

PD-AAT-680  
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**Micronutrients for Health  
Cooperative Agreement: 1997-2001**

**Center for Human Nutrition  
Department of International Health  
Johns Hopkins School of Public Health  
Baltimore, MD**

**Year 3 Annual Report  
1 October 1999 - 30 September 2000**

**Submitted by:**

**Keith P. West, Jr., Dr.P.H., Principal Investigator  
Alfred Sommer, M.D., Co-Principal Investigator**

**To:**

**Office of Health and Nutrition  
U.S. Agency for International Development  
Washington, DC**

This report was prepared under Project Number 936-5122.05 and Contract Number HRN-A-00-97-00015 between the Center for Human Nutrition (CHN), The Johns Hopkins School of Public Health, Baltimore, MD and the Office of Health and Nutrition, United States Agency for International Development, Washington DC.

**October 2000**

## Executive Summary

In June and July 1999 USAID-JHU meetings identified three large studies being carried out in Nepal, Bangladesh and Zimbabwe as priorities in FY'00. This Year 3 Annual Report, therefore, describes the major activities and accomplishments achieved in these important research programs. A few operational problems were encountered in achieving work plan benchmarks during the year, particularly in Zvitambo and JiViA. These were partly due to budgetary changes in response to USAID's financial constraints as well as challenges posed by the host country context. In addition, several minor activities that previously received CA support were either stopped or given minor support for completion. During FY'00 the CA supported, in full or part, these research efforts. Highlights of achievements during the third year of the CA include:

- From **NNIPS-2** in Nepal a large number of publications helped to keep global interest high in maternal vitamin A deficiency as a major, previously unrecognized public health problem in the developing world and the potential of vitamin A and beta-carotene to benefit maternal health and survival. Published scientific papers from NNIPS included those that addressed the –
  - Association between vitamin A and beta-carotene supplementation and the reduction of symptoms of illness in pregnant and lactating women;
  - Effects of vitamin A and beta-carotene supplementation among night blind women during pregnancy and their subsequent mortality;
  - Interactive effects of maternal cigarette smoking and vitamin A or beta-carotene supplementation on mortality related to pregnancy;
  - Responsiveness of dark-adaptation threshold to vitamin A and beta-carotene supplementation in pregnant and lactating women;
  - Lack of an effect of maternal low-dose vitamin A or beta-carotene supplementation on fetal loss and early infant mortality;
  - Interaction between iron and zinc among pregnant women;
  - Contribution of hookworms, malaria and vitamin A deficiency to maternal anemia and iron deficiency;
  - Twinning rates and survival of twins and their risk association with maternal vitamin A or beta-carotene receipt;
  - Effects of vitamin A and beta-carotene supplementation on maternal circulating retinol, tocopherol and carotenoid concentrations in pregnant and postpartum women;
  - Ethno-epidemiologic evidence of local food beliefs and their relation to night blindness; and
  - Impact of a small income on women's nutritional status and household food expenditures in rural Nepal.
- **NNIPS-3** completed enrollment of all subjects (i.e. 4998 pregnant women of an anticipated sample size of 5000) and, as of the end of FY 00, had monitored 90% of

all pregnancy outcomes and completed postpartum follow-ups on more than 75% of mothers and infants. Following standard ethical procedures for the conduct of clinical trials, an independent Data Safety and Monitoring Board (DSMB) met to review primary outcome and safety data in February 2000 and, finding all aspects of the study to be satisfactory and in compliance with guidelines for the protection of human subjects, recommended that the trial be continued until completion. The DSMB interim analysis revealed a modest maximum difference in birth weight between extreme treatment groups (60-75 g). Infant mortality up to 6 months of age for variable numbers of infants per treatment group was, however, 40% lower in two treatment arms compared with rates observed at that time in the other three arms. Treatment groups remain coded. The codes to NNIPS-3 supplements will be broken by Spring 2001.

- In **Bangladesh**, the **JiVitA** trial that will examine the impact of maternal supplementation with vitamin A and multiple micronutrients on maternal, fetal and infant health and survival underwent significant design changes as in-country preparations proceeded on schedule. In short, the trial has been divided into two phases (or trials) that both improve study efficiencies and accommodate interests to examine effects of a broader array of supplements on maternal and infant outcomes: (1) A trial that will focus on assessing impact of maternal vitamin A or beta-carotene supplementation on maternal mortality (N=54,000 pregnancies), now called *JiVitA-1* and (2) a second phased-in trial that will assess the effects of two combinations of maternal multi-micronutrient supplements on fetal and infant mortality (N=18,000 pregnancies), called *JiVitA-2*. The two phases together comprise the entire project called *JiVitA Bangladesh*. As these design changes have been put into place, the project has undergone formal recognition and approval by the Government of Bangladesh; main project offices have been rented, key staff hired, over 600 communities (~130,000 homes) mapped, addressed and computerized into an e-database, and most main forms, data collection procedures and manuals have been drafted for JiVitA-1. The project is poised to be formally launched during the 2<sup>nd</sup> quarter of FY01 in a phased manner. Once fully operational, JiVitA-1 will have ~750 Bangladeshi employees, over 650 of whom will be women. JiVitA-2, to start-up ~1 year later, will add another 250 employees, 85% of whom will be local women.
- In **India**, the **VASIN** trial to examine the impact of dosing newborns with 50,000 IU on infant mortality in Tamil Nadu completed its enrollment of ~15,000 pregnant women. This number includes the increased number of enrolled subjects that resulted from a DSMB recommendation in November 1999 to expand recruitment in order to detect an emerging difference in infant mortality rates with sufficient statistical power. All babies are expected to be born by the end of calendar year 2000, by which time a second Data and Safety Monitoring Board will have convened in Madras. We expect that close to final results will be available for their review and we expect to present the primary findings of this trial at the IVACG meeting in Hanoi in February 2001. The findings will directly answer the question of whether newborns in southern Asia should be dosed with vitamin A as part of a country's

infant and child survival strategy, as had been previously suggested by a USAID-funded trial by JHU and colleagues in Indonesia conducted several years ago.

- **Zvitambo (Zimbabwe)** represents the largest and most definitive field research project undertaken in Africa to assess the impact of early vitamin A intervention in infants and mothers on vertical transmission of HIV and infant death in both HIV+ and HIV- mothers and infants. During the past FY, recruitment of 14,110 mother-infant pairs was completed and clinic-based follow-up of enrolled mothers and infants for the first year after delivery is expected to be complete by March 2001. Evaluation of the counseling intervention to 'fully inform' women about infant feeding in the context of HIV is on-going. The project has, during the year, experienced setbacks from economic and political turmoil in the country including: i) hyperinflation that required the trial to cut the second year of postpartum follow-up in order to salvage the most important aspects of primary outcome follow-up during the first year of life; and ii) shortages of petrol and diesel and insecurity in the country side requiring the project to halt long distant rural visits to study defaulters for 8 months. Despite these setbacks, Zvitambo is expected to reveal substantial insight into the effects of neonatal and early postpartum maternal vitamin A supplementation on infant health and survival, transmission of HIV, the epidemiology and natural history of HIV/AIDS in mothers and children, efficacy of counseling and other forms of behavior modification attempts, and numerous other health issues facing women and their infants in HIV-endemic African settings. Findings are expected to emerge for several years beginning next year.
- **Micronutrient status assessment** continued to be advanced at JHU during the year, most notably with the emerging global recognition of maternal night blindness as a major indicator of vitamin A deficiency in women and the general population, stimulated by USAID-funded JHU work in Nepal. Secondly, dark adaptometry has been advanced over the past year as a new, non-invasive approach to assess vitamin A deficiency in the community and, finally, the use of the dried blood spot has continued to be evaluated as a practical assessment tool for assessing vitamin A status.
- **Global Leadership.** During FY 00, JHU faculty who are supported in whole or part by the USAID CA participated in numerous teaching programs within and outside of Johns Hopkins, served as consultants to various micronutrient projects (e.g., Thrasher review board, Institute of Medicine Dietary Reference Intake Panel, WHO committees, IVACG, UNICEF, MOST, MEASURE and other AID-supported sister projects) , presented findings of JHU CA research at scientific meetings such as the Experimental Biology 2000 meeting, a Nestles Workshop on Child Survival in St. Petersburg, Russia and the Rockefeller Foundation workshop on Child Health in NYC among others and were instrumental in helping to relaunch the INACG, that included the convening of an international expert group (in Belmont, MD) to provide a policy report on the current state-of-knowledge on the assessment, epidemiology, consequences and prevention of iron deficiency and anemia.

