field research project of this magnitude will be minimal, since the principal investigators have already conducted medical and food supplementation programs in rural areas and have expertise in dietary and anthropometric surveys. They include scientists from several disciplines with extensive experience in field

studies of the type proposed here. Moreover, the present proposal requests relatively little for scientific staff support. Most of the scientific staff will be supported principally from other sources.

## 11. Office Appraisal

This research is urgently needed since many LDC governments and donor agencies are currently involved in planning or implementing large scale nutritional interventions in malnourished populations without really knowing which of the possible interventions will produce the greatest benefit for the least cost. This new project represents a major TA/N effort to resolve this key nutrition questions. The project builds on the accumulated findings from AID supported INCAP studies (a) on the effect of maternal diet on development of the offspring and (b) the effect of corn fortification on nutritional status. It is proposed that the new research be carried out by INCAP which perhaps is the only institution having the capability, experience and "field laboratory" for carrying out the proposed study.

INCAP developed the project design and it was reviewed by TA/N and several independent experts who suggested a number of changes which are now incorporated into the design. TA/N considers the proposed research as having the highest priority and strongly recommends initiation of the project.

MILESTONE LIFE-OF-PROJECT SCHEDULE

	Year 1	Year 2	Year 3	Year 4	Year 5
Phase #1	(S) Δ			C	
Identification of Communities	(S) - C				
Health Care Program	(S)			C	
Intervention Decision Research	(S) Δ (C)				
Base Line Data Collection in Villages	(S) (C)				
Phase #2	(S)				(C)
Nutritional Interventions	(S)	Δ			C
Data Collection Following Nutritional Intervention	(S)				(C)
Preliminary Analysis and Publication of Results	(S)				(C)
Production and Quality Control of Food Supplements	(S) Δ				(C)
Phase #3				(S) - (C)	
Medical Care Program Turned Over To Ministry Of Public Health				(S) - (C)	
Final Analysis and Publication Of Data				(S)	(C)

WORKPLAN/CONTRACT BUDGET AND LIFE-OF-PROJECT COST ESTIMATE

	Year 1		Year 2		Year 3		Year 4		Year 5	
	<u>Man Mos.</u>	<u>Est'd Cost</u>								
<b>INPUTS</b>										
1. Salaries	280	160,000	520	215,000	520	230,000	520	250,000	144	100,000
2. Consultants	40	5,000	40	5,000	40	5,000	40	5,000	40	5,000
3. Fringe Benefits										
4. Overhead (18%)		62,460		81,720		84,420		88,020		32,400
5. Travel and Trans.	2	25,000	2	25,000	2	25,000	2	25,000	2	25,000
6. Allowance										
7. Other Direct Costs		44,000		142,000		142,000		142,000		
8. Equip., vehicles materials & supplies		98,000		44,000		44,000		44,000		
9. Publications		3,000		3,000		3,000		3,000		
10. Subcontracts										
11. Other direct costs		<u>15,000</u>		<u>20,000</u>		<u>20,000</u>		<u>20,000</u>		<u>50,000</u>
Total Costs by Inputs		<u><u>409,460</u></u>		<u><u>535,720</u></u>		<u><u>553,420</u></u>		<u><u>577,020</u></u>		<u><u>212,400</u></u>

RESEARCH AND DEVELOPMENT COMMITTEE

Minutes of the March 24, 1976 Meeting

Project: Effect of Protein-Calorie Interventions on Human Growth Retardation and Mortality Rates (New), 5 years, \$2,288,020

Contractor: Institute of Nutrition of Central America and Panama (INCAP)

Project Manager: Harold L. Rice, TA/N

Dr. Long, AA/TA, commented that the rationale was well defined for this project and suggested the proposal was ready for discussion.

The East Asia Bureau, V. C. Yoder, asked if the results would be transferable to rice diets in Asia, or if there should be a rice component in the study. Dr. Hornstein, TA/N, responded that the study is to evaluate nutrients and not specific commodity sources of nutrients, therefore the results should be transferable. He pointed out there are few places where such studies can be done and locality limits the choice of commodity. One treatment evaluation where commodity may be important, Dr. Rice said, is the comparison to determine if the population can consume enough of their staple diet to provide adequate nutrients.

