PN-ABA-036
ISN 69776

PRITECH

Technologies for Primary Health Care

Management Sciences for Health
1925 North Lynn Street
Suite 400
Arlington, Virginia 22209

PA-ABH-036
ISN 69774

PHASE I REPORT

LIQUID ORAL REHYDRATION SOLUTION (ORS)

PACKAGED ASEPTICALLY IN TETRA PAKS

IN PAKISTAN

A Report Prepared By PRITECH Consultants:
NANCY LAIBLE
ROLF CAMPBELL

During The Period:
MAY 1990

TECHNOLOGIES FOR PRIMARY HEALTH CARE (PRITECH) PROJECT
Supported By The:
U.S. Agency For International Development
CONTRACT NO: AID/DPE-5969-Z-00-7064-00
PROJECT NO: 936-5969

AUTHORIZATION:
AID/S&T/HEA: 12/10/90
ASSGN. NO: SUP 091-PA

TABLE OF CONTENTS

Page

Background.....1

Manufacturing Costs.....1

Distribution.....2

Retail Price.....2

Current Liquid ORS Technology in Pakistan.....4

Machinery.....6

Packaging Material.....7

Operation/Facility Expertise.....8

Chemical Analysis of Liquid ORS.....9

Material Structure Specifications.....13

Addendum

LIQUID ORS IN TETRA PAKS

PHASE I

Background on Liquid ORS Packaging in Pakistan

Liquid ORS manufacturing in Pakistan is feasible on existing Tetra Pak systems. This will be technically proven in Phase II. There are, however, several critical factors influencing what must be the ultimate objective of any initiative involving ORS: effectively delivering ORS into the hands of all people who need it (*). These factors are:

- Manufacturing Costs (packaging material costs and profit motivation to producers)
- Distribution
- Retail Price

While the scope of the immediate project focuses on establishing the technical feasibility of packaging liquid ORS on Tetra Pak machines, ultimate commercialization and use will hinge on these, at times, conflicting factors which I will briefly address.

Manufacturing Costs: Fixed costs reflecting facilities, capital investment in equipment and full time labor are expected to be absorbed by more extensive use of excess production capacity for liquid ORS, presumably during the ebb of dry season milk production. On the other hand, packaging material used for the Tetra Pak is expensive.

(*) Patterns of use, cultural influences, medical perspectives and so on have been extensively researched and reported elsewhere.

As a proportion of product cost for milk it is as high as 40%, for example. This imbalance could similarly make liquid ORS a relatively expensive product to produce. A single source of supply exists in Pakistan for Tetra Pak paper foil laminate so competitive bidding does not exist. Compounding this, import tariffs on foil can increase its cost a reported 120%. (Import tariffs on finished material from outside Pakistan are prohibitively high.) Tetra Pak Pakistan maintains that the material cost is competitive using international standards. Even so, material cost is a chronic source of complaint from some manufacturers and this might be expected to inhibit commercialization initiatives.

Distribution: Assuming an affordable product, a system of distribution must exist that provides outlets for liquid ORS. The customer base currently supporting the Tetra Pak milk business is not necessarily made up of the customers most in need of liquid ORS in a Tetra Pak. Researching, defining, and developing a distribution network that makes this form of ORS product available is an essential long term strategy.

Retail Price: An assumption exists that the profit motive will be the reason for manufacturers to produce liquid ORS in Tetra Pak once technical feasibility is confirmed. In fact, Colonel (Retd.) M. Akram Kahn, National Project Manager for the Control of Diarrhoeal diseases at the National Institute of Health forcefully emphasized his expectation that free market forces be the basis for an emerging liquid ORS business.

There is opportunity for prospective manufacturers to benefit from government ORS advertising funding and logo use. Still, manufacturing costs, and distribution that accesses the target customer must be paid for by someone. Milk in Tetra Paks is referred to as "rich man's milk" by some Pakistanis. The question of a needed, but also affordable product must be addressed if liquid ORS is expected to become a freestanding business opportunity.

