Building a Specialized Medical Food Supply Chain

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Dr. Susan Shepherd- Coordinator, Nutrition Working Group
Context:

- Quality assurance scheme for drugs in place
- Increasing use of Medical Devices and Food volumes

⇒ Implementation of a similar system for Medical Devices and Specialised Medical Food

⇒ Monique Dory: Coordinator for Medical devices Quality Assurance, MSF International

⇒ Odile Caron: Coordinator for Specialised Medical Food quality Assurance, MSF International
Nutrition Activity MSF 2005-2008

N° children treated for acute malnutrition* in MSF projects:

- 2005   >60,000
- 2006   120,000
- 2007   190,000
- 2008   415,000

*Includes SAM+MAM+RUF target blanket <3 years

MSF Nutrition activity mapping as of May 2009
Standard distribution of Weight-for-Height

Indiv Treatment Programs

Treatment Programs

BLANKET FEEDING TARGETED TO AGE GROUP
NB: does not include all RUTF used by field projects, ie RUTF sourced from local purchase in ’05-’08 not accounted here. RUTF sourced from UNICEF not included.
GOAL: Diversification of quality assured sources of specialized medical foods

- Development of detailed product specifications
- Development of a suppliers validation procedure
- Definition of a food suppliers validation team
RUTF Procurement Chain

MSF Supply/Log/Holland purchase in Europe

MSF Country missions local purchase

UNICEF donations in country

MSF Capital Warehouse

Projects

Purchaser

Specification File
Technical Specifications for RUTF

Based on specifications for F-100 therapeutic milk

Technical annex

Ready-to-use therapeutic foods

Ready-to-use therapeutic foods (RUTF) are high-energy, fortified, ready-to-eat foods suitable for the treatment of children with severe acute malnutrition. These foods should be soft or crushable and should be easy for young children to eat without any preparation. At least half of the proteins contained in the foods should come from milk products.

Nutritional composition

<table>
<thead>
<tr>
<th>Nutritional component</th>
<th>RUTF (per 100 g)</th>
<th>F-100 (per 100 g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moisture content</td>
<td>5% maximum</td>
<td>5% maximum</td>
</tr>
<tr>
<td>Energy</td>
<td>520-550 Kcal/100 g</td>
<td>100,000 Kcal/100 g</td>
</tr>
<tr>
<td>Proteins</td>
<td>10%-13% total energy</td>
<td>10%-20% total energy</td>
</tr>
<tr>
<td>Lipids</td>
<td>45%-60% total energy</td>
<td>25%-40% total energy</td>
</tr>
<tr>
<td>Sodium</td>
<td>120 mg/100 g maximum</td>
<td>100 mg/100 g maximum</td>
</tr>
<tr>
<td>Potassium</td>
<td>1,109-1,400 mg/100 g</td>
<td>500 mg/100 g</td>
</tr>
<tr>
<td>Calcium</td>
<td>300-800 mg/100 g</td>
<td>200 mg/100 g</td>
</tr>
<tr>
<td>Phosphorus (excluding phytate)</td>
<td>300-600 mg/100 g</td>
<td>200 mg/100 g</td>
</tr>
<tr>
<td>Magnesium</td>
<td>80-144 mg/100 g</td>
<td>50-100 mg/100 g</td>
</tr>
<tr>
<td>Iron</td>
<td>10-14 mg/100 g</td>
<td>5-10 mg/100 g</td>
</tr>
<tr>
<td>Zinc</td>
<td>11-14 mg/100 g</td>
<td>5-10 mg/100 g</td>
</tr>
<tr>
<td>Copper</td>
<td>1.4-1.8 mg/100 g</td>
<td>0.5-1 mg/100 g</td>
</tr>
<tr>
<td>Selenium</td>
<td>20-40 µg</td>
<td>10-20 µg</td>
</tr>
<tr>
<td>Iodine</td>
<td>70-146 µg/100 g</td>
<td>50-100 µg/100 g</td>
</tr>
<tr>
<td>Vitamin A</td>
<td>0.6-1.1 mg/100 g</td>
<td>0.2-0.4 mg/100 g</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>15-20 µg/100 g</td>
<td>0.5-1 µg/100 g</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>10-15 mg/100 g minimum</td>
<td>5 mg/100 g minimum</td>
</tr>
<tr>
<td>Vitamin K</td>
<td>15-30 µg/100 g</td>
<td>5-10 µg/100 g</td>
</tr>
<tr>
<td>Vitamin B1</td>
<td>0.5 mg/100 g minimum</td>
<td>0.2 mg/100 g minimum</td>
</tr>
<tr>
<td>Vitamin B2</td>
<td>1.6 mg/100 g minimum</td>
<td>1 mg/100 g minimum</td>
</tr>
<tr>
<td>Vitamin B6</td>
<td>6 mg/100 g minimum</td>
<td>3 mg/100 g minimum</td>
</tr>
<tr>
<td>Vitamin B12</td>
<td>1.6 µg/100 g minimum</td>
<td>0.5 µg/100 g minimum</td>
</tr>
<tr>
<td>Follic acid</td>
<td>200 µg/100 g</td>
<td>100 µg/100 g</td>
</tr>
<tr>
<td>Niacin</td>
<td>5 mg/100 g minimum</td>
<td>1 mg/100 g minimum</td>
</tr>
<tr>
<td>Fatty acids</td>
<td>3% of total energy</td>
<td>0.5% of total energy</td>
</tr>
<tr>
<td>n-6 fatty acids</td>
<td>2%-3% of total energy</td>
<td>0.5%-1% of total energy</td>
</tr>
</tbody>
</table>