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## 1. Introduction

The Micronutrients for Health Cooperative Agreement (MHCA) is a collaborative applied research, technical assistance and training project between The Center for Human Nutrition at the Johns Hopkins School of Public Health (JHU) and the Office of Health and Nutrition at USAID. Its original purpose is to provide global research leadership historically in vitamin A (VA) deficiency control, but over the past decade has expanded to include the prevention of other key micronutrient deficiencies, especially those of iron and zinc. The strategic goals and objectives of the MHCA are to advance micronutrient deficiency control through applied research aimed at protecting the health and survival of children (SO #3) and women of reproductive age (SO #2), reducing transmission of HIV/AIDS and other STDs (SO #4), and reducing the burden of re-emerging diseases (SO #5). This Annual Report covers the twelve month period from 1 October 99 through 30 September 00 (Fiscal Year 2000), covering activities proposed in the original five-year agenda (dated May 1996), modified by a letter to USAID (dated 2 June 1997) and new knowledge and ongoing discussions within JHU and with colleagues at USAID on emerging research priorities in micronutrient deficiency control.

The financial pipeline report for the JHU MHCA, which summarizes expenditures and funds remaining at the end of FY 00, is provided in **Appendix 1**. Commentary for the pipeline is provided in Section 7. PLEASE NOTE: The final pipeline analysis presented in this report excludes \$350,000 that, according to the Office of Health and Nutrition in late September 2000, was obligated by the USAID Mission in Bangladesh for FY 00, in support of the JiVitA maternal supplementation trial, that remains outstanding as of the date of preparation of this Annual Report.

## 2. Country Programs

During FY 00 the CA supported, in full or part, priority research activities in three main countries: Nepal, Bangladesh and Zimbabwe. This Year 3 Annual Report describes major activities and accomplishments by JHU in these research programs during the year. A checklist (**Appendix 2**) is attached which summarizes the degree to which planned goals specified in the Year 3 work plan were met during FY 00.

### 2.1 Nepal: NNIPS-2 and NNIPS-3

#### ***NNIPS-2***

Data from the NNIPS-2 maternal vitamin A and beta-carotene supplementation trial continue to be analyzed and published as papers that are helping to form a new basis of evidence for the importance of adequate maternal vitamin A nutrition in promoting the health and survival of women of reproductive age. Most visible this past year has been the recognition of the importance of a history of maternal night blindness as a practical, inexpensive indicator of maternal vitamin A deficiency and health and survival risk. NNIPS-2 data have clearly revealed, in this particular South Asian population, maternal night

blindness to be frequent (often affecting ~10% of pregnant women, as is now becoming evident elsewhere), associated with increased morbidity, poor infant outcome and, as reported in the American Journal of Epidemiology in September 2000, increased mortality risk of mothers for up to two years beyond the case pregnancy. Confirmation of this risk profile in other populations will establish maternal night blindness as an important indicator to be used in maternal and general health and nutrition services. As published in the Journal of Nutrition in October 2000, maternal anemia is likely caused by several prevalent factors, including iron deficiency, hookworm and malaria. Future publications from NNIPS-2 will elucidate vitamin A-iron deficiency interactions in predisposing women to anemia risk and associated consequences. Despite the positive effects observed in mothers, findings from the NNIPS-2 trial continue to reveal an equivocal role for maternal vitamin A status and beta-carotene supplementation in improving fetal and infant health and survival, although data from India and Zimbabwe will help resolve questions related to direct newborn supplementation with vitamin A. Peer-review scientific publications from NNIPS-2 are summarized in the Executive Summary of this Report with a full listing in the Appendix. Other papers either submitted for publication or in preparation address the association between maternal night blindness and infant mortality, effects of vitamin A and beta-carotene supplementation on non-maternal mortality, issues related to late pregnancy and second year post partum mortality of women, and other topics.

### ***NNIPS-3, Nepal***

This double-masked, cluster-randomized, controlled community trial is assessing the effect of multiple micronutrient supplementation during pregnancy on birth weight, infant and maternal morbidity, and early infant mortality. The trial has been providing women, starting in their first trimester, one of the following treatments: **(a)** vitamin A (1000 µg retinol equivalents, RE); **(b)** folate (400 µg) and vitamin A; **(c)** iron (60 mg), folate and vitamin A; **(d)** zinc (30 mg), iron, folate and vitamin A; and **(e)** multiple micronutrients (approximately 1 RDA of B-complex vitamins, vitamins C, E, K, and D, copper and small amounts of calcium and magnesium) including zinc, iron, folate and vitamin A. Women continue to be supplemented until 12 weeks of a live birth, or in the case of miscarriage, 6 weeks after the outcome.

NNIPS-3 is on-schedule having completed enrollment of all 4998 (of a planned sample size of 5000) pregnant women by January 2000. **Table 1** provides coded data reflecting participation and follow-up rates and **Table 2** provides coded data showing supplement consumption rates (i.e. compliance) across study groups. All pregnancies will have had an outcome by the end of October of 2000. On average, pregnancies were identified at ~7 weeks of gestation. Approximately 73% of birth weights were obtained at home within 24 hours as part of the birth assessment procedure, with an average birth weight of slightly more than 2500 grams and birth length of ~47 cm (**Table 3**). A first-10 day morbidity assessment (conducted on mothers and neonates) has been carried out after each live birth. These assessments will continue through early

November 2000. A 6-week postpartum home follow-up of infants and mothers has also taken place and will continue into January 2001. In a subsample of mothers, urine specimens have been collected at this visit for gonorrhea and chlamydia testing in laboratories at JHU. The 6-month postpartum follow-up for vital status will continue through April 2001, at which time infants will be assessed for prevalence of anemia, and severe anemia treated. This will mark the end of the field activities for NNIPS-3.

Data entry, checking and cleaning is currently ongoing with full force to catch up with data collection. The data will be clean and ready for analysis by May of 2001. Biochemical analysis of the approximately 1000 serum samples collected at baseline and follow-up will be completed for vitamin A, E, carotenoids, ferritin, folate, vitamin B12, iron, zinc, and copper by the end of December 2000. The biochemical analysis is being done at the Center for Human Nutrition in Baltimore.

*Data Safety and Monitoring Board Meeting (DSMB):* A DSMB meeting was held in February 2000 in Kathmandu, Nepal. The DSMB interim analysis revealed a modest maximum difference in birth weight between treatment groups with the most extreme mean birth weights (60-75 g). Infant mortality through 6 months of age was, however, 40% lower in two treatment arms compared with the rates in the other three arms, and with the mortality rate observed previously in this same population, indicating a lack of harm due to supplementation. The differences were not statistically significant, but this outcome will be further evaluated at the end of the study. Based on these results, the DSMB recommended that the study be continued until its completion.

