LNS Research Network Meeting Report
Rome, February 6, 2009

This report summarizes presentations and key discussion points from the first meeting of the LNS Research Network. Most presentations are also attached, in .pdf format. The LNS Research Network is at present a loosely organized group of researchers and practitioners with a common interest in exploring the potential of lipid-based nutrient supplements. The meeting was organized by the iLiNS Project (described in presentation #1) to provide a platform for exchange of information and ideas and for discussion.

The report includes:

- Meeting objective
- Remarks by Josette Sheeran, Executive Director of the World Food Programme
- Proposed objectives and operating principles for an LNS Research Network
- Summary of presentations and key discussion points
- Agenda
- List of participants

Meeting objective

To share information on current and planned research on lipid-based nutrient supplements (LNS) and issues related to use of LNS in programmatic settings.

Remarks by Josette Sheeran

Josette Sheeran greeted and thanked the group and underlined the importance of work on LNS, given there are still many unanswered questions. To put new World Food Programme (WFP) initiatives in context, she shared a brief history of the agency, beginning with the post-WW II aim of "connecting surplus to need". Over the years many lives have been saved, and WFP has built a global network: the "FedEx to the bottom billion". At the same time, available foods were not always well-matched to all the needs and preferences of the populations served. The goals were to make sure people got calories at the lowest cost, and to ward off starvation; WFP was "filling the cup".

Bringing the group up to date, Ms. Sheeran highlighted the magnitude of the challenges currently facing the agency, with 100 million people to feed and critical situations including in Darfur, Somalia, Zimbabwe and others. WFP is working relentlessly to meet these needs and often with very limited capacity. For example, it has less than a dozen nutritionists and only a handful of food technologists globally.

Ms. Sheeran also highlighted changes in WFP operations, as delivery of surplus food now represents less than 1% of WFP activity. WFP has moved towards buying food locally, and is now one of the largest food procurers in the developing world. In addition, concern has moved past "filling the cup" to ask: "What are we filling it with? Can it be sourced locally? Can it be sustainable? Can we "microtarget" within a camp?"

Her dream for the future is that responses can be shaped by realities in each country setting. WFP will identify the causes of food shortages/crises and also the local resources for response. If the food is in the market, cash and vouchers may be best; if there is no food, WFP can bring it in, but must recognize other constraints in advance. If there is no fuel/no water to cook, they must have something in the tool-box ready to go for those situations.

Right now, WFP needs "bang for the buck" answers on what can be added to rations. Based on what we already know about the window of opportunity (prenatally up to 2 years of age) and micronutrient needs, we must act and bring in the right products. In this context she offered encouragement and support for the efforts of the LNS Network.

LNS Research Network

During the first presentation (below and attached) Kay Dewey proposed objectives and operating principles for the LNS Research Network, highlighted here to provide a framework for all presentations:

Objectives:

- To provide technical information regarding the use of LNS to improve nutrition of vulnerable populations
- To facilitate timely exchange of knowledge and experience regarding use of LNS
- To foster rapid translation of new research findings on LNS into programs & policy

Operating principles:

- Rigorous scientific approach, evidence-based
- Open communication & access to information
- North-South partnerships & capacity building

Presentation #1

Overview of upcoming LNS research activities funded by the Bill and Melinda Gates Foundation (the "iLiNS Project")
Kay Dewey, University of California, Davis; and Per Ashorn, University of Tampere
(attached: *iLiNS overview 06 Feb 2009.pdf*)

Kay Dewey and Per Ashorn introduced the "iLiNS Project" (International Lipid-based Nutrient Supplements Project) which is comprised of a series of efficacy trials, socioeconomic studies and other activities aimed at enriching the evidence base for the use of LNS in prevention of undernutrition.

The key defining feature of LNS: lipids are the main source of energy (kilocalories). This differentiates LNS from other types of supplements. LNS are a family of products, ranging from those providing minimal energy (kcal) to those meant to supply a substantial proportion of needed energy; all provide multiple micronutrients and essential fatty acids, as well as macronutrients. Those that provide minimal energy may be designed for prevention while those that provide very substantial energy have been used in emergency settings and in treatment of acute malnutrition (in various settings).

The iLiNS Project is designed to achieve the following six objectives (detailed in attached presentation):

1. Develop LNS formulations for various target groups
2. Evaluate approaches to reduce the cost of LNS for infants & young children
3. Determine the optimal amount of zinc to include in LNS for infants & young children
4. Evaluate the efficacy of LNS products for pregnant & lactating women
5. Conduct socio-economic studies of LNS (demand, delivery systems, cost-effectiveness)
6. Coordinate efforts, build capacity and use results to inform nutrition policies and programs

The meeting reported here represents an activity under objective 6 of the iLiNS Project; during the 5-year life of the project, annual meetings will be organized to provide a forum for a group of researchers and practitioners, such as those gathered for the Feb. 6 meeting in Rome. The next 3 meetings will be

hosted in the country "homes" for the efficacy trials (Malawi, Ghana, and Burkina Faso) to facilitate participation by researchers and practitioners in those regions.