The Latin America Bureau, William Feldman, asked if the recent earthquakes in Guatemala had affected their national capability for conducting the study. The area being considered for the study is not located on a fault and was not affected by the recent quakes, Dr. Hornstein reported. The study will be done in "fincas" which are privately managed, thus government management capability will not be a factor. Although the Institute took some physical damage during the quakes, he said INCAP's capacity to do the study was not impaired.

Mr. Feldman further commented that the calorie-protein issue appears ultimately to become a question of total nutrition and asked for clarification. After reviewing briefly the interventions planned, Dr. Hornstein summarized the issue as a question of quality through quantity. If one can get the population to eat more, will the protein problem be solved? Can children especially eat enough to provide adequate nutrition?

The Africa Bureau, John Blumgart, through a letter from Dr. Cross, expressed concern that much of what this study proposes has been done previously. They are more concerned about utilization of the results and questioned if the interventions were applicable to LDC needs and could be afforded by them. Dr. Hornstein responded that the interventions

are not exotic and are applicable on a commercial or production basis. Although these variables have been studied in other ways he said we need to know how effective opaque-2 will be on a village basis. A lot has been learned from animal studies Dr. Rechcigl, TA/RES, pointed out, but has never been tested on a field basis with humans.

Dr. Long expressed concern that INCAP may be trying to study too many variables and get too many answers. Analysis of the many variables to be recorded must be closely scrutinized, and the role of check treatment villages in the design and follow-up requires careful review. Dr. Hornstein reported that INCAP has competent statisticians on its staff who are experienced in this kind of activity and TA/N has obtained external reviews of the experimental design which are favorable. Robert Birnberg, NE/DP, inquired if the 3 year study period was a scientific or a programmatic choice. Dr. Hornstein confirmed that the length of the study was objectively chosen.

Mr. Feldman inquired about implications and costs of manufacture or production to implement the products which may result from the study. Cost-effectiveness of the various interventions, Dr. Hornstein indicated, is part of the study. An implicit assumption relating to utilization is that governments will want to do something about this problem, as will industry. Dr. Rice commented that opaque-2 corn costs no more than the present corn, and soybeans not only yield more than the common bean in some areas but are better nutritionally. The capacity to grow soybeans on small farms is not limiting.

Mr. Feldman further suggested that evaluation and advising checks be built into the project. Dr. Rice confirmed that a feasibility review is built in during phase I, and Dr. Long recalled that RAC has a three-year limit on review and renewal.

Motion: That the project be approved.

Moved by V. C. Yoder and seconded by W. M. Feldman

Vote: Aye 5, Nay 0.

CERTIFICATION OF REVIEW  
AND  
SPECIAL IMPLEMENTATION OF INSTITUTIONAL ASSURANCE

The project titled "Effect of Protein-Calorie Interventions on Human Growth, Morbidity and Mortality" to be submitted on behalf of Drs. Robert E. Klein, Ricardo Bressani, Juan J. Urrutia, Reynaldo Martorell, Aaron Lechtig, and Charles Yarbrough to the Agency for International Development (AID) of the United States by the Pan American Health Organization/Institute of Nutrition of Central America and Panama has been reviewed by an assembled Institutional Review Board (IRB) whose signatures appear below in accordance with the requirements for regulations or protection of human subjects.

The IRB has determined to its satisfaction that the subjects of this activity will not be placed at risk. In arriving at the conclusion of no risk, the IRB reviewed the project in its entirety. Set forth below are the specific considerations and conclusions:

1. The families selected to participate in the study will be visited individually by a chief professional investigator who will explain in detail the degree of participation expected from them, that is:
  - a) Allowing their children to attend the health clinic on a specified date to be examined by health care personnel and by an anthropometrist.
  - b) Receiving on a specified date, the visit of an interviewer to collect information on home dietary intakes, morbidity, socioeconomic status and vital statistics.

