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UNITED NATIONS
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CONSULTANCY SERVICES FOR THE PROMOTION OF HIGH PRIORITY INDUSTRIES IN THE ARMENIAN SOVIET SOCIALIST REPUBLIC, USSR

TF/GLO/89/019

Technical report: Establishment of a production plant for disposable syringes *

Prepared by
the United Nations Industrial Development Organization

Based on the work of A. Bauer, UNIDO consultant

Backstopping Officer: M. Sanchez, Chemical Industries Branch

* This document has not been edited.

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1. **PLACE OF MEETINGS**

a) Institute of Armbiotechnology
Gyurdjan Street 14
City of YEREWAN

b) Existing Factory Building
Assigned for the Production of
Medical Articles
City of ABOVIAN

2. **PARTICIPANTS OF MEETINGS**

Dr. Edward M. HAKOPIAN	General Director of Corporation »Armbiotechnologia«
Dr. Vasil L. BARSEGIAN	Chief Engineer of »Armbiotechnologia«
Eng. Nikolay MEZENTSEV	Chief Engineer of »GIPROMED«, Kiev
Dr. Levon NEZSESIAN	Director of the Existing Factory (Building)
Mr. Suren KALSHIAN	Head of the Dept. for Foreign Affairs
Mrs. Ludmilla MAKAROVA	Engineer of the F.A. Dept., Interpreter
Mr. Alfred BAUER	UNIDO Consultant

3. BACKGROUND INFORMATION

Soviet Armenia has the geographical location in the southern part of the USSR adjacent to Turkey and Iran, covering an area of about 30,000 square km. The population in Armenia is 3.5 million and is expected to climb up to 4 million by the year 2000.

About 70 % of the population live in urban areas (Yerewan 1.2 million) and only 30 % of the population live in the country-side.

Following the disastrous earthquake on December 7, 1988, the idea was born to set up a plant for disposable medical articles - mainly disposable syringes and hypodermic needles.

Foreign donor institutions promised to financillay support this project. The Government of the Soviet Republic of Armenia consequently entrusted the Corporation »ARMBIOTECHNOLOGIA« to carry out the project implementation work.

The Corporation »ARMBIOTECHNOLOGIA« consists of the »BIOTECHNICAL RESEARCH INSTITUTE FOR AMINO ACIDS« and three Biochemical manufacturing plants. A fourth manufacturing plant project for the manufacturing of »clean acid« was stopped approximately 18 months ago. Parts of the already existing buildings are proposed to be used for the manufacturing of disposable medical articles. The factory site at the City of ABOVIAN is approximately 10-15 km north of Yerewan. The plant will later be called »FACTORY OF MEDICAL ARTICLES« and will be a member of the Corporation »ARMBIOTECHNOLOGIA«. All products of this plant will be delivered to the agency of the Ministry of Health, a company called »MEDTECHNICA«. This governmental institution is responsible for the country-wide distribution of the all kinds of medical articles according to instruction of the Ministry of Health.

The Corporation »ARMBIOTECHNOLOGIA« started the research work for possible and competent suppliers approximately 6 months ago.

Agency agreements with American institutions and consulting companies have been signed to find the most suitable supplier. A contract agreement with the West German company »PHARMAPLAN« for the supply of machinery and equipment has been elaborated and is ready for signature. It is the opinion of the Corporation »ARMBIOTECHNOLOGIA« that this West German company is the best partner to carry out the proposed project.

4. FEATURES OF THE PROJECT

To ensure a smooth and trouble-free realization of the complete project and due to the tight financial situation, the Armenian authorities proposed the following project implementation phases:

PHASE I: Implementation of a disposable syringe manufacturing plant, start-up and commercial production of the same within the shortest possible period.