**Table 1: NNIPS-3 Study Participation and Follow-Up  
(DSMB Data, February 2000)**

	T	X	G	Q	K	Total
Women under pregnancy surveillance	2540	2663	2682	2800	2579	13,264
Pregnancies enrolled with an outcome as of Dec 5, 1999	552	587	544	594	515	2792
Pregnancies ending in a miscarriage/stillbirth/ maternal death	153	142	144	138	124	701
Pregnancies ending in at least 1 live birth	399	445	400	456	391	2091
Twin pregnancies w/ both live births	3	4	5	6	4	22
Twin pregnancies w/ at least one live birth	0	0	1	3	1	5
Twin pregnancies w/ both stillbirths	0	0	0	0	0	0
Total live born kids as of Dec 5, 1999	402	449	405	462	395	2113
Infants alive as of Jan 21, 00	374	405	364	412	360	1914
Infants died as of Jan 21, 00	18	33	22	35	18	126
Infants vital status unknown after birth	10	11	19	16	17	73
Infants with birth weight < 24h	297 (74%)	333 (74%)	287 (71%)	322 (70%)	301 (76%)	1540 (73%)
Infants with birth weight > 24 h	72 (18%)	81 (18%)	77 (19%)	87 (19%)	65 (16%)	382 (18%)
Infants without birth weight	33 (8%)	35 (8%)	41 (10%)	53 (11%)	29 (7%)	191 (9%)

+ Excluding women in the hills, and 2 false positive pregnancies

4 kids with birth weight without time at measurement, excluded from the analysis

**Table 2: NNIPS-3- Supplement Consumption from Enrolment  
until End of Pregnancy by Allocation Group:  
Percent of All Possible Days  
(DSMB Data, February 2000)**

	T	X	G	Q	K
	n %	n %	n %	n %	n %
<b>OVERALL</b>					
0-<25%	66 (12.4)	57 (9.9)	62 (11.6)	73 (12.6)	61 (12.2)
25-<50%	56 (10.5)	47 (8.2)	57 (10.7)	52 (9.0)	42 (8.4)
50-<75%	86 (16.1)	83 (14.4)	81 (15.2)	97 (16.8)	80 (16.1)
75-100%	325 (60.9)	389 (67.5)	334 (62.6)	356 (61.6)	315 (63.2)
Total	533 (100)	576 (100)	534 (100)	578 (100)	498 (100)
p=0.69					
Median %	82.7	86.2	84.4	84.2	85.5
Mean tabs	121	131	122	127	126
# total days	159	168	160	169	166

**Table 3: NNIPS-3 - Mean Birth Weight, Length, and Head and Chest Circumference By Allocation Group (DSMB Data, February 2000)**

<b>Group</b>	<b>Mean weight (kg)</b>	<b>SD</b>	<b>95% CI</b>	<b>N</b>
T	2.606	0.425	2.558 - 2.654	297
X	2.621	0.431	2.547 - 2.668	333
G	2.549	0.422	2.500 - 2.598	287
Q	2.545	0.450	2.496 - 2.594	322
K	2.554	0.471	2.501 - 2.607	301
F <sub>4</sub> =2.08, p=0.0805				
<b>Group</b>	<b>Mean length (cm)</b>	<b>SD</b>	<b>95% CI</b>	<b>N</b>
T	47.28	2.59	46.99 - 47.57	297
X	47.55	2.16	47.32 - 47.78	333
G	47.27	2.44	46.99 - 47.55	287
Q	47.06	2.40	46.80 - 47.32	322
K	46.84	2.76	46.53 - 47.15	301
F <sub>4</sub> =3.68, p=0.0055				
<b>Group</b>	<b>Mean head circumference (cm)</b>	<b>SD</b>	<b>95% CI</b>	<b>N</b>
T	32.61	1.48	32.44 - 32.78	297
X	32.66	1.56	32.49 - 32.83	333
G	32.42	1.53	32.24 - 32.60	287
Q	32.32	1.44	32.16 - 32.48	322
K	32.41	1.51	32.24 - 32.58	301
F <sub>4</sub> =2.96, p=0.0189				

## 2.2 Bangladesh-JiVitA

This large field trial is now designed to fully replicate the NNIPS-2 study in a second malnourished population of women in South Asia, but with the difference of focusing the intervention to begin early in the first trimester of pregnancy through 3 months postpartum rather than continuously throughout the reproductive years. This is in part the result of some modifications in design over the past several months, as discussed with USAID HN officers in August 2000. As of last year, JiVitA had been planned as a 3-arm vitamin A, multiple micronutrient supplementation trial, thereby only replicating the vitamin A arm of NNIPS-2. Additional support from the Gates Foundation in recent months, has allowed a beta-carotene supplementation arm to be re-introduced. This, plus the opportunity to allow NNIPS-3 to inform the design of the multiple micronutrient arm in Bangladesh, has led us to now plan JiVitA as two phases: The first phase, now called JiVitA-1, will assess whether weekly maternal dosing with either vitamin A or beta-carotene from early pregnancy through three months postpartum, at recommended levels, reduces mortality related to pregnancy by at least 35 %. JiVitA-1 will begin in the field by February/March 2001. The second phase, JiVitA-2, will assess the impact of a daily maternal supplement with either a multiple micronutrient (similar to the nutrient composition proposed by UNICEF) or a smaller number of nutrients (to be determined based on NNIPS-3 findings) during pregnancy through 3 months postpartum on: (1) fetal loss due to miscarriage or still birth; (2) infant mortality under three months of age; (3) maternal obstetric and infectious morbidity; (4) infant infectious morbidity; (5) maternal and infant micronutrient status; (7) intrauterine growth and prematurity; and (8) postnatal infant growth to 3 months of age. JiVitA-2 will begin early in 2002.

Due to USAID budgetary constraints imposed upon JHU at the beginning of FY 2000, JHU deferred certain major start-up costs in Bangladesh until FY 01, especially those related to hiring large numbers of personnel and equipment in-country. Nonetheless, critical preparatory activities were completed during this fiscal year, including:

- **Ethical Reviews:** A protocol for ethical review was submitted to the Bangladesh Medical Research Council in Dhaka, and approval was obtained in January 2000.
- **Government Order/Memorandums:** After obtaining technical and ethical clearance of the protocol, steps were taken to have the JiVitA project formally approved by the Government of Bangladesh (GOB). The JiVitA project was included in the GOB's Operational Plan (August 2000), and this was followed by the signing of an Implementation Agreement (September 28, 2000) between the Line Director, Research and Development, Directorate General

of Health Services, Ministry of Health and Family Welfare, and JiViTA's host umbrella organization, Bangladesh Institute of Research for Promotion of Essential and Reproductive Health and Technologies (BIRPERHT). This Implementing Agreement serves as a formal Government Order from the GOB indicating its approval of the JiViTA project, recognizing the role and presence of JHU in this collaborative enterprise, and thereby giving the trial its formal legitimacy in Bangladesh. In addition, JHU and BIRPERHT signed a Memorandum of Agreement to Collaborate in July 2000 which lays the groundwork for maintaining close institutional linkages and collaboration over the next 5 years.

- **Office Facilities/Key staff:** During this fiscal year the project selected, rented and set up major JiViTA offices in Dhaka (liaison office), Rangpur (main project office/data entry center/residence) and Gaibandha Town (field station/residence). It also set up small sub-stations in selected areas throughout the 700 sq km study area. Recruitment, selection and hiring of key senior staff was accomplished including a Field Program Manager, Station Administrator, Research Nutritionist, Medical Epidemiologist, Data Center Manager and Chief Accounts Officer. Accounting procedures have been drafted and the chief accountant received training by the NNIPS chief accountant. Personnel policies have been drafted including job descriptions, leave, recruitment and hiring, performance review and termination procedures. Inventory, procurement and supplies issuance procedures are currently being finalized.
- **Community mapping and household addressing:** Over 600 local area maps, drawn to scale in 1932-35, were obtained, enlarged and used to map the location of households and assign unique addresses in the study area. Community mapping and addressing procedures that met study needs were developed and a manual of these procedures was developed. Over 80 field staff were hired (March 2000) and trained (April 2000) to conduct community mapping. Almost 200,000 homes were addressed (April to September), over 400 maps were completed, and mapping files were created to be used for supervisory, accountability, and operational use. The hard-copy maps were also scanned to form a computer-based template upon which households from the hardcopy maps could be entered using an AutoCAD program to create 'smart maps'. A team of 6 computer-based mappers were hired and trained in the AutoCAD program and have entered over 370 maps.
- **Data Management system:** The data management strategy was drafted and computer equipment/supplies/services in Dhaka and Rangpur were evaluated. Initial purchases of computer equipment were made, however others were deferred.
- **Vehicles:** Arrangements were made to rent vehicles for all of FY 00 as the project pursued the final approval of a Government Order and a Source of

Origin Waiver from USAID/Washington for the purchase of 3 4WD Toyota Land Cruisers. The purchase of motorcycles/bicycles was postponed for the 1<sup>st</sup> quarter of FY01.