Discussion:
Discussion centered on questions related to formulation of LNS products, and to study design.

Formulation:
Several points were raised concerning the advantages and disadvantages of dried skim milk (DSM) vs. whey/whey isolates. DSM is expensive and may be hard to source in Africa (full fat milk more available). Whey is less expensive but whey isolates may be needed and these are not so cheap. Both should be considered and local availability should be considered.

Q: Will the micronutrients provided by LNS for pregnant and lactating women differ from the UNIMMAP[1] formulation?
A: The formulation is still under discussion but it is likely to differ from UNIMMAP in several ways. iLiNS is considering higher doses of those micronutrients for which higher doses are quite safe; rationale is that RDA-level doses do not appear to restore micronutrient levels in depleted women. Other nutrient levels are constrained due to concerns about staying well below the UL[2] and/or due to taste issues. The formulation of the supplement is being reviewed nutrient-by-nutrient.

Efficacy trial designs:
Q: Why is supplement to lactating women discontinued when the child reaches 6 mo of age?
A: At 6 mo, we can start supplementing the child directly. It is possible that there would be added benefit to the mother to continue her own supplement; we do not know. There are cost issues and it is already ambitious to provide supplementation during pregnancy and first 6 mo of lactation.

Q: Programmatically we have been supplementing children up to 24 or 36 mo of age. What is the rationale for stopping at 18 mo?
A: This is the period of greatest vulnerability. Results from previous studies in Malawi showed severe stunting eliminated during this age span (with 50 g/day supplement) and impacts were sustained for at least 2 years.[3] It is possible there would be added benefit to continuing but there is a big cost issue. We aim to see how much can be accomplished focusing on the key window of opportunity. We aim to find the lowest cost intervention that is still efficacious. Programs can of course supplement for longer or to a wider age group if they can afford to do so.

Q: Why not split the 12 mo of supplementation into 2 hunger seasons instead of into 12 consecutive months?
A: An interesting idea but one cannot do everything; we are not doing this. Also, the micronutrients are needed throughout the year, not just during the hungry season.

Q: Why consider cost at all in the design? Why not aim high and aim to eliminate stunting, learn the whole range of possibility and then consider cost?

[1] The UNIMMAP supplement is the UNICEF/WHO/UNU international multiple micronutrient preparation, and provides the Recommended Dietary Allowance (RDA) of 15 vitamins and minerals.

[2] UL=Tolerable Upper Intake Level; this is the highest average daily intake likely to pose no risk of adverse effects.

[3] Phuka JC, Maleta K, Thakwalakwa C, et al. *Postintervention growth of Malawian children who received 12-mo dietary complementation with a lipid-based nutrient supplement or maize-soy flour.* American Journal of Clinical Nutrition 2009; 89(1):382-90. Epub 2008 Dec 3.

A: To some extent this is the reason for the study arm that supplements during pregnancy, lactation to 6 mo, and 6-18 mo (child) – to see what can be achieved when targeting all of these age periods. It was also the rationale for the 50 g dose in earlier Malawi studies; 50 g was considered the largest dose that would not interfere with breastfeeding. Yet the cost issue is real.

Presentations #2-#6: Current or planned research on efficacy of LNS

There was very little time for discussion of presentations, so the notes below summarize main points and refer the reader to the available presentations.

Presentation #2

"The effect of a lipid-based nutritional supplement on birth outcome: a randomized controlled trial in rural Burkina Faso"

Huybregts, LF[a], Roberfroid, D[b], Lanou H[c]., Meda N[c]., Van Camp, JH[a] & Kolsteren, PW[a,b]
[a] Dep. Of Food safety and Food Quality, Ghent University, Belgium
[b] Child Health and Nutrition Unit, Prince Leopold Institute of Tropical Medicine, Antwerp, Belgium
[c] Centre Muraz, Bobo-Dioulasso, Burkina Faso
(no presentation attached)

Fetal growth is an important determinant of child health in developing countries. Low birth weight (<2500g; LBW) is regarded as an important predictor of infants' morbidity and mortality.[4,5] Multiple micronutrient supplementation during pregnancy showed an modest increase in birth size. Most studies evaluating food supplementation during gestation showed also a limited effect on birth size.
The objective was to test the effect of a fortified lipid-based nutritional supplement (LNS) enriched with multiple micronutrients compared to a multimicronutrient tablet in terms of birth weight and birth length in pregnant African women.