Beyond these three essential business factors, a very extensive group of involved organizations will add complexity to coordinating a successful commercialization of Liquid ORS. These are:

Group	Role
Ministry of Health	Approval
National Institute of Health	Supportive
USAID	Supportive & Funding
PRITECH	Supportive & Funding
WHO	Standards, Advising
Tetra Pak	Consulting
Dairies	Implementation, Commercialization Interest
Pharmaceutical Corporation	New Outside Competition
Land O'Lakes	Facilitating & Implementation

Liquid ORS in Tetra Paks has no status as an approved regulated product at this time. Regulation may involve packaging form and sizes, product formula, and product definition as a pharmaceutical which in turn will dictate where it can be sold.

Further complexity will be added if an international pharmaceutical corporation follows through on their expressed interest in liquid ORS manufacturing in Pakistan.

Current Liquid ORS Technology in Pakistan

No aseptically packaged liquid ORS product is currently commercially available in Pakistan. The three dairies visited who have the Tetra Pak system are technically capable of packaging liquid ORS.

From a technical capability standpoint the Tetra Pak TBA10 machine can process and pack liquid ORS. The laminate specification currently in use (attached) is acceptable for liquid ORS containment. The dairies have each demonstrated excellent technical competence through the present processing and packaging of buffalo milk. Two Pakistan dairies have been identified where past attempts to package liquid ORS in Tetra Paks have been made.

Chaudhry Dairies Ltd. packed a 1 litre test run in 1989. Retained samples on site appear intact today. Other samples from this run were discovered to leak after shipment which I did not personally witness. I am not aware of any post packaging analysis of product and packaging integrity in terms of shelf life, storage conditions or distribution abuse simulation.

Chaudhry has had past problems with packaging material quality that causes machine downtime and field "bloat" (failed milk packages) of Tetra Paks.

They do not presently perform incoming quality control on material, but do maintain a file of samples representing extreme quality deviations.

I will be working with Chaudhry to show them some test procedures and devices that will characterize incoming packaging material attributes. This will help them pinpoint the actual cause of packaging performance or machine problems.

Chaudhry would be a good choice for a working partner to demonstrate liquid ORS in a Tetra Pak feasibility and they are willing to participate.

Pakistan Dairies Ltd. (Green's) recently packed a (flavored) 250 ml Tetra Pak test run and retained unstressed samples appeared intact at this time. Records of conditions and past pack analysis were not made. No abuse stress was done or is planned. As stated, we are not aware of any commercially available liquid ORS in Pakistan. Pakistan Dairies Ltd. is another good willing working partner candidate.

A third dairy, Milkpak Ltd., has not attempted a liquid ORS trial, but has also expressed a commitment to performing one for this project. They would be interested in filling the Tetra Pak tetrahedron shaped package.

In all three cases the principal project focus will be experimenting with and documenting ORS processing conditions, packaging machine conditions, finished package integrity, and stability and quality of finished product.

Visits and interviews with these three dairies using Tetra Pak aseptic systems (Chaudhry, Milkpak, Pakistan Dairies) has revealed that a solid base of technology exists in Pakistan suitable for the packaging of liquid ORS. "Technology" refers specifically to:

1. Machinery
2. Packaging Material
3. Operator/Facility Expertise
4. Process Conditions, Formula, and Packaging Performance (to be determined and confirmed Phase II)

1. <u>Machinery</u>:

   All plants use a Tetra Pak model TBA10 machine (250, 500, and 1 litre sizes) this model differs from machines conventionally used in the U.S. and Europe, e.g., in that it produces a Tetra Pak with side seal seams, no ribbon of seal polymer is added on the machine, speeds are slightly reduced and operations are purportedly less complex. None of these should negatively influence the finished package integrity and in fact may actually produce a more rigid package.