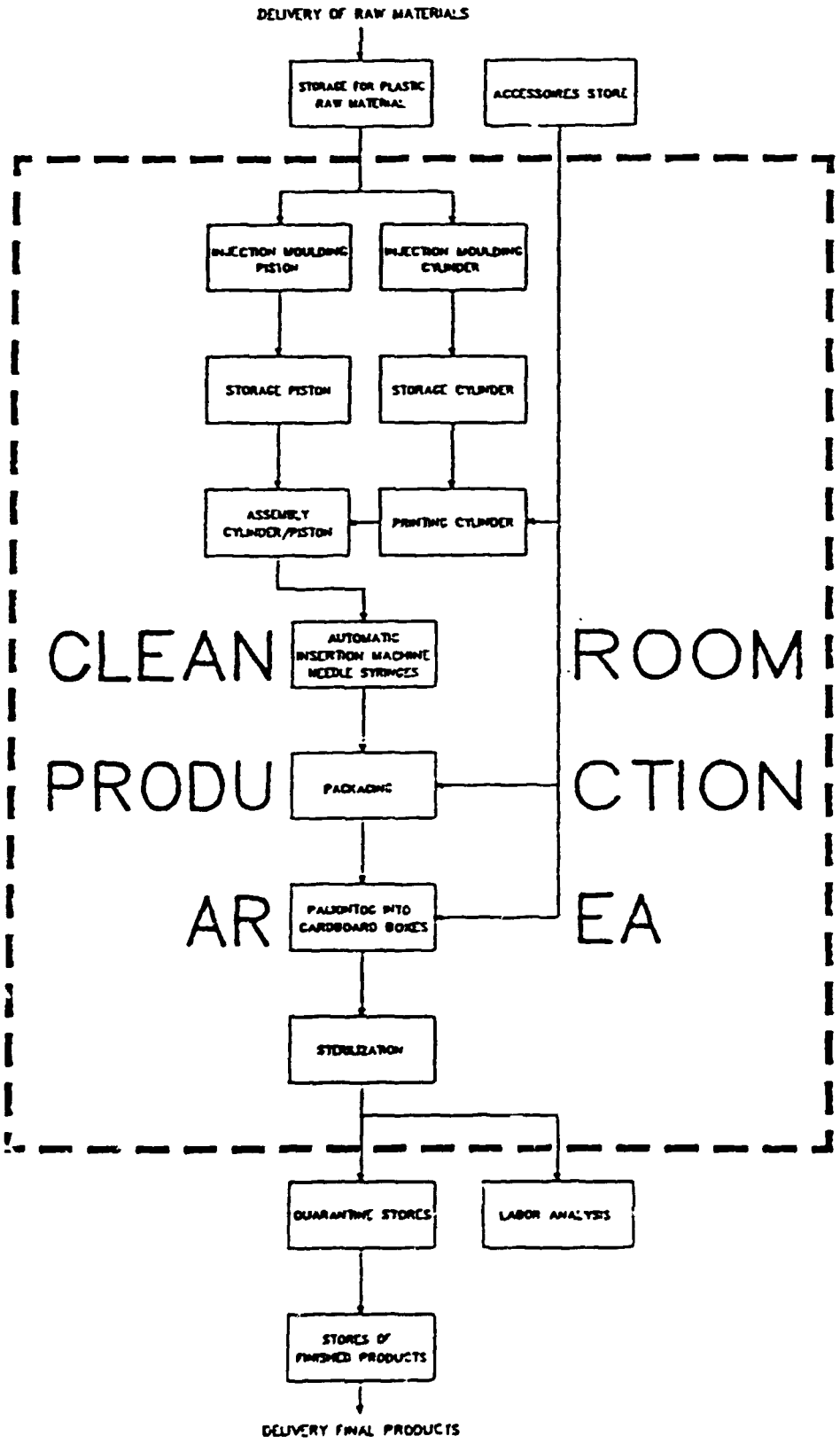
PHASE II: Implementation of hypodermic needles manufacturing plant, start-up and commercial production of the same as soon as the financial situation allows.

PHASE III: Implementation of a manufacturing plant for disposable medical systems approximately 6 to 12 months after successful start-up and operation of Phase I and II.

All three project phases should be implemented separately and independently, only the capacity of the sterilizing unit should be sufficient for all medical articles produced and implemented with the first phase.

UNIDO activities in the field were concerned with the discussions for the installation of disposable syringes production (Phase I).
General analysis for future programmes with the Armenian authorities were conducted. It is recommendable to continue with the establishement programme in the future.

5. DISPOSABLE SYRINGE PRODUCTION FLOW SHEET



6. GENERAL

Disposable syringes are used with as well as without a silicone rubber ring between the piston and the cylinder.