A randomized controlled trial including 1300 pregnant women in the Houndé district, Burkina Faso. The LNS provided the 370kcal per day and contained the UNIMMAP[6] multiple micronutrient formulation. The control group was given a tablet containing the UNIMMAP. Supplement intake was directly observed.

Newborns in the LNS group were slightly heavier (31g; $p>0.05$), but significantly taller (5 mm; $p<0.05$). The proportion of LBW in the LNS group was slightly lower (OR 0.79; $p>0.05$). The treatment effect was homogeneous over the whole birth weight and birth length distribution. No effect treatment effect was found on the incidence of preterm delivery.

In conclusion, this study found that the administration of LNS compared to multi-micronutrient supplementation, to pregnant women increased birth length significantly.

[4] Ashworth A. *Effects of intrauterine growth retardation on mortality and morbidity in infants and young children.* Eur J Clin Nutr 1998;52(suppl): S34–41.

[5] Black RE, Allen LH, Bhutta ZA, et al. *Maternal and child undernutrition: global and regional exposures and health consequences.* Lancet 2008; 371:243– 60.

[6] UNICEF/UNU/WHO. *Composition of a multi-micronutrient supplement to be used in pilot programmes among pregnant women in developing countries.* New York, NY: UNICEF, 1999.

Presentation #3

"Research with LNS in the Gambia"
Kay Dewey presented on behalf of Andrew Prentice, London School of Tropical Hygiene and Medicine (no presentation attached)

Andrew Prentice sent materials describing two studies:

Study 1:
A randomized trial to investigate the effects of pre-natal and infancy nutritional supplementation on infant immune development in rural Gambia (The ENID Trial: Early Nutrition and Immune Development)
PI: Dr Sophie Moore
Design:
Randomized controlled trial; n=800 1st trimester pregnant women
Subjects will be randomized into 4 groups:

i. A ready to use protein energy (PE) supplement (unfortified LNS)
ii. PE + multiple micronutrient (MMN) (LNS)
iii. MMN only
iv. Iron-folate only (FeFol control = usual standard of care, as per Gambian Government guidelines)

Then infants re-randomised at 6 mo to LNS vs unfortified placebo.

Primary outcomes: Thymic size by ultrasound and vaccine responses. More detailed cellular immunology in subgroups.
Secondary outcomes: growth, morbidity.

Study 2:
A randomized trial to investigate the effects of physician prescribed lipid-based multiple micronutrients on the health of children presenting to a primary health care centre in The Gambia.
PI: Dr Stefan Unfer
Design:
Clinic-based randomized controlled trial of 750 infants and 1500 children. Subjects are all children self-presenting to clinic (NB no selection on basis of nutritional status in this trial).
Subjects will be randomized into 3 groups:

i. 12 wk LNS supplementation;
ii. 6 wk LNS supplementation followed by 6wk placebo
iii. 12 wk placebo

Primary outcome: Repeat clinic visits.
Secondary outcomes: growth, morbidity

Sub-study of children with lower respiratory tract infection (LRTI):
n=50 LRTI+LNS
n=50 LRTI-LNS
n=50 control+LNS
n=50 control-LNS

Outcomes are detailed mucosal immunology.

Presentation #4

"Valid Nutrition's LNS Research Program"
Victor Owino, Valid Nutrition
(attached: *Valid Nutrition LNS Research Program Rome 06 Feb 2009.pdf*)

Victor Owino presented an overview of Valid Nutrition including mode of operation and principles. He then described a set of planned research activities exploring acceptability, efficacy and effectiveness of several new ready-to-use (RUF) food products.

These are:

- Maize -Soya-Sorghum RUF with a small amount of milk powder for use as a complementary food (RUCF) among infants and young children 6-24 months old (dose 200 kcal/day; efficacy trial)
- Maize-Soya-Sorghum RUF with a small amount of milk powder for use as supplementary food (RUSF) among children 6-59 months old (dose 750 kcal/day; efficacy trial)
- Maize -Soya-Sorghum RUTF with no milk powder for treatment of severely acutely malnourished children 6-59 months old (dose 200 kcal/kg/day; effectiveness trial)
- Maize -Soya-Sorghum RUTF-HIV with no milk powder for treatment of malnutrition among HIV-infected adults (dose 2000 kcal/day; efficacy trial)

Acceptability tests have been satisfactorily completed (a question was raised regarding the difference in age between the target age group for RUSF and the age group for acceptability testing). Next there will be adjustments of ingredients and of the vitamin-mineral pre-mix, and then the efficacy and effectiveness trials.