The added minerals should be water-soluble and should not form insoluble components when mixed together. The food should have a mineral composition that will not alter the acid-base metabolism of children with severe acute malnutrition. In particular, it should have a moderate positive non-metabolizable base sufficient to eliminate the risk of metabolic acidosis. The non-metabolizable base can be approximated by the formula: estimated absorbed minerals (sodium + potassium + calcium + magnesium) - (phosphorus + chloride). The mineral mix recommended for F100 by WHO is an example of a mineral mix with a suitable positive non-metabolizable base.

The product should be free from objectionable matter. It must not contain any substance originating from microorganisms or any other poisonous or deleterious substances, including antinutritional factors, heavy metals or pesticides in amounts that may represent a hazard to health.

Maximum toxin levels

<table>
<thead>
<tr>
<th>Toxin</th>
<th>RUTF (per 100 g)</th>
<th>F-100 (per 100 g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aflatoxin</td>
<td>0 µg maximum</td>
<td>5 µg maximum</td>
</tr>
<tr>
<td>Microorganisms content</td>
<td>100,000 µg maximum</td>
<td>100,000 µg maximum</td>
</tr>
<tr>
<td>Coliform test</td>
<td>negative in 1 g</td>
<td>negative in 1 g</td>
</tr>
<tr>
<td>Clostridium perfringens</td>
<td>negative in 1 g</td>
<td>negative in 1 g</td>
</tr>
<tr>
<td>Yeast</td>
<td>negative in 1 g</td>
<td>negative in 1 g</td>
</tr>
<tr>
<td>Molds</td>
<td>negative in 1 g</td>
<td>negative in 1 g</td>
</tr>
<tr>
<td>Pathogenic Staphylococci</td>
<td>negative in 125 g</td>
<td>negative in 125 g</td>
</tr>
<tr>
<td>Salmonella</td>
<td>negative in 1 g</td>
<td>negative in 1 g</td>
</tr>
<tr>
<td>Listeria</td>
<td>negative in 15 g</td>
<td>negative in 15 g</td>
</tr>
</tbody>
</table>

Note: Although RUTF is rich in F100, the mixture off F200 can be found in Management Booth Information Manual for Physicians and other health workers. World Health Organization. Geneva, 2000 (available at <http://www.who.int/information-manual-management-nutrition-eng.pdf>).

Elements of Specification File

- GMP
- Primary material specs
- Additives, partial
- Product specifications, incomplete
- Safety
- Packaging and labeling
- Stability studies
- Acceptability and Efficacy trials
- Certificate of Analysis
Where to set the specification?

Crude fibre: used 5 g/100 g maximum:
- CAC/GL 08-1991

Phytate: zinc molar ratio. No spec


Where to set the specification?
- Current spec based on tolerance of 20 ppb in peanuts
- High/medium/low level toxicity

Postweaning exposure to aflatoxin results in impaired child growth: a longitudinal study in Benin, West Africa.


How best to monitor aflatoxin levels?
- Qualitative testing – immunochromatographic rapid tests
- Quantitative testing - HPLC
### Certificate of Analysis/Release

#### Reference values

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moisture content</td>
<td>&lt;2.5%</td>
</tr>
<tr>
<td>Energy value</td>
<td>520-550 kcal/100 g product</td>
</tr>
<tr>
<td>Protein content</td>
<td>10-12% total energy</td>
</tr>
<tr>
<td></td>
<td>13-16% by weight</td>
</tr>
<tr>
<td>Fat content</td>
<td>45-60% total energy</td>
</tr>
<tr>
<td></td>
<td>33-36% by weight</td>
</tr>
<tr>
<td>Carbohydrate content, by calculation</td>
<td>43-48% by weight</td>
</tr>
<tr>
<td>Mineral content</td>
<td>3-4% by weight</td>
</tr>
<tr>
<td>Tracer element</td>
<td></td>
</tr>
<tr>
<td>potassium</td>
<td>1100-1400 mg/100 g</td>
</tr>
<tr>
<td>vitamin C</td>
<td>&gt;or = to 50 mg/100 g</td>
</tr>
</tbody>
</table>