All of this will be explained to them in terms that their cultural characteristics and level of education requires for a good understanding.

The head of the family will then be asked to make the decision to participate in the study on a free voluntary basis.

Conclusion: The IRB felt that under the circumstances this is the best which can be done in terms of "informed consent" and that it is appropriate. The commitment of the subjects will not interfere with their normal lives in any measurable way.

The inhabitants of the six communities, whether they decide to participate or not in the study, will benefit from the following services:

- a) Free preventive and curative medical care. This will be staffed by nurses under the supervision of a physician.
- b) Availability of food supplements. Five communities will receive combinations of proteins and/or calories. All groups, including the control group, will benefit from supplements containing vitamins and minerals.

Conclusion: The IRB concluded that the members of these communities would benefit from the activities contemplated within the study.

General Considerations:

The IRB analyzed the potential benefits that the project results may yield. It was remarked that, if the evaluation plan is carried out as proposed, the information obtained will be of great significant value for Health Planners in many underdeveloped countries.

The members of the IRB are listed below. None of the signatories has a vested professional interest in this activity that conflicts with the principle of independent, objective review.

I certify that this review was carried out in accordance with the requirements of Part 46, Protection of Human Subjects of Title 45 of the Code of Federal Regulations of the United States.

25 March, 1976

\_\_\_\_\_  
(Date of IRB approval)

\_\_\_\_\_  
 Signature of authorized institutional official)      25 March, 1976  
 (Date)

Carlos Tejada V.      Director, INCAP  
 \_\_\_\_\_  
 (Name)      (Title)

Institute of Nutrition of Central America and Panama (INCAP)  
 \_\_\_\_\_  
 (Name of Institution)

Av. Barrios 11-88, Guatemala City, Guatemala, C.A.  
 \_\_\_\_\_  
 (Address)

2762, Guatemala City  
 \_\_\_\_\_  
 (Telephone Number)

*Ivan Beghin*

---

Ivan Beghin, M.D.  
Chief, Division of Applied Nutrition, INCAP

---

Fernando Viteri, M.D.  
Chief, Division of Biomedics, INCAP

*Marina Flores*

---

Marina Flores, M.S.  
Chief, Dietary Research Unit, Division of Applied Nutrition, INCAP

*Gustavo Leal*

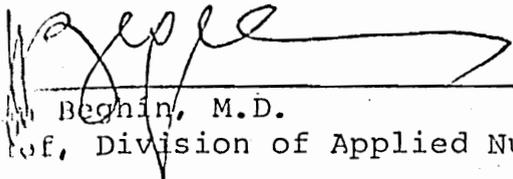
---

Gustavo Leal, D.D.S.  
Professor of Dentistry, University of San Carlos, Guatemala

*Luis Octavio Angel*

---

Luis Octavio Angel, M.D., M.P.H.  
Chief, Division of Education, INCAP

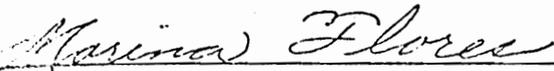


Beghin, M.D.  
Chief, Division of Applied Nutrition, INCAP

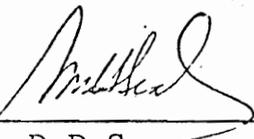


Fernando Viteri, M.D.  
Chief, Division of Biomedics, INCAP

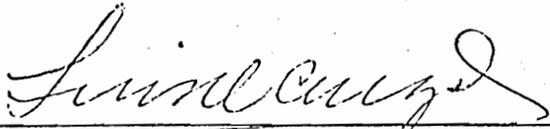
Designated Representative  
Benjamin Torún, M.D., Ph.D.  
Associate Chief  
Division of Biomedics, INCAP



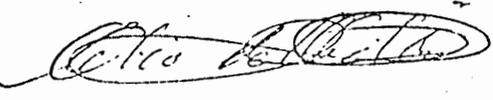
Marina Flores, M.S.  
Chief, Dietary Research Unit, Division of Applied Nutrition, INCAP



Gustavo Leal, D.D.S.  
Professor of Dentistry, University of San Carlos de Guatemala