Presentation #5

"Acceptability and effectiveness of chickpea sesame based ready to use therapeutic food (cs-rutf) in malnourished HIV positive adults: Results of a pilot programme"
Paluku Bahwere, Valid International
(attached: *Valid - Acceptability effectiveness of cs-rutf HIV pos adults 06 Feb 2009.pdf*)

Paluku Bahwere described an observational (non-controlled) study of 60 HIV+ adults referred by volunteers and given 3 months of nutritional support (500 g/d of chick-pea sesame RUTF) delivered through existing home-based care structures. Criteria for selection were body mass index (BMI) <17 and/or mid-upper arm circumference (MUAC) < 22 cm.

Study questions:

- RUTF acceptability?
- What are the clinical effects of RUTF?
    - Nutritional status including body composition
    - Activity and quality of life
    - Survival

The RUTF was well accepted; some complained it was too sweet, a few said too salty or too oily, but acceptance as measured by consumption was good (average intake 300 g/d). Study subjects gained weight and fat-free mass; fat deposition was not disproportionate to fat-free mass gain. With weight gain there were associated improvements in physical activity. There was a group of non-responders (~30%) and this will be explored further. There were no major side effects.

Presentation #6

"Randomized controlled trial (RCT) with adult HIV patients in Jimma, Ethiopia"
Christian Mølgaard, University of Copenhagen
(attached: *RCT with adult HIV patients in Jimma Ethiopia 06 Feb 2009.pdf*)

Christian Mølgaard summarized key results of several previous studies undertaken along with his colleagues, which have led up to a current planned randomized controlled trial. Previous studies have:

1. Reviewed evidence for a growth-stimulating effect of milk, associating milk protein fractions with IGF and insulin; and
2. Assessed advantages and disadvantages of including whey vs. skim milk powder in blended fortified foods.

It has been suggested that whey may have positive immune modulating effects but these effects have not been conclusively demonstrated. Currently, the group is planning a randomized clinical trial with the main objective:

- To assess the effects of a whey-containing nutritional supplement to HIV infected patients commencing antiretroviral treatment (ART) on general and HIV specific treatment outcomes

Study design: participants will be stratified by baseline BMI (with BMI < 16 excluded and treated) and assigned to receive RUTF with whey protein, RUTF with soy protein, or delayed RUTF (only if baseline BMI is > 17.5).

Primary outcomes: Lean body mass; grip strength; physical activity
Secondary outcomes: HIV load; CD4 count; adherence to ART; risk of IRIS; S-IGF-I levels; quality of life

Presentations #7-#10: Research on use of LNS in programmatic settings

The afternoon presentations focused on past, on-going, or planned use of LNS in programs. As with the morning session, the first afternoon presentation (#7) was a longer overview and was followed by some discussion. For the subsequent presentations (#8-#10) time for discussion was quite limited. The notes below summarize main points and refer the reader to the available presentations.

Presentation #7

"LNS in programs: FANTA-2 research and overview of current programmatic uses of LNS"
Camila Chaparro, Food and Nutrition Technical Assistance II Project (FANTA-2)
(attached: *Overview of LNS in programs 06 Feb 2009.pdf*)

Camila Chaparro summarized planned work to be undertaken by the FANTA-2 Project and their partners. Activities include:

- Research on the effectiveness of LNS for the prevention of stunting
- Active participation in the LNS Research Network, including contributions to a web-based clearinghouse for technical information on LNS
- Tracking/mapping of on-going programmatic use of LNS and any associated research (operational; effectiveness)

Under the first activity (effectiveness research) FANTA-2 will evaluate impact of LNS when delivered in several programmatic settings (vs. in more controlled setting of efficacy trials). Outcomes to be assessed will include:

- Biological
    - Growth: length/height, weight
    - Stunting, underweight
    - Micronutrient status: iron, vitamin A
    - Anemia
    - Motor and cognitive development
- Operational effectiveness
    - Program delivery
    - Caregiver exposure and practice
- Cost effectiveness
    - Costs related to product, transportation, personnel time (entire delivery system)

The second activity – active participation in the LNS Research Network – reflects recognition of current strong interest in LNS, including for "prevention", accompanied by confusion over a growing variety of products. There is also confusion over appropriate uses and, at present, a still limited evidence base for use of LNS in prevention. The LNS Research Network provides an opportunity to share experiences and research results and this may ultimately result in clear guidance on the use of LNS in programs.

The third and related activity – tracking/mapping of on-going programmatic use of LNS and associated research – has already begun and first results were presented. Dr. Chaparro presented a brief overview of programs and programmatic research recently completed, underway, or planned by several organizations (Action Contre la Faim (ACF), Médecins Sans Frontières (MSF), WFP, and UNICEF; see attached .pdf for details). Through communication with implementing groups, FANTA-2 will contribute to the LNS Research Network and may also help identify and communicate research priorities for use of LNS in programmatic settings.