#### Microbiologic analysis at 30 degrees

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total flora of aerobic mesophilic bacteria</td>
<td>&lt;10,000/g product</td>
</tr>
<tr>
<td>Coliform test</td>
<td>negative in 1 g product</td>
</tr>
<tr>
<td>Clostridium perfringens</td>
<td>negative in 1 g product</td>
</tr>
<tr>
<td>Yeast</td>
<td>maximum 10 in 1 g product</td>
</tr>
<tr>
<td>Mould</td>
<td>maximum 50 in 1 g product</td>
</tr>
<tr>
<td>Pathogenic staphylococci</td>
<td>negative in 1 g product</td>
</tr>
<tr>
<td>Salmonella</td>
<td>negative in 25 g product</td>
</tr>
<tr>
<td>Listeria</td>
<td>negative in 25 g product</td>
</tr>
<tr>
<td>Total aflatoxins</td>
<td>5 ppb maximum</td>
</tr>
</tbody>
</table>
Evolving Food safety standards:
- aflatoxin control (other fungal pathogens/toxins?)
- Emerging food-borne pathogens, ie Cronobacter sakazakii
- Other issues associated with new recipes (soy isolate)

Standards for efficacy trials for new recipes
- Weight gain only current standard
- Need to assess accrual of lean-tissue

Stability testing – accelerated?

Acceptability/Palatability testing
GOAL: Diversification of quality assured sources of specialized medical foods

- Development of detailed product specifications
- Definition of a food suppliers validation team
- Development of a suppliers validation procedure
- Manufacturer pre-selection
- Manufacturer GMPs audit
- Product approval
- Final approval
- Contract agreement (orders)
Food suppliers validation procedure at MSF

Interested producer

Interesting producer?

⇒ Potential interest for MSF programs?
Interesting producer?

Potential interest for MSF programs?

Criteria:

- Location (strategic interest for MSF)
- Nutritional products meet with MSF specifications
- Capacity to supply in due time
- Competitive price (estimate)

Questionnaire (GMP)

⇒ Manufacturer Pre-selected (or not)
Food suppliers validation procedure at MSF

SCHEME PROPOSAL:

- Manufacturer pre-selection
- Manufacturer GMPs audit
- Product approval
- Final approval
- Contract agreement (orders)
Audit of Manufacturer Pre-selected

- Covering hygiene concerns, quality management, traceability systems, staffs training, recording systems, validation of control measures, level of control verification, monitoring of control measures, premises & equipment

- References / standards (same as Unicef)
  - Codex alimentarius
    - The rating of the findings (non conformities)
    - The corrective actions plan proposed

⇒ **Manufacturer passed GMPs audit**
Audit of Manufacturer Pre-selected

✓ Permission to share the audit reports, corrective action plans between Unicef and MSF (same standards) requested from the manufacturer

✓ BUT MSF makes its OWN final decision

MSF is NOT a normative organisation and we don’t want to be seen as one.
SCHEME PROPOSAL:

- Manufacturer pre-selection
- Manufacturer GMPs audit
- **Product - Manufacturer approval**
- Final approval
- Contract agreement (orders)
- Complete batch analysis (by MSF):

- Moisture content
- Energy value
- Protein content
- PDCAAS
- Fat content (Omega 3 & 6 fatty acids)
- Carbohydrate content
- Phytate level
- Antitrypsin level

- Minerals (sodium, potassium, calcium, zinc)
- Vitamins (vit. A, D, B6, C)
- Microbiology (total aerobic mesophilic flora, coliform test, clostridium perfringens, yeast, mould, pathogenic staphylococci, salmonella, listeria)
- Total aflatoxins

⇒ Product approved (or not)
SCHEME PROPOSAL:

- Manufacturer pre-selection
- Manufacturer GMPs audit
- Product approval
- Final approval
- Contract agreement (orders)
Manufacturer GMPs audit

+ Product approval

+ 1st order feed back from the program

= Final approval
SCHEME PROPOSAL:

- Manufacturer pre-selection
- Manufacturer GMPs audit
- Product approval
- Final approval
- Contract agreement (orders)
Contract agreement (orders) with Purchasers (separated from Quality Assurance)

- Directly by the programs

- Via the supply centres
Criteria for Supplier Selection

- Product meets MSF’s specifications
- Produced within codex, ISO... standards
- Pricing
- Manufacturer strategically located
- Production capacity/reactivity
- ...

Thank You