Luis Octavio Angel, M.D., M.P.H.  
Chief, Division of Education, INCAP



Eusebio del Cid Peralta, M.D.  
Director, Health Services  
Ministry of Public Health  
Guatemala

ASSURANCE OF COMPLIANCE

REGULATIONS ON PROTECTION OF HUMAN SUBJECTS

1. The Pan American Health Organization/Institute of Nutrition of Central America and Panama will comply with established principles for protection of human subjects, accordingly:

2. This Institution has established and will maintain an Institutional Review Board (IRB) competent to review projects and activities that involve human subjects. The Board shall determine for each activity as planned and conducted whether subjects will be placed at risk and if risk is involved, whether:

The risks to the subject are so outweighed by the sum of the benefit to the subject and the importance of the knowledge to be gained as to warrant a decision to allow the subject to accept these risks;

The rights and welfare of any such subjects will be adequately protected;

Legally effective informed consent will be obtained by adequate and appropriate methods in accordance with the provision of the regulation;

The conduct of the activity will be reviewed at timely intervals.

3. This Institution will provide for Board reviews to be conducted with objectivity and in a manner to ensure the exercise of independent judgment of the members. Members will be excluded from review of projects or activities in which they have an active role or conflict of interest.

4. This Institution will encourage continuing constructive communication between the Board and the activity director as a means of safeguarding the rights and welfare of the subjects.

5. This Institution will have available the facilities and professional attention required for subjects who may suffer physical, psychological, or other injury as a result of participation in an activity.

6. This Institution acknowledges that it will bear full responsibility for the proper performance of all work and services including the use of human subjects under any grant or contract covered by this assurance, including continuing compliance with pertinent state or local laws, particularly those concerned with informed consent.

7. This Institution will maintain appropriate and informative records of the Board's review of applications and activities, of documentation of informed consent, and of other documentation that may pertain to the selection, participation, and protection of subjects and to the review of circumstances that adversely affects the rights or welfare of individual subjects.

8. This Institution will at least annually reassure itself through appropriate administrative overview that its practices and procedures designed for the protection of the rights and welfare of human subjects are being effectively applied.

9. This special assurance of compliance applies specifically to the activity entitled "Effect of Protein-Calorie Interventions on Human Growth, Morbidity and Mortality" submitted by the Pan American Health Organization/Institute of Nutrition of Central America and Panama to the Agency for International Development of the United States.

Carlos Tejada V.  
Director, INCAP

The members of the Institutional Review Board (IRB) for the project "Effect of Protein-Calorie Interventions on Human Growth, Morbidity and Mortality" are listed below.

I certify that this review was carried out in accordance with the requirements of Part 46, Protection of Human Subjects of Title 45 of the Code of Federal Regulations of the United States.

25 March, 1976

(Date of IRB approval)

25 March, 1976

(Signature of authorized institutional official)

(Date)

Carlos Tejada V.

(Name)

Director, Institute of Nutrition of Central America and Panama

(Title)

Institute of Nutrition of Central America and Panama (INCAP)

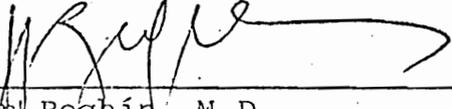
Name of Institution

Apartado 11-88, Guatemala City, Guatemala, C.A.

(Address)

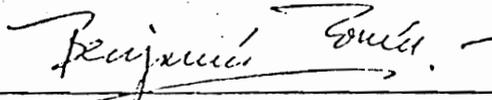
43762, Guatemala City

(Telephone Number)



---

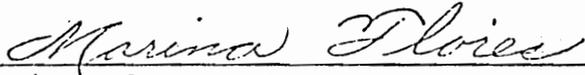
Ivan Bechín, M.D.  
Chief, Division of Applied Nutrition, INCAP



---

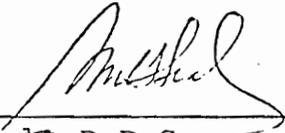
Fernando Viteri, M.D.  
Chief, Division of Biomedics, INCAP