- **Field Procedures/Forms:** In April 2000, field procedures and forms began being drafted and reviewed by senior project personnel. These forms were tested and further refined in September 2000. Finalization of basic study forms will occur during the 1<sup>st</sup> quarter of FY01. Also, in September, a manual of operations, drawing heavily on experiences gained from NNIPS-2 and NNIPS-3 studies in Nepal, was drafted and is currently being translated.
- **Community preparation:** The process of informing the public in the Gaibandha/Rangpur communities about JiVitA started in FY 99 by holding several months of meetings with district, thana, union and mauza representatives and other community groups. From April to September, Community Advocate Teams (CATs) were formed from the field staff engaged in community mapping. These teams met with community leaders, school teachers, local NGOs and other community groups to introduce the project to the >200 mauzas.
- **Supplement production:** As part of the CA budget reduction program, JHU offered to find external funds to support production of the initially anticipated 22 million supplements needed for the JiVitA trial. JHU negotiated with CIDA to support the production, bottling, labeling and shipment of these supplements at a total estimated cost of ~\$525,000. A grant for this amount was approved by the IDRC/MI in July 2000, but the agreement contained numerous clauses with which JHU could not comply, stalling the funds disbursement. In the interim, JHU has decided that JiVitA-1 would, given the changes to supplement women with either vitamin A or  $\beta$ -carotene, entail weekly oil-based capsule supplementation, thereby decreasing the number of supplements required by 85%, or ~3.3 million for a total of 54,000 pregnant women. Supplements required for JiVitA-2 will be based on daily micronutrient use by 18,000 pregnant women. These changes have decreased to the anticipated cost to \$440,000 requested from the IDRC/MI. Negotiations have continued on issuance of this grant.

### 2.3 India-Vitamin A Supplementation in Newborns Study (VASIN)

The VASIN study is a collaborative undertaking of the Center for Human Nutrition at Johns Hopkins University and the Aravind Children's Hospital in Madurai, India.

Its purpose is to evaluate the impact of vitamin A dosing of infants within the first few days of life on early infant mortality, morbidity, and growth. It is designed as a community-based randomized trial in which infants are enrolled at the time of birth and assigned to receive either 25,000 IU of vitamin A or placebo on two

consecutive days. The target time for treatment is within 48 hours of birth, but given the logistical difficulties involved, we enroll and dose infants up to one month after birth.

As of the week ending Sept. 9, 2000, a total of 14109 pregnant women have been identified, of whom 14055 (99.6%) have agreed to participate in the study. Two hundred forty-eight of these women permanently migrated out of the study area prior to delivering their infant. A total of 12097 deliveries have occurred among enrolled women, of which 328 resulted in a stillborn infant, leaving a total of 11769 live births. Two hundred forty-two of these live born infants have died prior to our teams being able to enroll and dose them. In addition, 826 infants migrated out of the study area and 16 infant's parents refused to participate prior to our enrolling and dosing the child leaving a total of 10,685 infants available for enrollment and dosing. 99.6% of these have received the full treatment assignment of two doses. An additional 277 infants have died during the study period for a total of 519 deaths. A total of 7303 children have completed the study follow-up period of 6 months. As expected in a community-based study as opposed to one in which only infants born in a particular facility are included, a large proportion (46.6%) of these deaths occurred within the first day or two of life and prior to our ability to provide the assigned treatment. All children are followed until 6 months of age and then discharged from the study and dosed with 100,000 IU of vitamin A.

Enrollment of pregnant women has finished and we expect all babies to be born by the end of calendar year 2000. The next meeting of the Data and Safety Monitoring Board will be in the first week of December, 2000 in Madras. We expect that close to final results will be available for their review and we expect to present the primary findings of this trial at the IVACG meeting in Hanoi in February 2001.

#### **2.4 Zimbabwe-ZVITAMBO**

The Zimbabwe Vitamin A for Mothers and Babies project is a randomized placebo controlled clinical trial among 14,000 mother-infants pairs to determine the impact of administering single oral doses of vitamin A to mothers and neonates in the immediate post partum period on three outcomes: (1) infant mortality; (2) mother-to-child HIV-transmission during breast feeding; and (3) maternal HIV infection during the post partum year. This is a collaborative study between The University of Zimbabwe, the Harare City Health Department, The Montreal General Hospital Research Institute and The Johns Hopkins School of Hygiene and Public Health and is co-funded with CIDA.

This year has been a tumultuous one for Zimbabwe with numerous impacts on the ZVITAMBO trial:

- The economy has been devastated by hyperinflation (50-70%). At the same time, the local currency was artificially fixed to the US\$ from December 98–August 00. Government salaries (which include the University of Zimbabwe to which ZVITAMBO salaries are tied) were raised 25% in January 1999, 17% in July, 1999 retroactive to January 1, and 85% from January 1 2000. This last increase alone represented an increase of US\$700,000 to the project budget. After prolonged negotiations with USAID and CIDA, the decision was made to cut the last year of the project in order to salvage the most important aspects of the primary outcomes which will be obtained with 12 months follow up. Thus, beginning June 1, 2000 women-infant pairs were only followed to 12 months. Staff cuts began that month with 45 staff losing their jobs June 30; an additional 45 are being cut between July and December 2000.
- Beginning in February 2000 and continuing to the present, President Mugabe has paid “war veterans” to occupy white-owned farms. This brought violence and insecurity throughout the country and greatly slowed agriculture that is the economic backbone of the country and its primary source of foreign currency. With forex reserves depleted, shortages of many commodities on which ZVITAMBO depends ensued– most importantly petrol and diesel. Long queues at service stations became the norm. Insecurity in the rural areas together with lack of petrol made it impossible to conduct long distance rural visits to our defaulters from February 1 – September 1 of this year. When petrol has been available, we have continued defaulter visits in Harare and have now caught up on these. We began in September working on the backlog of long distance visits, although acute petrol shortages are again predicted for late October.

**Recruitment:** Recruitment was completed on January 29, 2000 with a total of 14, 110 mother-infant pairs enrolled.

**Follow up:** Follow up has continued at the clinics, but home visiting of defaulters was interrupted due to political unrest and lack of petrol.

**Laboratory facilities:** The PCR laboratory completed analysis of the maternal-to-child transmission rates for the infants of the first 1000 HIV+ mothers enrolled and submitted these results to the DSMC for review. The Vitamin A laboratory completed retinol analyses of serums from mothers in Substudy A. However, in July internal politics at the UZ forced the vitamin A lab to relocate and it has since been operating in a temporary facility. Fortunately, the Vice Chancellor of the UZ has personally taken an interest in promoting this lab and has found funds within the university budget to convert an office into the vitamin A laboratory.

**Counseling:** The counseling intervention to “fully inform” women about infant feeding in the context of HIV was implemented beginning September 1, 1999. Thus, 2744 of the 14,000 women enrolled in ZVITAMBO were “exposed” to this intensive education and counseling which included male outreach, the

incorporation of infant feeding messages into antenatal sensitization and recruitment, a reminder of the relevance of knowing ones HIV status to making good infant feeding decisions at the first follow up visit, health education to encourage exclusive breast feeding and safe sex during lactation for women who do not want to know their HIV status, and individualized counseling on various feeding options (including replacement feeding, expressed and heat-treated breast milk, early breast feeding cessation, and safer breast feeding practices) for known HIV+ women. The outreach and teaching materials developed collaboratively with the City Health and Ministry of Health have been used in national seminars to train health workers. UNICEF has paid to have the main outreach brochure, "Can Mothers pass HIV to their infants during breast feeding?" mass produced, adding its logo to the back. Evaluation of the counseling intervention includes a knowledge assessment at the 3-month visit and a practices assessment at the 12-month visit. A subgroup of 224 women who were counseled on "safer breast feeding" were visited within 2 weeks of instruction in their homes for a "skills assessment" to determine how well mothers are able to implement these recommendations. In-depth interviews are being conducted on all known HIV+ women and a subset of HIV- and HIV unknown women enrolled during the counseling intervention period to determine why families made the feeding decisions they did, and who was involved in the decision making.

### **3. Micronutrient Status Assessment**

#### **3.1 Dark Adaptometry**

This method has been under development at JHU for the past several years, however it gained considerable prominence in the past year with the publication of additional data from Nepal in the American Journal of Clinical Nutrition in August 2000 on its validity to reflect vitamin A-deficiency induced impaired dark adaptation, among women participating in NNIPS-3. During the year additional DA instruments were produced and are in the process of being distributed to potential collaborators in several countries who are committed to following a standard protocol for testing the instrument's reliability and validity in different populations and in the hands of different groups of investigators. Current plans call for collaborative studies to be done in Haiti, Kenya, Tanzania, Viet Nam and Guatemala.