Discussion:
Representatives of the implementing agencies were in attendance and could offer reflections on experiences and problems faced. Key areas of discussion included questions on various products; questions on the issue of sharing within the household (beyond targeted individual) or outside the household; challenges in field settings both to distribution and evaluation; and technical challenges with product development.

Range of products in use:
Proliferation of products has caused confusion; a specific question was asked about differences in formulation and intended use between Supplementary'Plumpy (SP) and Plumpy'doz (PD).
A: SP was developed for use with moderately malnourished individuals and provides a large amount of energy (~500 kcal in 92 g daily dose); it has no milk; PD was designed as a rainy season supplement, to prevent acute malnutrition and treat borderline cases. In PD, the vitamins and minerals are more concentrated and the daily ration has less energy (40 g daily dose; ~250 kcal). PD has milk and is closer to Nutributter®.

Issue of sharing/selling of LNS products:
MSF/Niger: The situation varies; in 2007 MSF felt there was not much shared beyond targeted individuals; in 2008 the food security situation was worse and PD became a family resource, and as such was shared.

Project Peanut Butter/Malawi: Focus group results suggested that something like 80% of LNS reached the target child, compared to about 50% of corn-soy blend.

Q: Has anyone explored the effect of packaging on extent of sharing?
A: MSF: Small sachets were more likely to end up sold in local markets because the family could sell a small amount yet also keep some; larger tubs were not showing up in the markets.

Challenges in field settings:
UNICEF reported challenges to evaluating efforts in two settings. In Somalia, with lots of acute malnutrition and few contacts, impacts were impossible to document due to the nature of the situation. In Madagascar: Could not design/develop protocol for evaluation in time to accompany urgent need to distribute (in advance of the hungry season).

Technical challenges:
WFP described challenges with product development in India. There were challenges both with formulation/stabilization and with packaging. These took some time to work out but they now aim to produce (private company), distribute and scale up and plan both efficacy and effectiveness work. The product is similar to PD (~50 g, less for younger children) and the target is children in ICDS.[7]

Presentation #8

"Preventive Supplementation with RUF: the MSF experience in Niger"
Géza Harczi, MSF
(attached: *Preventive supplementation w RUF MSF Niger 06 Feb 2009.pdf*)

Géza Harczi presented results from a recently published cluster randomized controlled trial implemented in 2006-2007 in Niger[8], and presented study design and preliminary results from a second, prospective study that followed on from the RCT in 2007-2008.

First he described the context for the work of MSF and their focus on "hunger hotspots" – that is locations with high under-five mortality and high prevalence of stunting and wasting. In these contexts, ready-to-use foods (RUF) can be an important component of treatment, but are expensive and difficult to provide at scale. To date, documentation of RUF used preventatively at population-level is rare.

In this context, MSF designed and implemented a cluster-randomized trial comparing a 3-month ration of Plumpy'nut® to a null control. The timing of the ration was during the hungry season, with the following primary hypothesis:

[7] "Started by the Government of India in 1975, the Integrated Child Development Scheme (ICDS) has been instrumental in improving the health and wellbeing of mothers and children under 6 by providing health and nutrition education, health services, supplementary food, and pre-school education". Source: http://motherchildnutrition.org/india/program-outline.html accessed 3 March, 2009.

[8] Reference: S Isanaka, N Nombela, A Djibo, et al. *Effect of Preventive Supplementation With Ready-to-Use Therapeutic Food on the Nutritional Status, Mortality, and Morbidity of Children Aged 6 to 60 Months in Niger: A Cluster Randomized Trial***.** JAMA 2009; 301(3):277-285.

- Village level supplementation with Plumpy'nut® in months prior to harvest would reduce incidence of wasting (global, severe) in children 6 to 60 months

Other outcomes measured included stunting, morbidity, and mortality. Analyses adjusted for age, sex, and nutritional status at baseline, as well as accounting for cluster design. MSF reported a 36% reduction in wasting relative to control group, and a 58% reduction in severe wasting; no significant effect on stunting or morbidity. They concluded that the findings support effectiveness of short-term supplementation with RUTF in preventing acute wasting.

In 2007, the RCT was interrupted and a follow-on study was designed with the following main objective:

- To examine the effect of two different preventive strategies in reducing severe wasting in children 6 to 36 months old in Maradi, Niger:
    - Active distribution of Plumpy'nut® for 4 mo during hungry season (dose 500 kcal/day)
    - Passive distribution of Plumpy'doz for 6 mo prior to and during hungry season (dose 250 kcal/day)

The intent was to identify if the 2nd approach – cheaper per child – could prevent wasting as well as the active distribution of the higher dose Plumpy'nut®. Preliminary analyses show no difference in impact on global wasting, and some suggestion that the first approach may have performed better than the second in preventing severe wasting. Analysis is not completed.