Designated Representative  
Benjamin Torún, M.D., Ph.D.  
Associate Chief  
Division of Biomedics, INCAP



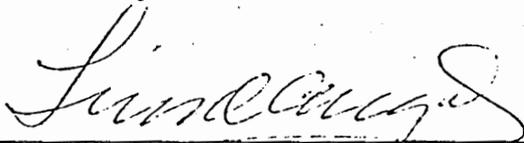
---

Marina Flores, M.S.  
Chief, Dietary Research Unit, Division of Applied Nutrition, INCAP



---

Gustavo Leal, D.D.S.  
Professor of Dentistry, University of San Carlos de Guatemala



---

Luis Octavio Angel, M.D., M.P.H.  
Chief, Division of Education, INCAP



---

Eusebio del Cid Peralta, M.D.  
Director, Health Services  
Ministry of Public Health  
Guatemala

AID 1350-1X  
(7-71)

DEPARTMENT OF STATE  
AGENCY FOR  
INTERNATIONAL DEVELOPMENT

1. Cooperating Country  
TAB 311,600

Page 1 of Pages

2. PIO/T No.  
931-17-560-625-73-

3.  Original or  
Amendment No. \_\_\_\_\_

PIO/T

PROJECT IMPLEMENTATION  
ORDER/TECHNICAL  
SERVICES

4. Project/Activity No. and Title  
Effect of Protein-Calorie Interventions on  
Human Growth Retardation and Mortality  
Rates (INCAP/PAHO; AID-ta-C-1342)

DISTRIBUTION

5. Appropriation Symbol  
72-11X1023

6.A. Allotment Symbol and Charge  
402-31-099-00-22-51

6.B. Funds Allotted to:  
 A.I.D./W  Mission

7. Obligation Status  
 Administrative Reservation  Implementing Document

8. Funding Period (Mo., Day, Yr.)  
From 9/8/76 To 12/29/77

9.A. Services to Start (Mo., Day, Yr.)  
Between Ongoing and \_\_\_\_\_

9.B. Completion date of Services  
(Mo., Day, Yr.) 12/29/77

10.A. Type of Action  
 A.I.D. Contract  Cooperating Country Contract  Participating Agency Service Agreement  Other

10.B. Authorized Agent  
AID/W

Estimated Financing		(1)	(2)	(3)	(4)
		Previous Total	Increase	Decrease	Total to Date
\$1.00=					
11. Maximum A.I.D. Financing	A. Dollars	0	37,000	0	37,000
	B. U.S.-Owned Local Currency				
12. Cooperating Country Contributions	A. Counterpart				
	B. Other				

13. Mission References

14. Instructions to Authorized Agent  
The Office of Contract Management is requested to amend the contract, AID-ta-c-1342, with the Pan American Health Organization in order to provide funds in the amount of \$37,000 to fully fund Phase I of the project approved by the Research Advisory Council. The work scope of this project remains the same.

15. Clearances - Show Office Symbol, Signature and Date for all Necessary Clearances.

A. The specifications in the scope of work are technically adequate  
TA/N, S.G. Kahn *[Signature]*  
TA/N, I. Hornstein *[Signature]*

B. Funds for the services requested are available  
TA/RES, M. Rechcigl *[Signature]*

C. The scope of work lies within the purview of the initiating and approved Agency Programs  
TA/N, F. J. Levinson *[Signature]*

D. TA/PPU: Evelyn C. McLeod *[Signature]*  
TA/PPU, M. Mozynski *[Signature]*

E. TA/N, L. Rudel

F.