#### **3.2 Dried Blood Spot**

JHU has been working with Neal Craft in North Carolina on further developing the DBS for assessing vitamin A status for the past several years, during which significant advances have been made. A first publication appeared describing the technique and values it generates on serum retinol in health US subjects in February 2000. A second appeared (not coauthored by JHU) in the American Journal of Clinical Nutrition from Guatemala in August. We currently are preparing another paper on data from women in NNIPS, which shows strong

linear correlation between the DBS and standard phlebotomy derived serum retinol determinations. Work will continue to publish data in the coming year to help establish the technique.

### **3.3 History of Maternal Night Blindness**

JHU has been working with a large number of groups over the past year to disseminate standardized questions for assessing a history of maternal night blindness during pregnancy in the previous 3 years. This technical assistance, coupled with several publications from Nepal on the validity and associations of a history of maternal XN, has led to the method being incorporated into DHS and MICS surveys throughout the world in the past year, with plans to expand its use in the future.

## **4. Core Activities**

USAID-supported core activities at JHU provide laboratory, data management, and administrative backup to country research programs. Under core support JHU faculty also prepare publications of research findings, attend and present findings at scientific meetings, provide technical assistance, staff international committees, teach courses that address micronutrients in health and carry out other consultative functions that comprise the Center's global leadership activities in micronutrient deficiency control.

### **4.1 Laboratory**

During the year, the Center for Human Nutrition Micronutrient Analysis Laboratory continued to process a large volume of samples and carried out a wide range of biochemical analyses in support of the MHCA-supported field trials. These included:

#### **NNIPS-3 samples (Nepal):**

- Serum retinol, vitamin E and carotenoids were analyzed on ~1000 pregnant women.
- In cooperated with Dr. Richard Semba's laboratory, ~1000 samples were analyzed for serum iron, zinc and copper.
- ~ 1000 Samples from baseline collections were analyzed for serum folate and vitamin B<sub>12</sub> using newer developed microbiological methods.
- Determinations of serum homocysteine concentration have been completed in ~1200 samples collected from baseline and ~800 samples collected from follow-up period.
- Serum vitamin B<sub>6</sub> concentrations have been determined in ~200 samples using HPLC method.
- Serum ferritin was measured in ~1200 samples collected from baseline, and ~800 samples from follow-up periods.

#### **NNIPS-2 samples (Nepal):**

- A serum-based assay of malandialdehyde (MDA) concentration was developed by HPLC in the Center's nutrition laboratory over the year as an

index of lipid peroxidation, and performed in serum from ~600 NNIPS-2 women during pregnancy. The results suggested that  $\beta$ -carotene supplementation may have reduced oxidative stress in pregnancy, evident by an ~15% lower serum MDA concentration in carotenoid recipients compared to women who received vitamin A or placebo. The results were presented at Experiment Biology 2000 meeting.

**Hi-B vaccine and vitamin A study (El Salvador):**

- ~600 serum samples were analyzed for retinol, vitamin E and carotenoids levels (carried out as a result of previous commitments to this study).

**TAPP/ONEPLUS, Zanzibar/Tanzania:**

- The commercial kits for serum ferritin determination were evaluated between different manufactures for the purpose of quality assurance. The actual measurement of serum ferritin has been carried out in the field.

**Analytical methods development**

- **Serum folate and vitamin B<sub>12</sub>:** Analytical methods for determining serum folate and vitamin B<sub>12</sub> have been set up using a microbiology assay on microtiter plates.
- **Serum vitamin B<sub>2</sub> and B<sub>6</sub>:** A rapid, and highly sensitive method for serum vitamin B<sub>2</sub> and B<sub>6</sub> by HPLC has been developed.

## **4.2 Data Management**

The Data Management Core provides support to MHCA projects by providing database design for planned projects, data management in the US and on-site for projects in the data collection phase, and data analysis for projects whose field work is complete but for which analytic questions remain. The following activities were undertaken during Year 3:

**Design and implementation of a data management system for JiVita.**

During the past year, the Data Management Core has designed a data management system for JiVita. Parts of the system that can be implemented (given the progress made in field activities) have been put in place. This system includes, for the first time, networking of data entry activities. Reliable hardware vendors were identified and bids for hardware reviewed. The purchase of some hard and software, both locally and within the US was completed. This was not all of the purchasing needed, but was enough to set up a system for scanning, processing and electronically storing maps of the study area, which can later be linked to specific records in the study data base. This system also allows for electronic "clean" versions of the scanned maps to be printed for use in the field, after updating them with exact locations of households within study areas, and the household numbers assigned to these by the mapping teams. A data center has been designed for the Rangpur office, with appropriate electrical outlets, and

furniture to support the center and its data entry activities. Several data entry personnel have been hired and trained to clean the electronic maps. Some of these personnel will be shifted to other data entry and management tasks once the mapping activities are completed. A new systems manager was hired. This person will be responsible for the maintenance of the network of computers for data entry and management. Since forms testing is not yet complete, the task of producing data entry programs has not yet started. However, the software selection is complete, and the approach to data entry and management has been identified. Email capabilities for the Rangpur office are critical to the smooth operation of the study, and the process of identifying how best to set up email is underway.

### **Data management and analysis for NNIPS-3.**

This has been ongoing during year 3, since data collection has continued during this period. The remaining data entry and management programs have been written and the data center in Kathmandu is continuing with the remaining data entry. The Data Management Core provided data analysis expertise during this period for the Data Safety and Monitoring Committee which took place in February, 2000, in Kathmandu. Analysis of the main study outcomes (outside of the Data Safety and Monitoring committee) will not take place, since data collection is not yet complete.

### **Data management for ZVITAMBO.**

These activities continued in year 3. Quality control programs for follow-up forms have been implemented and a detailed analysis plan has been developed. Basic tabulations have been run without breaking the treatment codes.

### **Data analysis for NNIPS-2 and other MHCA studies.**

The major files and variables from the NNIPS-2 database have been cleaned and edited. A number of analyses have been done and papers written (see publication list). The VASIN study has been continuing with modest data management and analysis input from the Data Management Core. Analyses of TAPP study data from Zanzibar have also been completed in the past year.

### **Maintenance of databases and provision of data to researchers.**

The Data Management Core has continued to maintain databases and their documentation from previous studies which are accessed by ourselves and others. Acknowledgment of USAID is requested for any publications arising from these data collaborations. Data provided to other researchers in the past year is given below.

### **Internal to Johns Hopkins**

- 1) Data from NNIPS-1 was provided to Dr. David Bishai for his analysis of how vitamin A supplementation can alleviate poverty associated mortality in Nepal.

- 2) Data from Al Sommer's Indonesian longitudinal studies and NNIPS-1 and data have been provided to the Biostatistics department for use as example data sets for their introductory sequence of courses.
- 3) Data from NNIPS-1 were provided to Dr. Daniel Scharfstein of the Biostatistics Department at Johns Hopkins, for a Bayesian efficacy analysis of the impact of supplementation on growth.

#### **External to Johns Hopkins**

- 1) Aceh study data were provided to a doctoral student of Dr. Bengt Muthen at the University of California, Los Angeles for application of a new statistical method of analysis of this type of controlled trial (one in which no placebo was used).
- 2) The Indonesian longitudinal data was also provided to Dr. Sylvia Richardson, Chair of the Department of statistics at Imperial College, London, for application of new statistical methods for longitudinal data.
- 3) Data from NNIPS-1 was provided to Dr. Els Goetghebeur of Ghent University, Belgium, and Dr. Juni Palmgren of the Karolinska Institute, Sweden, for efficacy analysis of NNIPS-1 infants data using a new statistical method. This analysis appeared in Life Time Data Analysis, Volume 6, pp 107-121, 2000.
- 4) Data from Aceh were provided to Dr. Don Ruben, Chair of Statistics at Harvard, for efficacy analysis of clustered data using a Bayesian approach, the results of which have been published in the Annals of Statistics.