Recently, however, the production of two-part disposable thermoplastic syringes - i.e. without a sealing ring - consisting of the cylinder and the piston has become generally accepted, because a chemical influence of the drugs by the sealing material is avoided, hygienically flawless production is guaranteed, and production costs can additionally be lowered when this design is used. By using disposable one-way syringes, the risk of contamination during filling and decanting as well as during the cleaning and storage of conventional syringes is avoided.

REQUIREMENTS OF DISPOSABLE ARTICELS

The average consumption of disposable syringes and hypodermic needles in Europe are as follows:

7 - 8 pcs. disposable syringes/annum/inhabitant
and
9 - 10 pcs. hypodermic needles/annum/inhabitant

for other countries you may calculate with:

5 - 6 pcs. disposable syringes/annum/inhabitant
7 - 8 pcs. hypodermic needles/annum/inhabitant

DISTRIBUTION OF THE VARIOUS SYRINGE SIZES BY PERCENT

The syringe sizes mainly used are 2 ml, 5 ml, 10 ml, and 20 ml. For special purposes, such as tuberculin and insulin injections, syringes with 1 ml and/or 2 ml with a special graduation are manufactured.

Many years of experience have shown the following percentage distribution for the use of disposable syringes.

	2 ml	5 ml	10 ml	20 ml
Austria	42 %	28 %	2 %	8 %
FRG	49 %	24 %	20 %	7 %
Sweden	67 %	18 %	7 %	8 %

DESIGN

The disposable plastic syringes for medical purposes in Europe are made according to DIN 13098.

The syringes can be manufactured either with a Rekord or Luer cone. The required moulds can be designed in such a way that syringes can be manufactured with a Rekord as well as a Luer cone. The cone insert can be exchanged in the mould.

The needle cone at the 2 ml syringes is centric, alternatively centric or eccentric at the 5 ml syringes, and at all the other syringes, the needle cone is eccentrically located.

RAW MATERIAL

Both components can be made of PP (Polypropylene). In most cases, however, the piston of the syringe is made of HDPE (high-density Polyethylene), more rarely of PS (Polystyrol).

Owing to the required higher slideability of the surface, the PP for the cylinder must meet special qualifications:

Homopolymeric Polypropylene, especially modified for low surface friction (by means of an internal lubricant which diffuses to the surface after conditioning). The internal lubricant can be added to the Polypropylene by means of a Masterbatch - sliding agent concentration - (3 - 5 %). The material must correspond to DIN 13 098 (the German specification for disposable syringes).

MACHINES REQUIRED FOR THE PRODUCTION OF SYRINGES

A production line consists of:

- injection moulding machine for the manufacture of the cylinder
- injection moulding machine for the manufacture of the piston
- automatic printing machine for printing the graduation
- automatic assembly machine for assembling the cylinder and the piston
- packaging machine for individual packaging
- sterilizer for sterilizing with ethylene oxide or gamma radiation
- various conveying facilities for raw material, compressed air system, cooling water preparation plant, internal transport system, and additional facilities and equipment.

7. PRODUCTION PROCESS

The production of the syringes should, if possible, be effected in 3-shift operation - this would lead to one-hundred-percent utilization of the machines.

It is recommended that a production line be acquired for each syringe size, so that no mould-change-overs are necessary on the machines.
The sequence of production should be designed so that the operating personnel touches neither the individual parts nor the finished syringe. Only the packed syringe that comes in the sales carton would come into contact with the personnel.

The raw material polypropylene and polyethylene for the cylinder and the piston are continuously fed to the injection-moulding machines by means of a conveyer.
The individual parts manufactured on the injection-moulding machines (pistons, cylinders) are intermediately stored for at least 12 hours in the plastic collecting container after the automatic separation from the sprue. The cylinders stored in the collecting container are now conducted to the printing machine.

The printed cylinders subsequently reach the assembly machine via a conveyor or again via a collecting container. The pistons are brought to the assembly machine from intermediate storage via the plastic collecting containes in the same way.
The cylinders and the pistons are put together on the assembly machine.

The assembled syringes are again subsequently brought to the inserting device of the packaging machine by means of a conveyor. Depending on the syringe size, a certain number of syringes at once are packed in a so-called blister package. The individually packed syringes are packed in sales cartons depending on the packaging unit.

Placement in the sales cartons can be performed manually or, for larger-scale production, fully automatically.

Further packaging in export-cartons (approx. 10 sales cartons) is performed manually, or fully automatically for larger-scale production.