Discussion:
During a brief discussion, a question was raised as to whether for study #2 there could be an analysis per kcals delivered. MSF confirmed there is more analysis to do and also acknowledged that it is controversial whether or not giving an RUTF-size dose of energy (~500 kcal/d) to non-malnourished infants and young children is a good idea.

Presentation #9

"Effectiveness of a child-centered approach in primary health care: A randomized controlled trial in rural Burkina Faso"
Patrick Kolsteren
(attached: *Child centered approach in PHC – RCT in Burkina Faso 06 Feb 2009.pdf*)

Patrick Kolsteren presented plans for a randomized controlled trial to be undertaken in Houndé District, Burkina Faso. The intervention is systemic in nature and includes LNS only in treatment of severe acute malnutrition.

Background
Malnutrition is high in the district (34% stunting and 14% wasting among underfives) and early feeding practices are poor (lack of diversity; first food is usually unenriched millet porridge). Implementation of nutrition interventions is currently very poor, along three dimensions:

- *Communicational dimension*
  Health workers lack essential skills in patient-centred communication for nutrition counselling and child health promotion

- *Functional dimension*
  Nutrition dimension of the IMCI[9] program is often neglected by health workers; there is a need for a revised strategy for growth promotion as opposed to growth monitoring alone, with fewer but better contacts

- *Structural dimension*
  Need to reorganise treatment of malnutrition and improve case detection in communities

Specific examples of delivery failures in Houndé District were described (see attached presentation). An intervention has been designed to address constraints in all three dimensions.

Evaluation Design
Pair-matched, cluster-randomized controlled trial; six pairs of health facilities will be matched on the basis of accessibility, functioning criteria and population characteristics

Evaluation methods
The evaluation will based on the program theory. Intervention processes will be assessed in a sub sample of 4 health facilities using:

- structured observations of health facilities activities
- regular meeting in the health facilities
- interviews of caregiver and health workers
- cross-sectional survey

Outputs
- Health worker communication and management skills improved
- Health providers' knowledge of nutrition counselling and practices improved
- Caregiver knowledge of nutrition and complementary feeding practices improved
- Caregiver satisfaction with health care
- Caregiver compliance with recommended feeding practices

Outcomes
- Decreased child morbidity
- Improved child dietary intake
- Improved child nutritional status
- Improved child psychosocial development

Presentation #10

"Use of LNS in refugee populations"
Caroline Wilkinson, Office of the United Nations High Commissioner for Refugees (UNHCR)
(attached: *Use of LNS in refugee populations 06 Feb 2009.pdf*)

Caroline Wilkinson presented background on nutrition interventions in refugee populations, and described general plans for work commencing in 2009, when UNHCR plan to work on nutrition issues particularly in seven countries/refugee settings. In some settings people have been in camps for decades, and malnutrition may have an intergenerational aspect. However, on the other side there is some buffering from seasonal hunger. Rates of global acute malnutrition vary across settings; rates also vary but are generally quite high.

[9] IMCI=Integrated Management of Childhood Illness

UNHCR works in partnership with other agencies and organizations to:

- Prevent, control and reduce micronutrient deficiencies
- Improve nutritional status
- Enhance general well being of the children including growth and development

The intervention strategy under development for the seven countries/settings will be tailored to each specific context and include a range of products and interventions. Micronutrient powders, LNS, and fortified complementary foods will all be used alone or in combination with other interventions (counseling on infant and young child feeding, deworming, sanitation, insecticide treated bednets, others).

Monitoring and evaluation will include:

- Assessment of anemia in different age groups
- Anthropometric measurements
- Associations with child motor development indicators
- Investigation of causes and trends

Three questions were raised for general discussion:

- What duration of supplementation, especially in protracted refugee situations?
- Daily dosages by age group?
- How to avoid negative impacts on breastfeeding (displacement)?

These issues were not specifically resolved in discussion, with the exception that a concrete suggestion was made for younger infants. One could use Nutributter® for infants 6-11 mo, and Plumpy'doz for those 12 mo and older; Nutributter® is a 20 g dose and provides half the energy of Plumpy'doz. It was noted that cutting the dose of Plumpy'doz in half is not recommended for infants 6-11 mo because of their high needs for iron and some other nutrients.

Q: Will UNHCR assess micronutrient status for anything other than iron?
A: Not in these sites, but in a study in Kenya they will look at other micronutrients.