#### **General Data Management Core Activities**

The Data Management Core also provides ongoing maintenance and trouble-shooting for all MHCA computing locally and abroad, which includes PC's, the SUN mini-computer, and laboratory computing. The Core sets standards for hard and software selection for the group, as well as maintenance of computer security and security of electronic transfer of data from field sites to Hopkins.

### **4.3 Publications**

During calendar year 2000 JHU published or has in press 39 manuscripts that reported findings from its applied vitamin A, iron and anemia, zinc and other dietary and nutritional research programs (**Appendix 3**). We expect these publications will provide needed evidence upon which USAID and other agencies can continue to develop and shape micronutrient deficiency prevention and control policies and programs.

### **4.4 Technical Assistance**

On a regular basis, JHU nutrition faculty provide technical assistance and policy guidance to international agencies such as UNICEF, WHO, IDRC, HKI, IEF, ICDDR, MOST, and IFPRI. Technical assistance is a crucial component of collaborative work with JHU's national partners in Nepal, India, Bangladesh, Tanzania, Zimbabwe and elsewhere, and forms a valuable linkage with UN agencies, NGOs (including sister

projects supported by USAID HN), the private sector and other groups. The following activities illustrate the breadth of technical assistance rendered by JHU faculty during the past fiscal year. A more comprehensive list is provided in **Appendix 4**.

- Alfred Sommer continues to chair and lead the IVACG Steering Committee as it prepares for its 25<sup>th</sup> Anniversary meeting in Hanoi, Viet Nam in February 2001, and provides global policy guidance for the control of vitamin A deficiency. Keith West continued to serve as an IVACG steering committee member.
- Keith West served on the Advisory Board and met throughout the year with the MEASURE Project to assist in developing a US strategy for the 10-year anniversary of the World Summit for Children, to be celebrated at the Special Session of the UN planned in September 2001.
- Parul Christian and Robert Black served as invited speakers and research consultants at the Indo-US Micronutrient Research Conference held in New Dehli, India, in February 2000 to plan a new joint research program on micronutrient deficiency control.
- Rebecca Stoltzfus was appointed as a founding member of the “new INACG” that will provide global policy guidance for the control of iron deficiency and anemia. In that capacity Dr. Stoltzfus also co-organized the “Belmont Meeting”, an expert conference held in Belmont, Maryland in May 2000, that led to the publication of a state-of-the-situation report on the control and prevention of iron deficiency and control of anemia.
- Rolf Klemm served as a consultant to UNICEF to develop the use of the dried blood spot method for assessing vitamin A status in conjunction with a planned tetanus toxoid survey to be carried among pregnant women in two states in India in FY 2001.
- Parul Christian provided technical assistance to MACRO, International to insert a standard set of questions on assessing maternal night blindness into the core module of the DHS and in the MICS surveys.
- Keith West served as a member of the Dietary Reference Intake Micronutrient Task Force, Vitamin A Subpanel, for the Institute of Medicine, National Academy of Sciences, which will publish the new DRIs for multiple micronutrients in December 2000.
- Alfred Sommer provided guidance throughout the year to Maryland congressional representatives on directions needed to be taken by the US government on vitamin A and micronutrient deficiency control.

#### 4.5 Teaching

During the past twelve months, Drs. West, Gittelsohn, Stoltzfus, Christian, Shankar, Tielsch and Black taught courses in the School of Hygiene and Public Health which include extensive material on vitamin A, iron, zinc and other micronutrient deficiencies. Classes over the past year that have focused on advancing skills and knowledge on micronutrient deficiency prevention were taught by faculty in the following courses:

<u>Course Title</u>	<u>Faculty Member</u>	<u>Role</u>
International Health 2	James Tielsch Joanne Katz	Instructor Instructor
Nutrition During Life Stages	Rebecca Stoltzfus	Instructor
International Nutrition	Keith West Parul Christian	Instructor Instructor
Principles of Human Nutrition	Keith West Rebecca Stoltzfus	Lecturer Lecturer
Assessment of Nutritional Status	Kerry Schulze Joanne Katz Keith West	Instructor Lecturer Lecturer
Disease Surveillance	James Tielsch	Instructor
Summer Studies Institute	Joanne Katz	Lecturer
Summer Program (Columbia, MD)	Keith West	Lecturer

A listing of guest lectures on micronutrient deficiencies given outside of JHU by faculty is listed in **Appendix 5**.

#### 4.6 Global Leadership

Global leadership is hard earned. Many of the above activities undertaken by JHU faculty contribute to the global leadership role of JHU in preventing micronutrient deficiencies. It is a role that is shared with USAID HN as vital partners in this international public health effort, that increasingly is attracting and engaging “new players” to achieve prevention goals. Each year global leadership work is carried out through the conduct of research that is essential to move micronutrient policies forward (i.e., NNIPS trials, Zvitambo, VASIN, Zanzibar studies, JiVitA Bangladesh), and regular dissemination of findings through peer review journals (see Appendix 3) and international health and nutrition conferences (e.g., Experimental Biology Meeting, ICN).

Faculty provide highly visible leadership by serving as editors and reviewers for leading journals (e.g., Rebecca Stoltzfus serves as Associate Editor for the Journal of Nutrition; Keith West is on its editorial board; Jim Tielsch, Joanne Katz and Al Sommer serve on editorial boards of several leading health sciences journals), actively participating in professional societies as members and officers (e.g., ASNS, SINR, APHA, ASE), international task forces and consultative groups (IVACG, INACG, WHO and other UN Advisory Boards, IOM DRI committees); by providing authoritative guidance to the private non-commercial sector (e.g., to USAID-funded partners such as MOST, MEASURE, the CORE Group, MACRO/DHS, HKI, etc) and to multinational corporate partners (e.g., Monsanto, Roche, Procter and Gamble, Nestle, Kellogg, Rexall/Sundowner and Unilever in the past year); by engaging private sector foundations to assume leading roles, technically and financially, in the fight against micronutrient malnutrition (e.g., the Bill & Melinda Gates Foundation, Task Force Sight and Life of Roche, Unilever Health Institute) and by making deliberate efforts to disseminate the "micronutrient story" to a wide array of lay audiences as a means to reach and influence public opinion about international health work in general and micronutrient deficiency control in particular (e.g., Anderson TV documentary in Nepal, to be televised in 2001; Baltimore Sun 3-part front page series on JHU work in Nepal; lay articles written for the Xerophthalmia Club Bulletin and industry publications, etc). The latter activities help to educate the US public world citizenry in general about the need to support efforts to prevent vitamin A and other micronutrient deficiencies. JHU faculty view this role as a tradition initiated for the field of nutrition by EV McCollum decades ago.

Listings of meetings and travel of JHU CA-supported faculty in carrying out the research, technical assistance, teaching and global leadership agenda of the CA are provided in **Appendices 6 and 7**, respectively.

#### **5. Faculty Changes**

During the year Drs. Anu Raj Shankar and Amy Rice departed Johns Hopkins as full-time faculty on the Baltimore campus to assume in-country positions with Helen Keller Worldwide in Indonesia. Both Drs. Shankar and Rice contributed immensely to the MHCA research, teaching and technical assistance program at JHU over the past several years, particularly to our understanding of the roles of vitamin A and zinc supplementation in reducing the morbidity burden of malaria and the roles of post-partum maternal vitamin A and  $\beta$ -carotene supplementation in improving vitamin A status of mothers and infants in the first year of life, respectively. Both have retained adjunct appointments in the Center of Human Nutrition and Department of International Health. Given the strong collaborative ties between JHU and HKI, their appointments will serve to strengthen JHU-HKI collaboration on micronutrient deficiency control in Indonesia and elsewhere in Southeast Asia in years to come.

#### **5. Cooperative Agreement Baseline Report (Pipeline)**

Appendix 1 contains the Cooperative Agreement Baseline Report. Total cumulative obligations through September 30, 2000, including the pipeline left in the CA

budget as of 1 October 1999, amounted to \$10,931,021. **PLEASE NOTE:** This total does not include \$350,000 that was to have been obligated by the USAID Mission in Bangladesh in support of the JiVitA Project. It is our understanding from USAID HN, as of 28 September 2000, that the monies were obligated by the Mission and processed by the Contracts Office at USAID/W in early September but that the funds had not been transferred due to a backlog of work at that time. JHU was assured that the funds would be forthcoming as a final modification to the FY 00 CA account.