The export-cartons are provided with a sterilization control strip and go to the sterilization department.

After sterilization, samples are taken from each sterilization batch and subjected to a bacteriological and biological examination. After passing this examination, the syringes are cleared for dispatch.

CONDITION OF THE PRODUCTION AREA

The workrooms in which the disposable syringes are manufactures should be provided with wall covering that can be easily and safely cleaned and is resistant against acids and alkaline solutions. According to GMP or FDA standard the concept of the room should correspond to a Class 10,000 as per US Federal Standard 209d.

All floors must be jointless and easy and safe to clean.

Doors and windows must have tight joints.

The rooms proper should have an overpressure of 10 - 15 mm water column compared with their environment.

For the air conditioning of the rooms, 12 - 15 circulations of the air per hour should be provided.

The working temperature should be 20 - 22° C at a relative humidity of 50 percent. For purifying the air, one ultraviolet lamp is required for approx. 20 - 25 m2. This particularly also applies to the laboratory rooms, which should be directly irradiated with UV light during non-working hours.

Necessary equipment like temperature and humitiy writers, particle counter, air samplers, etc. should be available.

After the end of the working shift or on holidays, the rooms should be cleaned, possibly with a disinfectant solution, then fumigated with thriethyleneglycol ($HO\text{-}CH_2\text{-}CH_2\text{-}O\text{-}CH_2\text{-}CH_2\text{-}O\text{-}CH_2\text{-}CH_2\text{-}OH$).

Fumigation should be effected as follows:

A faience dish provided with the appropriate quantity of thriethyleneglycol is placed on a tripod and the triethyleneglycol evaporated with a spirit burner.

8. REQUIREMENT OF DISPOSABLE MEDICAL ARTICLES IN ARMENIA

Out of a wide spectrum of disposable medical articles the representatives of the Corporation »ARMBIOTECHNOLOGIA« and the UNIDO Consultant agreed that the most essential items are the following:

a) Disposable syringes

b) Hypodermic needles

c) Disposable medical systems

- blood transfusion sets
- blood taking sets
- catheters

The following quantities of disposable medical articles are necessary in Armenia according to local Ministry of Health:

a) approx. 60 million disposable syringes per annum

1 ml	15.0 %	9 million/annum
2 ml	30.0 %	18 million/annum
5 ml	30.0 %	18 million/annum
10 ml	15.0 %	9 million/annum
20 ml	10.0 %	6 million/annum

b) approx. 75 million hypodermic needles per annum

0,8 mm x 38 mm	80.0 %	60 million/annum
0,6 mm x 26 mm	7.5 %	13 million/annum
0,5 mm x 16 mm	2.5 %	2 million/annum

c) approx. 1.1 million disposable medical systems

Blood transfusion sets	500,000 sets/annum
Blood taking sets	500,000 sets/annum
Intravenous catheters	50,000 sets/annum
Subelavian catheters	50,000 sets/annum

9. PRODUCT CHARACTERISTICS

Based on the research activities of the Corporation and the recommendations of the UNIDO Consultant, it was agreed that the disposable syringes proposed for production have to show the following characteristics:

- disposable syringes made of thermoplastic materials like polypropylene and polyethylene
- 2 part syringe system (consisting of plunger and cylinder) for 2 ml, 5 ml, 10 ml and 20 ml
- 3 part syringe system (consisting of plunger, rubber sealing and cylinder) for 1 ml using silicone rubber
- hot printing of the syringe graduation
- 2 different graduations (children, diabetes) for the syringe sizes 1 ml and 2 ml
- Luer cone for the syringe adaptor and the needle hub
- centrically located adaptor cones for 1 ml and 2 ml syringes and excentrically located ones for 5 ml, 10 ml and 20 ml
- EO-gas sterilization system for all medical articles produced
- single, peelable packing units for each syringe, needle respectively medical system set

10. RAW MATERIALS

10.1 Indigenous raw material

According to the Corporation and the opinion of the UNIDO Consultant the following raw material used for the proposed production of disposable syringes should be obtained locally (USSR):

Disposable syringes

Cylinder	:	Homopolimeric Polypropylene
Plunger	:	High-density Polyethylene
Rubber seal	:	Silicon rubber sealing for 1 ml syringe

10.2 Imported raw material

Disposable syringes

Cylinder	:	Sliding agent (Masterbatch) = US $ 4.- kg
Printing	:	Hot printing foil = US $ 7.-/reel (122 m)
Assembly	:	Silicone liquid (spraying agent) = US $
Packing	:	Packing paper (59-60 g) with grid licquer (EO-gas pervious) width 415 mm = US $ 0.4/m^2

These materials should be imported from abroad. It is possible to acquire them from West Europe resp. USA.