Future research needs

Following morning presentations on efficacy research and afternoon presentations on the use and effectiveness of LNS in programmatic settings, the group was asked to identify key questions for future research efforts. A variety of technical and operational issues were identified and for some, participants could share current efforts to address. Some issues also generated further discussion on experiences and current knowledge.

Questions and issues below are roughly grouped into: Biological questions; safety/quality control questions and issues; implementation/operational questions (although some topics spanned several of these).

Biological questions

1. Need for research to document relationships between nutrition and malaria, nutrition and tuberculosis, and to test approaches to integrate nutrition into malaria and TB interventions.

   LNS research should address malaria status/iron delivery.

   With respect to malaria: does MSF have data that can speak to this concern (risks of supplementing with iron in endemic areas), from past or on-going work? The study described in presentation #8 (Isanaka et al., 2009) did not find elevated prevalence of malaria but authors noted further research is warranted.

2. Need more information on the relationship of other exposures to stunting: smoke exposure; aflatoxin contamination.

3. Need more research on the impact of effects of anti-nutrients/plant-based ingredients on bioavailability of micronutrients for infants/young children.

   What should we be measuring to understand which LNS ingredients may interfere with absorption in a way that lessens potential to impact growth?

4. We may have limited impact on stunting with LNS alone. Can we explore what we can achieve with combined health/nutrition interventions? (this issue has both biological and operational dimensions).

Safety/quality control issues and questions
These issues were raised in context of the current US salmonella problem in peanut products. Kay asked Mamane Zeilani (Nutriset) to first respond on this issue. The discussion followed from there.

5. Mamane commented on risk of salmonella and on safety protocols. Microorganisms are very unlikely to multiply in fat-based spreads but if contamination occurs, the pathogens can survive. It is important to note that the infective dose for salmonella is very low. Nutriset procotols are very strict and include: testing on arrival of ingredients, by an external lab; frequent sampling and testing; systems are in place for both ingredients and products. There is a 12-year record with no positive tests.

6. The UN statement on Community-Based Management of Severe Acute Malnutrition (CMAM)[10] speaks to this; requires the same safety standards as for production of infant formula. UNICEF also works with producers and suppliers, including inspection of quality control systems and regimes; joint inspections. UNICEF, MSF, WFP, others are all involved in quality control guidance. New producers are mushrooming out. However if they don't follow and demonstrate meeting clear standards set by UNICEF, others, then these large purchasers will not buy.

[10] *Community-based management of severe acute malnutrition: A Joint Statement by the World Health Organization, the World Food Programme, the United Nations System Standing Committee on Nutrition and the United Nations Children's Fund*, 2007: http://www.who.int/child_adolescent_health/documents/pdfs/severe_acute_malnutrition_en.pdf, accessed 3 April 2009.

7. Smaller scale and community-based production: how strict can quality control procedures be?

   Valid experience in Malawi: With NGO support small scale production can meet standards.

   Project Peanut Butter experience in Malawi: at two levels, factory and small-scale – since 2002, no aflatoxin and no worrying microbiology results. Emphasized that monitoring / testing alone cannot assure safety, it's how you select ingredients.

   Experience in Burkina: Aflatoxin levels in groundnut in local markets were quite high. But with HACCP system and good supervision, small scale production, including hand sorting, met safety standards.

8. Other issues with regulation

   MSF: Problem is that there is no normative body. We (UNICEF/MSF) have become a normative body by default and we do not want the role or the risk. Small producers must self-regulate; for the big ones we need a system.

   WFP: Need policies at national level. Quality assurance must be proactive. We need a separate meeting on this issue.

Implementation/operational questions

9. Need to know more about linking use of LNS to other components of programs, especially educational/communications components

   Current efforts to address this/follow-on discussion:
   The Maternal Infant and Young Child Nutrition working group (MICYN, a sub-group of the Ten-year Strategy for the Reduction of Vitamin and Mineral Deficiencies) will issue a "Code for Dummies" to give guidance on how the International Code of Marketing of Breast-milk Substitutes speaks to packaging, marketing, and distribution of fortified products used during the period of complementary feeding. Specifically, what does the Code say about what should be conveyed on packaging for LNS, and also for micronutrient powders and other supplements and products? Aim is to inform private sector – they may not be "bad actors" but can still be ignorant of the issues; need to make this accessible.

   iLiNS is considering developing guidance on "minimum messages" for conveying 1. Via packaging and 2.When LNS is delivered in programmatic contexts. Examples of possible issues to cover in "minimum messages": safe and appropriate use of products; messages ensuring products "do no harm" to breastfeeding; products do not replace food/varied diet.

   We can look at and learn from how this issue has been addressed to date (e.g.social marketing research, process, and messages for Grandibien in Niger; social marketing/packaging for micronutrient powders). We need to partner with social marketing experts.