Total cumulative expenses as of September 30, 2000 were \$8,713,107 leaving a balance of \$2,217,914 as of 1 October 2000, the beginning of FY2001. For FY00, a total of \$2,952,903 was expended generating a burn-rate of \$ 246,075 per month. Planned expenditures for FY01 amount to \$ 3,329,370, with a projected monthly burn-rate of \$277,448. Given these projections it is estimated that the new FY 01 pipeline, as of 1 October 2000, will cover projected CA expenses for ~8 months or up to May 2001.

# Appendices

**Appendix 2:  
Checklist of JHU Progress Against the  
Year 3 (FY00) Proposed Work Plan**

<b>Project</b>	<b>Proposed Activity in Year 4 Workplan</b>	<b>Current Status</b>
NIPPS-3	<ul style="list-style-type: none"> <li>• Pregnancy enrollment</li> <li>• Birth and first 10 d assessment</li> <li>• Dosing and 6 wk postpartum visit</li> <li>• 6 mo. follow-up for vital status</li> <li>• 6 mo. follow-up of infant anemia status</li> <li>• Data entry and cleaning</li> <li>• Biochemical analysis</li> <li>• DSMC</li> </ul>	<ul style="list-style-type: none"> <li>✓</li> <li>✓</li> <li>✓</li> <li>on-going</li> <li>on-going</li> <li>on-going</li> <li>on-going</li> <li>✓</li> </ul>
JiViTA	<ul style="list-style-type: none"> <li>• Ethical Review, approval and GOB gov't order</li> <li>• Set up offices and hire key staff</li> <li>• Develop mapping procedures</li> <li>• Design and set up data management system</li> <li>• Procure vehicles</li> <li>• Develop field procedures/forms</li> <li>• Community preparation</li> <li>• Community meetings</li> <li>• Mapping of communities and numbering households</li> <li>• Hire/train distributors</li> <li>• Census taking</li> <li>• Pregnancy surveillance</li> <li>• Supplement production/shipment</li> </ul>	<ul style="list-style-type: none"> <li>✓</li> <li>✓</li> <li>✓</li> <li>on-going</li> <li>x</li> <li>on-going</li> <li>✓</li> <li>✓</li> <li>✓</li> <li>x</li> <li>x</li> <li>x</li> <li>x</li> </ul>
Zvitambo	<ul style="list-style-type: none"> <li>• Recruitment</li> <li>• Follow up</li> <li>• Male outreach program</li> <li>• QC implemented for Follow up forms</li> <li>• Data shop audit</li> <li>• DNA PCR diagnosis of babies born to first 1000 HIV+ mothers</li> <li>• RNA PCR diagnosis of plasma &amp; milk of substudy A mothers</li> <li>• Vitamin A analysis of Substudy A specimens</li> <li>• Vitamin A analysis of Substudy B specimens</li> <li>• Refinement of current analysis plan</li> <li>• Intensive monitoring phase of infant feeding counseling intervention</li> </ul>	<ul style="list-style-type: none"> <li>✓</li> <li>on-going</li> <li>on-going</li> <li>on-going</li> <li>✓</li> <li>✓</li> <li>on-going</li> <li>on-going</li> <li>X</li> <li>on-going</li> <li>on-going</li> </ul>

Key: ✓=completed  
X=not accomplished  
In progress=in progress

## Appendix 3

### Year 2000 Publications

#### *Peer-reviewed Journal Articles (published, in press, or submitted)*

##### Vitamin A

Almekinder J, Manda W, Soko D, Lan Y, Hoover DR, Semba RD: Evaluation of plasma retinol-binding protein as a surrogate measure for plasma retinol concentrations. *Scand J Clin Lab Invest* 2000;60(3):199-203.

Choi JK, Akib A, Munasir Z, Permaesih, Komala, Muherdiyantiningsih, Martuti S, Muhilal, Semba RD: Effects of vitamin A supplementation with measles vaccine on lymphocyte subsets in young infants. *J Nutr Immunology* 2000 (in press).

Christian P, West KP Jr, Khattry SK, Katz J, Kimbrough-Pradhan E, LeClerq SC, Shrestha SR: Interactive effects of cigarette smoking and vitamin A or  $\beta$ -carotene supplementation on mortality related to pregnancy in rural Nepal. *AJPH* 2000 (submitted).

Christian P, West KP Jr, Khattry SK, Katz J, Kimbrough-Pradhan E, LeClerq SC, Shrestha SR, Sommer A: Association of maternal night blindness with early infant mortality in Nepal. (submitted 1999)

Christian P, West KP Jr, Khattry SK, Katz J, LeClerq SC, Kimbrough-Pradhan E, Dali SM, Shrestha SR: Vitamin A and  $\beta$ -carotene supplementation reduces symptoms of illness in pregnant and lactating Nepali women. *J Nutr* 2000;130(11): (in press).

Christian P, West KP Jr, Khattry SK, Kimbrough-Pradhan E, LeClerq SC, Katz J, Shrestha SR, Dali SM, Sommer A: Night blindness during pregnancy and subsequent mortality among women in Nepal: effects of vitamin A and  $\beta$ -carotene supplementation. *American Journal of Epidemiology* 2000;152:542-547.

Coles CL, Rahmathullah K, Kanugo R, Thulasiraj RD, Katz J, Santosham M, Tielsch JM: Effect of vitamin A supplementation on pneumococcal carriage in South Indian infants. *Journal of Nutrition* 2000 (submitted).

Congdon NG, Dreyfuss ML, Christian P, Navitsky RC, Sanchez AM, Wu LSF, Khattry SK, Thapa MD, Humphrey J, Hazelwood D, West KP Jr: Responsiveness of dark-adaptation threshold to vitamin A and  $\beta$ -carotene supplementation in pregnant and lactating women in Nepal. *Am J Clin Nutr* 2000;72(4):1004-1009.

Craft NE, Haitema T, Brindle LK, Yamini S., Humphrey JH, West KP Jr: Retinol analysis in dried blood spots by HPLC. *J Nutr* 2000;130:882-885.

Hadi H, Stoltzfus RJ, Dibley MJ, Moulton LH, West KP Jr, Kjolhede CL, Sadjimin T: Vitamin A supplementation selectively improves linear growth of Indonesian preschool children: results from a randomized controlled trial. *Am J Clin Nutr* 2000;71:507-513.

Humphrey JH, Rice AL: Vitamin A supplementation of young infants. *Lancet* 2000;356:422-424.

Katz J, West KP Jr, Khattry SK, Pradhan EK, LeClerq SC, Christian P, Wu LSF, Adhikari RK, Shrestha SR, Sommer A: Maternal low-dose vitamin A or  $\beta$ -carotene supplementation has no effect on fetal loss and early infant mortality: a randomized cluster trial in Nepal. *Am J Clin Nutr* 2000;71:1570-1576.

Ng EWM, Congdon NG, Sommer A: Acute sixth nerve palsy in vitamin A treatment of xerophthalmia (Letter). *Br J Ophthalmol* 2000;84:931-932.

Rice AL, Kjolhede CK, de Francisco A, Stoltzfus RJ: Evaluation of serum retinol, the modified relative dose response (MRDR) ratio, and breast milk vitamin A as indicators of response to postpartum maternal vitamin A supplementation. *Am J Clin Nutr* 2000;71:799-806.

Semba RD, Muhilal, West KP Jr, Natadisastra G, Eisinger W, Lan Y, Sommer A: Hyporetinolemia and acute phase proteins in children with and without xerophthalmia. *American Journal of Clinical Nutrition* 2000;72(1):146-153.

Shankar AV, Gittelsohn J, Pradhan R, Dahal B, West KP Jr: Night blindness, diet and health in Nepalese children: An ethno-epidemiological investigation of local beliefs. *Ecol Food Nutr* 2000;39:1-25.

Solon FS, Klemm RDW, Sanchez L, Darnton-Hill I, Craft NE, Christian P, West KP Jr.: Efficacy of vitamin A-fortified wheat-flour bun on the vitamin A status of Filipino schoolchildren. *Am J Clin Nutr* 2000;72:738-744.