There is nothing in this TBA10 machine's design that would prevent the packaging of liquid ORS. While Tetra Pak has not run ORS on this model of machinery, they have done some feasibility testing and liquid ORS manufacturing in some areas of the world on other models.

A meeting with Tetra Pak Pakistan was held with the result that they have offered any form of technical support we may need to execute a liquid ORS feasibility confirmation run in Pakistan.

2. Packaging Material:

The material specified (attached) and available through Tetra Pak is produced in Pakistan by Packages Ltd. There are no alternative structures or sources of supply to be considered for two reasons: First, no other converters other than Packages laminates such a structure and second, import tariffs on a completed film would be prohibitively high. No incoming quality control tests are done on this material by users. If line failures are attributed to web quality defects the user plant negotiates with Tetra Pak/Packages for credit or replacement of material. There is concern among some users regarding consistent film quality while others reported no problems. Tetra Pak reported that they regularly have film quality confirmed at their headquarters in Lund, Sweden, according to standardized tests applicable throughout the world.

Film quality is as essential to a successful liquid ORS product as it is to milk. There are currently milk package failures in the field usually evidenced by package "bloat" caused by gas producing micro organisms, but the causes can be from multiple sources and the frequency is not documented.

Based on the manifest success overall of the Tetra Pak milk package and an analysis of liquid ORS ingredients, it is believed that currently available specified film structures in Pakistan will successfully contain liquid ORS and preserve quality during storage. This will be proven during Phase II trials.

Should unforeseen compatibility problems be revealed through empirical tests, Tetra Pak shares the commitment to succeed with ORS and would, I believe, customize specifications as needed.

3. Operation/Facility Expertise:

Fortunately for this project we have arrived toward the end of a long learning curve during which plant personnel have gained experience, equipment has been debugged, and the productivity of these sophisticated Tetra Pak systems is assured.

Given clearly specified process operating conditions and product formula, any of the plants visited can dependably produce liquid ORS in Tetra Paks.

4. Process Conditions, Formula and Packaging Performance (Product Behavior and Vulnerabilities): These aspects of technology are the essence of the present project objective and thus to some extent are as yet unknowns. The existing knowledge base has been presented in this report.

Chemical Analysis of Liquid ORS

Objectives:

1. Prepare an ORS solution which is heat treated to model an aseptic process.
2. Determine effects of heat treatment on bacteria intentionally added to the ORS solution.
3. Determine the capability of the aseptic ORS solution to support bacterial growth after exposure to potentially contaminating conditions.

   a. Open to air for 24 hours.

   b. Supplemented with bacterial culture.

Methods:

I. Composition and Preparation of ORS Solution

For these studies the ORS-citrate formulation recommended by the WHO was chosen. The solution was made as follows:

	Grams/Liter
Sodium Chloride	3.5
Trisodium Citrate Dihydrate	2.9
Potassium Chloride	1.5
Glucose, Anhydrous	20.0

All ingredients were dissolved in sterile distilled water. The solution was colorless with a pH of 8.05.

II. Bench-scale Aseptic Processing of ORS

1. The prepared ORS was divided in half.
2. As a challenge to the method of aseptic processing, one portion was supplemented with Escherichia coli strain #431 at a population estimated to be 500,000 to 1,000,000 per ml. The second portion was unsupplemented.
3. Both portions were then subjected to a heat treatment at 200°F, (93°C) for 10 seconds by immersion in a water bath. Timing of the treatment was begun when the ORS reached the desired temperature.
4. Prior to and following the heat treatment, aliquots were removed from the ORS solutions for cultural analysis to detect surviving organisms.

Results:

Heated ORS	E. Coli Added	Bacteria Per Milliliter of ORS
No	No	68
No	Yes	780,000
Yes	No	<1
Yes	Yes	<1

In addition, heat treatment did not affect the color or appearance of the ORS solutions.