16. For the cooperating country: The terms and conditions set forth herein are hereby agreed to

17. For the Agency for International Development

18. Date of Signature

Signature and date:

Signature: *[Signature]*  
John Gunning

Title: Chief, Program and Analysis  
Division, TA/PPU

9/8/76

DEPARTMENT OF STATE  
AGENCY FOR  
INTERNATIONAL DEVELOPMENT

PIO/T

PROJECT IMPLEMENTATION  
ORDER/TECHNICAL  
SERVICES

2. PIO/T No. 931-17-560-625-73 3.  Original or Amendment No. \_\_\_\_\_

4. Project/Activity No. and Title  
Protein Calorie Interventions

DISTRIBUTION

5. Appropriation Symbol  
72-11X-1023 6.A. Allotment Symbol and Charge  
402-31-099-00-22-61 6.B. Funds Allotted to:  
 A.I.D./W  Mission

7. Obligation Status  
 Administrative Reservation  Implementing Document 8. Funding Period (Mo., Day, Yr.)  
From 6/30/76 To 9/1/76

9.A. Services to Start (Mo., Day, Yr.)  
Between 6/30/76 and 7/7/76 9.B. Completion date of Services (Mo., Day, Yr.)  
9/1/76

10.A. Type of Action  
 A.I.D. Contract  Cooperating Country Contract  Participating Agency Service Agreement  Other

10.B. Authorized Agent  
AID/W TA/N

Estimated Financing		(1) Previous Total	(2) Increase	(3) Decrease	(4) Total to Date
\$1.00=					
11. Maximum A.I.D. Financing	A. Dollars		213,000		213,000
	B. U.S.-Owned Local Currency				
12. Cooperating Country Contributions	A. Counterpart				
	B. Other				

14. Instructions to Authorized Agent  
CM/COD is requested to negotiate a contract with the Pan American Health Organization in order to carry out the services specified herein.

This PIO/T addresses a three year project at an estimated total cost of \$1,500,000. The Research Advisory Council (RAC) has approved the Phase I of the project for a period of 18 months at an approximate funding level of \$650,000 with the provision that RAC suggestions concerning design, food sources, data analysis, etc., be considered.

FY 76 funding in the amount of \$213,000, is provided at this time for start-up cost and village surveys.

15. Clearances - Show Office Symbol, Signature and Date for all Necessary Clearances.

A. The specifications in the scope of work are technically adequate  
TA/N: H.L. Rice *[Signature]* B. Funds for the services requested are available  
TA/PPU: E. McLeod *[Signature]* 5/27/76

C. The scope of work lies within the purview of the initiating and approved Agency Programs  
TA/N: I. Hornstein *[Signature]* D.  
TA/PPU: M. Mozynski

E. TA/N: A. Pound *[Signature]* F.  
TA/RES: *[Signature]* 5-28-76

16. For the cooperating country: The terms and conditions set forth herein are hereby agreed to  
Signature and date:  
Title:  
17. For the Agency for International Development  
Signature: John Gunning, TA/PPU  
Title: Chief, Program Division  
18. Date of Signature  
5/25/76

*Handwritten notes:*  
Contact needs \$13,000  
either this Rice is pretty sure  
to use \$13,000, or that the  
was amended to \$100,000  
can do this or that  
5-5-77  
AP [Signature]

PIO/T

Project/Activity No. and Title  
Protein-Calorie Intervention

SCOPE OF WORK

19. Scope of Technical Services

A. Objective for which the Technical Services are to be Used

The principal purpose is to determine, in populations with dietary limitations, the relativeness effectiveness of increasing protein quantity or protein quality and quantity, or caloric intake under actual field conditions.

B. Description See Attached Project Statement: Items 8 and 10 and Page 38 for Budget.

C. Technicians

(1) (a) Number

(b) Specialized Field

(c) Grade and/or Salary

(d) Duration  
of Assignment  
(Man-Months)

INCAP has the necessary resources for this research.

Consultants will be provided as provided in the Budget to cover a review at the end of the first year--none are needed during the period of this PIO/T.

(2) Duty Post and Duration of Technicians' Services

N/A

(3) Language requirements

N/A

(4) Access to Classified Information

No access to classified information is required.