Yamini S, West KP Jr, Wu L, Dreyfuss ML, Yang D-X, Khattry SK: Circulating levels of retinol, tocopherol and carotenoid in Nepali pregnant and postpartum women following long term  $\beta$ -carotene and vitamin A supplementation. *European Journal of Clinical Nutrition* 2000 (under review).

#### Vitamin A and HIV

French AL, Kirstein LM, Massad LS, Semba RD, Minkoff H, Landesman S, Palefsky J, Young M, Anastos K, Cohen MH: The association of vitamin A deficiency with cervical squamous intraepithelial lesions in HIV-infected women. *Journal of Infectious Diseases* 2000;182:1084-1089.

Tang AM, Smit E, Semba RD, Nina S, Lyles CM, Li D, Vlahov D: Improved antioxidant status among HIV-infected injecting drug users on potent antiretroviral therapy. *Journal of Acquired Immune Deficiency Syndrome* 2000;23(4):321-326.

#### Iron Deficiency and Anemia

Christian P, Khattry SK, LeClerq SC, Shrestha SR, Kimbrough-Pradhan E, West KP Jr: Iron and zinc interactions among pregnant Nepali women. *Nutr Reviews* 2000 (accepted for publication).

Dreyfuss ML, Stoltzfus RJ, Shrestha JB, Pradhan EK, LeClerq SC, Khattry SK, Shrestha SR, Katz J, Albonico M, West KP Jr: Hookworms, malaria and vitamin A deficiency contribute to anemia and iron deficiency among pregnant women in the plains of Nepal. *J Nutr* 2000;130(10):2527-2536.

Fishman SM, Christian P, West KP Jr: The role of vitamins in the prevention and control of anaemia. *Public Health Nutrition* 2000;3(2):125-150.

Iyer JK, Shankar AH, Stoltzfus RJ, the TAPP Research Team, Sullivan DJ Jr: Protection from malaria by anemia-associated elevations in erythrocyte protoporphyrin IX. *JCI* (submitted 1999).

Montresor A, Albonico M, Khalfan N, Stoltzfus RJ, Tielsch JM, Chwaya HM, Savioli L: Field trial of a haemoglobin colour scale: an effective tool to detect anaemia in preschool children. *Tropical Medicine and International Health* 2000;5(2):129-135.

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#### Articles by Others Using Our Data

Korhonen P, Loeys T, Goetghebeur E, Palmgren J: Vitamin A and infant mortality: beyond intention-to-treat in a randomized trial. *Lifetime Data Analysis* 2000;6:107-121. (Joanne Katz providing data from Vitamin A trial)

## Appendix 4

### Technical Assistance (TA)

Name	Nature and Purpose of TA	Dates
Alfred Sommer	Provided direction to IVACG Steering Committee as the Chair	Oct 99-Sept 00
Keith West	<p>Provided policy guidance to IVACG Steering Committee as a Member</p> <p>Assisted Measure Project to develop US Strategy for 10<sup>th</sup> Anniversary of World Summit for Children</p> <p>Served as a member of the Dietary Reference Intake Micronutrient Task Force, Vitamin A Sub-panel, Institute of Medicine, National Academy of Sciences</p>	<p>Oct 99-Sept 00</p> <p>Oct 99-Sept 00</p> <p>Oct 99-Sept 00</p>
Rebecca Stoltzfus	<p>Appointed as founding member of the "new" INACG</p> <p>Co-organized the "Belmont Meeting" which brought together iron deficiency and anemia experts and drafted a state-of-the-situation-report on the control and prevention of iron deficiency and control of anemia</p>	May 2000
Joanne Katz	<p>Provided TA to Aravind Eye Hospital, Drs. Kim &amp; Narendra on vitamin A programs</p> <p>Provided assistance to BIRPERHT, Dr. Halida Akhter in the drafting of NIH grants</p> <p>Assisted Moorfields Eye Hospital, Richard Wormald in a meta analysis of vitamin A trials (CO chraine collaboration)</p>	<p>Nov 1, 1999</p> <p>April 12, 2000</p> <p>May 8, 2000</p>
Parul Christian	<p>Served as research consultant to the Indo-US Micronutrient Research Conference</p> <p>Assisted MACRO International to insert a standard set of question on assessing maternal night blindness into core DHS and MICS survey modules</p>	February 2000
Rolf Klemm	Assisted UNICEF-India in the design of a survey using the dried blood spot method to assess VA status in post-partum women	Oct 99-Sept 00

## Appendix 5

### Lectures

Date(s)	Name	Title/Audience/Place
Jan 6, 2000	Joanne Katz	Survey methods for nutrition, JHU-Nutritional Assessment course
Jan 24-25, 2000	Keith West, Jr.	"Evaluation of programs: interventions to reduce micronutrient deficiencies. State-of-the-art of bio-assessment," Nat'l Academy of Science, Washington, DC
Feb 7, 2000	Joanne Katz	Sample size considerations in field trials, JHU-Field Trials course
Feb 9, 2000	Joanne Katz	Critique of NNIPS-2 study findings, JHU-Field Trials course
Feb 10-12, 2000	Parul Christian	NIH/USAID/CDC sponsored workshop on "Indo-US collaboration on maternal & child health & nutrition research." Indian & US scientists, Hyderabad, India
April 12, 2000	Keith West, Jr.	Speak at dinner meeting for Monsanto in Atlanta, GA
May 2-3, 2000	Parul Christian	Kellogg sponsored mini-symposium on "role of vitamins in combating iron deficiency anemia." Caracas, Venezuela
Sept 3-7, 2000	Keith West, Jr.	Nestle Nutrition Workshop Lecture, St. Petersburg, Russia
Sept 18, 2000	Keith West, Jr.	"Measure" World Summit, Rockefeller Center, New York

## Appendix 6

### Meetings

Date(s)	Name	Purpose	Location
Nov 18-19, 1999	Keith West, Jr.	Institute of Medicine meeting	Washington, DC
Dec 9-12, 1999	Keith West, Jr.	"World Summit Goals," USAID-Child Survival Development	Washington, DC
Jan 24-25, 2000	Keith West, Jr.	Nat'l Academy of Science conference, "Biological & Clinical Data Collection in National surveys: Potential and Issues"	Washington, DC
Mar 23-24, 2000	Keith West, Jr.	IVACG Steering Committee	Washington, DC
April 14-18, 2000	Parul Christian, Tiang Jiang	Present a paper at the FASEB meeting	San Diego, CA
April 14-18, 2000	Keith West, Jr.	FASEB meeting	San Diego, CA
April 30-May 5, 2000	Joanne Katz	ARVO meetings	Ft. Lauderdale, FL
May 31, 2000	Keith West, Jr.	UNICEF-State of the World's Children	New York
Aug 24-25, 2000	Keith West, Jr.	IVACG Steering Committee	Washington, DC
Sept 3-7, 2000	Keith West, Jr.	Nestle Nutrition Workshop	St. Petersburg, Russia

## Appendix 7

### Travel

Dates	Name	Country	Purpose
Sept 29-Oct 11, 1999	Joanne Katz	Nepal	NNIPS-3
Sept 29-Oct 16, 1999	Keith West	Nepal, Bangladesh	Visit projects
Feb 8-Mar 10, 2000	Parul Christian	India, Nepal, Bangladesh	Give a talk and to visit project in Nepal and Bangladesh
Feb 19-Mar 9, 2000	Joanne Katz	Nepal, Bangladesh	NNIPS-3, JiVitA
Feb 23-March 17, 2000	Keith West, Jr.	Nepal, Bangladesh	Visit projects
Feb 23-Mar 4, 2000	Rolf Klemm	Nepal	Visit Sarlahi and observe field procedures for NNIPS-3
Mar 5-April 9, 2000	Rolf Klemm	Bangladesh	Planning for JiVitA. Recruit, select, and hire field staff, train field staff to undertake community mapping and household addressing, supervise field work
Aug 18-Sept 24, 2000	Parul Christian	Nepal, Bangladesh	Visit project sites
Sept 5-Nov 19, 2000	Rolf Klemm	Bangladesh	Orient senior staff, draft manuals and forms, pretest forms, oversee procurement, supervise mapping and sectoring
Sept 8-16, 2000	Keith West, Jr.	Bangladesh	Visit project