Conclusions:

Chemical Composition: The constituents of ORS are chemically inert and should be very stable in combination with each other. Because there are no proteins present, the prospect of Maillard reactions between protein amino groups and the carbonyl group on the glucose is avoided. In addition, choosing the ORS-citrate formulation eliminates the potential decomposition caused by interactions between glucose and sodium bicarbonate which can occur in the ORS-bicarbonate formulation, particularly under tropical heat and humidity conditions.

In addition, it is noted that the sodium chloride level is inadequate to inhibit growth of potential microbial contaminants, whereas the glucose provides an energy source for these organisms.

Microbiological Concerns: There are few microorganisms (<100 per ml) present in the freshly prepared ORS. The glucose component may allow growth of these contaminating bacteria if they are not inactivated.

Using aseptic process conditions above (140°C, 10 seconds), these organisms will be readily killed.

While it is believed that the chemical composition will yield a very stable product with a shelf life of one year, there remains the possibility for some product changes over time. These changes would be in appearance and/or flavor. The ideal unflavored ORS is a clear liquid with a bland sweet-salty taste. Changes that may occur are:

1. Color change to a clear light brown. This may be caused by thermal processing or storage at high temperatures when glucose isomerizes or polymerizes. Possible solution is to control process and storage temperatures or add a color to mask effect.

   Another possible cause of non-enzymatic browning may be the presence of organic residue from the kill of microbes during processing. This would leave protein to interact with the glucose aldehyde resulting in browning. A solution would be employing a .2 micron filter up line from thermal processing to remove organics.

2. Clouding or sedimentation. "Hard" water containing minerals such as iron, calcium and magnesium may form an insoluble precipitate under certain conditions or cloud the solution which would be a harmless aesthetic problem. If this were to occur demineralization through filtering or softening would correct it.

3. Acidification of the solution (<4.6) with citric or malic acid for example, may have some advantages for either preventing or masking the effects of long term storage. A lower pH would permit lower processing temperatures with less risk of glucose browning.

   Acidification used in conjunction with color and flavor addition would produce a very palatable product with reduced risk for microbial outgrowth in storage and after opening. Any browning would be masked. The physiological impact of acidified ORS has not yet been investigated for this report.

Next Steps:

1. The ORS solutions described above will be stored at room temperature and monitored weekly for visual changes in color and appearance.

2. A portion of the heated (no bacterial supplement) sample will be purposely opened and exposed to the room environment for a period of 24 hours. This sample will be monitored for bacterial contaminants by cultural analysis immediately and after a four week incubation at room temperature.

3. Heated ORS will also be intentionally inoculated with a bacterial culture at approximately 100,000 per ml and monitored for bacterial survival/growth after room temperature incubation for 24 hours and four weeks.

4. The heat treatment on ORS supplemented with *Escherichia coli* will be repeated using 180°F for 5 seconds.

Material Structure Specifications (Attached)

These are straight forward specifications, yet circumstances surrounding their selection are important to an understanding of a long term liquid ORS business.

The ORS solution described above is not reactive with the product contact polyethylene film under anticipated conditions of processing and use. The material shown is the same specification as that currently used for juice Tetra Pak packaging.

The structure at least meets and, I believe, exceeds barrier properties needed to provide shelf life for extended storage stresses. For this reason an informed prediction can be made that this specification will contain liquid ORS very acceptably, which is fortunate because there is only one manufacturer of Tetra Pak material in Pakistan and two basic material specifications for structures (one for milk and one for juices). The manufacturer "Packages" is 49% owned by Tetra Pak and 51% owned by a Pakistan business.

As alluded to above, there has been controversy between some dairy users and this single source supplier over pricing, quality, and performance. Price is allegedly too high to be profitable, film quality problems at times impinge on machine productivity, and packaging performance in distribution occasionally leads to product failure.