(5) Dependents

N/A

Will

Will Not

Be Permitted to Accompany Technician

D. Financing of Technical Services

(1) By AID - \$ 105,000

(2) By Cooperating Country -

AID 1350-1X (9-70)	Cooperating Country Guatemala	PIO/T No.	Page 3 of 5 Pages
PIO/T	Project/Activity No. and Title Protein Calorie Intervention		

20. Equipment and Supplies (Related to the services described in Block 19 and to be procured outside the Cooperating Country by the supplier of these services)

A. (1) Quantity	(2) Description	(3) Estimated Cost	(4) Special Instructions
	Vehicles, laboratory and office equipment for field stations and analytical supplies will be required early in the project.	\$98,000	

B. Financing of Equipment and Supplies

(1) By AID - \$ 98,000

(2) By Cooperating Country -

21. Special Provisions

- A. This PIO/T is subject to AID (contracting) (PASA implementation) regulations.
- B. Except as specifically authorized by AID, or when local hire is authorized under the terms of a contract with a U.S. Supplier, services authorized under this PIO/T must be obtained from U.S. sources.
- C. Except as specifically authorized by AID/W, the purchase of commodities authorized under this PIO/T will be limited to the U.S. under Geographic Code 000.
- D. Other (specify): Office supplies available locally.

Soy Ethics Committee Approval is attached.

1. International Travel

No international travel will be undertaken unless prior approval has been granted by the Office of Nutrition, Technical Assistance Bureau, AID with the concurrence, to be obtained by the Office of Nutrition of the Participating Agency Staff, Office of Contract Management, AID.

PIO/T

Project/Activity No. and Title

Protein Calorie Interventions

22. Reports by Contractor or Participating Agency (Indicate type, content and format of reports required, including language to be used if other than English, frequency or timing of reports, and any special requirements)

No reports will be required during the life of this PIO/T.

Annual reports in English will be required within thirty days of the anniversary date of the contract.

Annual report guidelines are attached.

Twenty copies should be submitted to AID/W, TA/N.

One copy of all original data or punch cards and tapes, and of all necessary data accession instructions are the property of AID to be made available within 60 days of AID's written request.

23. Background Information (Additional information useful to Authorized Agent and Prospective Contractors or Participating Agency; if necessary cross reference Block 19.C(4) above.)

Project Leaders: Dr. Robert Klein and Dr. Ricardo Bressani

Investigators: Dr. Charles Yarborough and Dr. Martorell.

Carretera Institute of Central America and Panama

Roosevelt Zona 11, Apartado Postal 1188

Telephone: 43-76-23

24. Relationship of Contractor or Participating Agency to Cooperating Country and to AID

A. Relationships and Responsibilities

INCAP is the Regional Institute of PAHO covering C. A.

B. Cooperating Country Liaison Official

For PAHO -- Dr. Carlos Daza, Director of Nutrition Telephone: 331-4302

C. AID Liaison Officials

For ROCAP, Mr. Larry Heilman

AID/W Harold L. Rice, Research Officer, Irwin Hornstein, Deputy Director, TA/N

AID 1350-1X  
(9-73)

Cooperating Country

Guatemala

PIO/T No.

Page 5 of 5 Pages

PIO/T

Project/Activity No. and Title

Protein Calorie Interventions

LOGISTIC SUPPORT

25. Provisions for Logistic Support N/A

A. Specific Items (Insert "X" in applicable column at right. If entry needs qualification, insert asterisk and explain below in C. "Comments")

	IN KIND SUPPLIED BY		FROM LOCAL CURRENCY SUPPLIED BY		TO BE PROVIDED OR ARRANGED BY SUPPLIER
	AID	COOPERATING COUNTRY	AID	COOPERATING COUNTRY	
(1) Office Space					
(2) Office Equipment					
(3) Housing and Utilities					
(4) Furniture					
(5) Household Equipment (Stoves, Refrig., etc.)					
(6) Transportation in Cooperating Country					
(7) Transportation To and From Country					
(8) Interpreter Services/Secretarial					
(9) Medical Facilities					
(10) Vehicles (official)					
(11) Travel Arrangements/Tickets					
Other: (specify)					
(12)					
(13)					
(14)					
(15)					

B. Additional Facilities Available From Other Sources

APO

PX

COMMISSARY

OTHER (specify, e.g., duty free entry, tax exemption)

N/A

C. Comments