   Comment/Note of caution: this raises broader issue of communication; health workers may have 2 seconds with the mother and new products are just a new complication.

Communication to motivate mothers/others: we need to know what is compelling to them, this is not likely to be "your child will not be stunted". iLiNS will aim to answer this question via qualitative work and will gain insights for settings where those studies are undertaken.

10. We need to address the lack of information on women and on strategies to prevent micronutrient undernutrition. How can we reach adolescents, before early marriage, early pregnancy? How to reach them if they are not in school?

11. We need more clarity on when to choose which type of intervention. When are multiple micronutrient powders more appropriate than LNS? Competing/complementary technologies are causing a lot of confusion.

12. We need more research on implementation and on how to achieve better training and supervision in the public sector. Outreach to community may be the weak link in many efforts (gave example of Western Sahel – underutilization of available services).

Strategies to optimize collaboration and communication between researchers and stakeholders

The final discussion of the day focused on collaboration and communication, and a possible role for an LNS Research Network, to include those in the room but also other interested researchers and practitioners. Kay Dewey reviewed the objectives and operating principles introduced during the first presentation (see above).

Adopting objectives and operating principles

There were no objections to the objectives and operating principles as stated. The World Health Organization noted interest in remaining involved, but there will be new representation.

Clarification of objectives

Regarding the first objective ("To provide technical information regarding the use of LNS to improve nutrition of vulnerable populations") there was a request for clarification: will there be a forum/site where people can get replies to questions? Or will the information be "one-way"? Kay Dewey indicated that there are limited resources for responding to questions, so in general information will flow one way (e.g. via the iLiNS website, which will have limited interactivity).

Additional objectives

One additional objective was suggested and discussed: To what extent will research be harmonized? For example, will there be harmonization of protocols? Will there be peer review of protocols?

In regard to the latter (peer review): this could be quite onerous and it is not clear how it could work in practice. It was noted that *The Lancet* offers free review of protocols for clinical trials.

People shared positive experience with harmonization of the UNIMMAP trials. This ensured that information on the same outcomes was available across trials. In this instance raw data were also shared and people were careful, there were no problems that resulted from this. Importantly, this also allowed characterization of how populations in different sites differed at baseline.

The iLiNS Project will share protocols via the website; for us this follows our principle of open communication. Others can do this if they wish, but we recognize some may not like to do this because of the effort involved in developing protocols.

It was noted that sharing research protocols is fine, but that this does not ensure quality of implementation; quality will vary and this can lead to conflicting results.

In conclusion, there was consensus on the objectives and operating principles, with the addition that we will encourage sharing of protocols.

LNS Research Network Meeting

Rome, February 6, 2009

Agenda

Objective: To share information on current and planned research on lipid-based nutrient supplements (LNS) and issues related to utilization of LNS in programmatic settings

8:30 Welcome and introductions

9:00 Overview of upcoming LNS research activities funded by the Bill and Melinda Gates Foundation (Kay Dewey and Per Ashorn)

9:45 Discussion

10:15 Remarks by Executive Director of the World Food Programme, Josette Sheeran

10:30 Coffee break

10:50 Other current or planned research on efficacy of LNS

a) Patrick Kolsteren & Lieven Huybregts (Institute of Tropical Medicine, Belgium) "Efficacy of LNS supplementation during pregnancy: a randomised controlled trial in rural Burkina Faso"
b) Kay Dewey, presenting for Andrew Prentice (London School of Tropical Hygiene and Medicine) “Research with LNS in the Gambia”
c) Victor Owino (Valid Nutrition) “Valid Nutrition’s LNS research program”
d) Paluku Bahwere (Valid International) “Acceptability and effectiveness of chickpea sesame based ready to use therapeutic food (cs-rutf) in malnourished HIV positive adults: Results of a pilot programme”
e) Christian Mølgaard (Univ Copenhagen) “RCT with adult HIV patients in Jimma, Ethiopia”

12:15 Lunch

1:45 Research on use of LNS in programmatic settings

a) Camila Chaparro (FANTA-2) “LNS in programs: FANTA-2 research and overview of current programmatic uses of LNS” [30 min]
b) Géza Harczi (Epicentre, France) “Preventive supplementation with RUF: the MSF experience in Niger”
c) Patrick Kolsteren & Lieven Huybregts (Institute of Tropical Medicine, Belgium) "Effectiveness of a child-centered approach in primary health care: a randomized controlled trial in rural Burkina Faso”
d) Caroline Wilkinson (UNHCR) “Use of LNS in refugee populations”

3:30 Coffee break

3:50 Future research needs

4:30 Strategies to optimize collaboration and communication between researchers and stakeholders

5:00 Adjourn

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