Tetra Pak maintains that material is fairly priced in context with material sold in other countries, that film quality must meet standards and tests actually conducted at Tetra Pak headquarters in Sweden and that productivity loss and product failure result more from a long learning curve at the dairies perfecting the operation of a complex Tetra Pak system. It is Tetra Pak's position that problems are diminishing and will continue to diminish for this reason.

The paper substrate used for the Tetra lamination is produced at this supplier with a requirement that a proportion of the base pulp be provided by recycled paper products (an admirable solid waste initiative). As a result, shorter fibers are incorporated into the paper which can influence stiffness, strength, and machinability.

Tetra Pak is adamant in standing behind the quality and consistency of this material and with no evidence to the contrary must be believed. They are an extremely credible and committed force in the world packaging community.

The structural success of a package from manufacture to market is minimally dependant on three additional key factors that directly influence the performance of a correct material specification selected for product protection and compatibility, distribution strength, and machining performance:

1. Compliance with the specification by the material supplier - a consistently correct, quality structure.

2. Machinery designed for specified process conditions and capable of forming the material into a package of good integrity at consistent levels of productivity.

3. Machine operators and maintenance personnel who are trained, and a vigilant program to use and care for the machinery as designed.

Failure or deviation in any of these four key areas puts packaging integrity at risk. For reasons explained above our packaging material specification is now a given, but one that is expected to function well. Factors 1, 2, and 3 are equally critical to the immediate objective and will be scrutinized and to the extent possible, documented during Phase II. I am confident that these key factors are being effectively controlled at all dairies visited.

Discontinuities or "pinholes" in the inner polyethylene laminate layer (E) are critical defects and will cause product/package failure.

The control and responsibility for laminate quality resides with the sole supplier.

Function of Tetra Pak Laminate Layers (See attached drawing)

a. Outside polyethylene surface: protection of paperboard from moisture, abrasion. Protection of printing ink. Machining properties of slip and flexibility.

b. Base paperboard: provides a carrier for barrier laminates, structure and strength, scoring and folding base to form a carton shape.

c. Polyethylene tie layer: bonds aluminum foil to paper base web.

d. Aluminum foil: gas, moisture and odor barrier, functions to facilitate induction heat sealing method used.

e. Ionomer: EAA or "surlyn" foil primer coat or layer prevents penetrant product molecules from reaching foil. Especially required for acidic fluids.

f. Polyethylene inside surface: protects aluminum foil from product and prevents flex cracking, adds flexibility to overall structure, functions to create a fusion heat seal when heated during induction sealing, serves as inert, safe product contact surface.

TETRA PAK LAMINATE SPECIFICATION - JUICE

Machine Model TBA 10	250 ML	500 ML	1000 ML
a. Polyethylene Outside Layer	12 +\- 2 MC	12 +\- 2 MC	12 +\- 2 MC
b. Paperboard	185 GSM +\- 15 GSM (.305 MM)	235 GSM +\- 15 GSM (.380 MM)	235 GSM +\- 15 GSM (.380 MM)
c. Laminating TIE Layer Polyethylene	25 +\- 2 MC	25 +\- 2 MC	25 +\- 2 MC
d. Foil	6.65 +\- .05	6.65 +\- .05	6.65 +\- .05
e. Ionomer Layer			
f. Polyethylene Inside Layer	45 +\- 2 MC	45 +\- 2 MC	45 +\- 2 MC
Width	289 +\- 1 MM	305 +\- 1 MM	473 +\- 1 MM

GSM = Grams/Square Meter
MC = Microns
MM = Millimeters
ML = Milliliters

CRITICAL PERFORMANCE (Product identity and conditions of use)

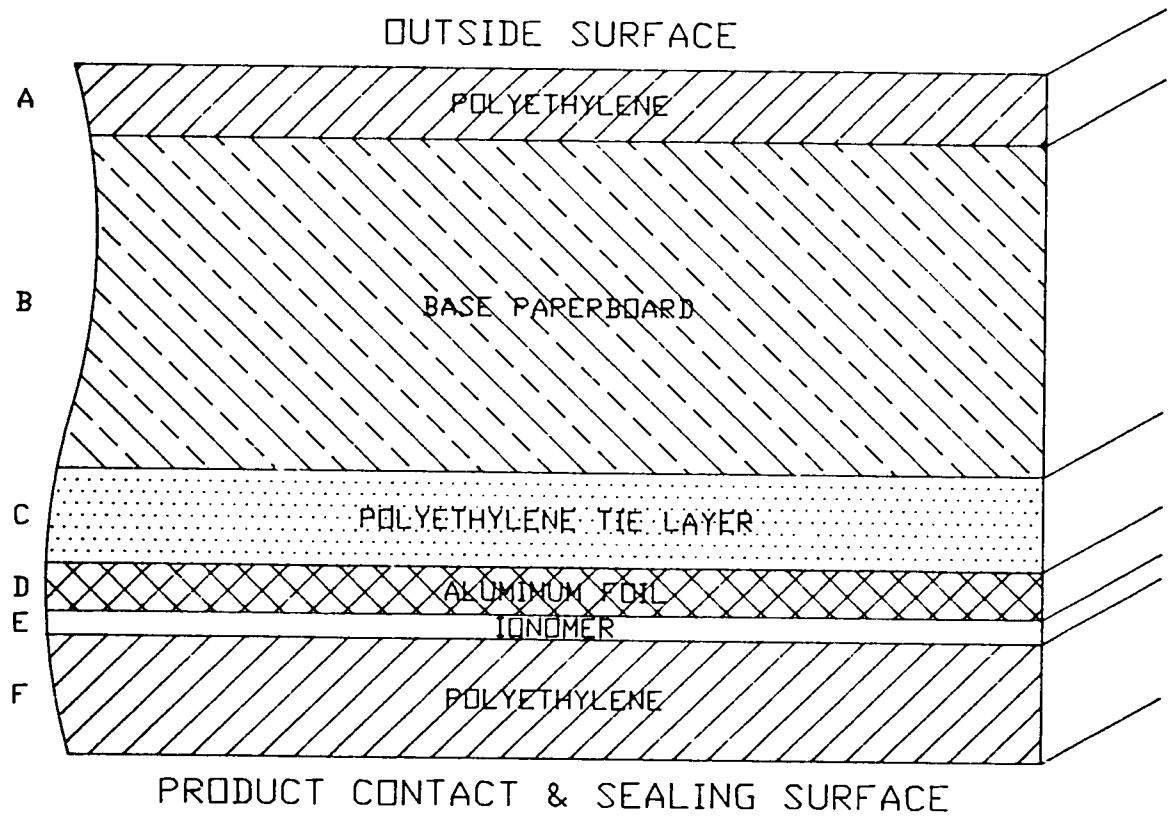
The above laminate structure is intended to contain a liquid Oral Rehydration Solution (ORS) for a period of six months at 40°C. The solution pH is 8, the solution formula is:

Percentage	ORS - citrate	Grams/litre
12.55	Sodium chloride	3.5
10.39	Trisodium citrate, dihydrate	2.9
5.38	Potassium chloride	1.5
71.68	Glucose, anhydrous	20.0
100.00	Total	27.9

The above solution will be heat treated for sterility, cooled and filled aseptically.

Acidification of this formula to <4.6 will also be compatible with this packaging material.

TETRA PAK LAMINATION LAYERS
FOR JUICE PACKAGING



AutoCAD DRAWING FILENAME	TPAK-2
DRAWING NUMBER	
LAND O' LAKES, INC.	
DRAWING TITLE	TETRA PAK LAMINATION LAYERS-JUICE
SCALE:	NONE
DATE:	5/30/90
DRAWN BY:	Frank K.
SHEET:	

15