10.3 Technical Specification of raw material

Granulate for syringe cylinder

Homopolimeric Polypropylene

Melting index	:	230 °C/2.16 N= 7,0-9,0 g/10 min 230 °C/5.00 N= appr. 32 g/10 min 190 °C/5.00 N= appr. 13 g/10 min
Density	:	0,90 - 0,91 g/cm^3

Vicot softening point A (10N)	:	150 - 154 °C
B (50N)	:	84 - 86 °C
Heat deformation temperature		
A (0,46 MPa)	:	80 - 90 °C
B (1,82 MPa)	:	50 - 58 °C
Melting temperature	:	162 - 165 °C

Granulate for syringe plunger

High density Polyethylene

Melting index	:	190 °C / 2,16 N = 7-9 g/10 min
		230 °C / 2,16 N = 30-32 g/10 min
		230 °C / 5,00 N = 12-14 g/10 min
Density	:	0,961 - 0,964 g/cm^3
Vicat softening point A (10N)	:	152 - 156° C
B (50N)	:	86 - 88° C
Heat deformation temperature		
A (0,46 MPa)	:	80 - 90° C
B (1,82 MPa)	:	50 - 60° C
Melting temperature	:	160 - 170° C

Sealing ring for 1 ml plunger

Pharma rubber on silicone basis

Bottom foil for packing

PA/PE foil
30 micron PA/50 micron PE or
30 micron PA/70 micron PE

sealing temperature approx. 110 °C - 140 °C at 3 kp/cm^3

Top foil for packing

Peelable paper gas-permeable
59 g paper / 11 g grid lacquer or
60 g paper / 10 g grid lacquer

sealing temperature approx. 110 °C - 140 °C at 3 kp/cm^3

Sliding agent (for PP-granulate)

Masterbatch sliding agent at the basis of clean Oleamides
i.e. Maxithen PP 7051/050
(Dosing: approx. 4 % of Masterbatch and 96 % PP)

Printing foil

Hot printing foil for PP cylinder

Assembly accessory

Silicone liquid (spraying agent for assembly machine)

10.4 **Raw Material Consumption**

for approx. 1 million syringes:

a) Plastic raw material

2 ml cylinder	: PP	:	approx. 1,500 kg
	Sliding agent	:	approx. 75 kg
2 ml plunger	: PE	:	approx. 1,350 kg
5 ml cylinder	: PP	:	approx. 2,680 kg
	Sliding agent	:	approx. 100 kg
5 ml plunger	: PE	:	approx. 2,900 kg

b) Hot printing foil (1 ml 51 or 122 m)

2 ml	: 111 prints/m	:	9,000 m
5 ml	: 83 prints/m	:	12,050 m

c) Packing foil (bottom & top web 420/415 mm)

2 ml	:	13,500 m
5 ml	:	15,000 m

d) Sterilizing gas

approx. 1,000 - 1,300 g/m^3 of sterilizer volume.

11. BUILDING FACILITIES AND SPACE REQUIREMENTS

11.1 Existing Building

As already mentioned in the Preamble (Background Information) there is an existing factory building complex, approximately 10-15 km north of Yerewan in the City of ABOVIAN.

The building complex consists of several single and multistoried buildings out of which one was chosen by the Corporation for the accommodation of the proposed manufacturing plant.

The four-storied building has not been completed and is, therefore, unused. The basic structure of the building consists of prefab concrete element construction. The interior work of the building and the partly existing equipment installation for a different project have been stopped and have to be removed to the requirements.

Dimensions of building : 30 m x 66 m

Further to this situation, the building has to be completed and adapted to the requirements of a disposable medical article plant and finally to the recommendations of the executing contractor.

Due to the already existing building structure and the therefore existing static limits, the weight and measurements of the production machinery are restricted to:

- max. height : approx. 3,5 meters
- max. weight : approx. 7,5 tons/m^2

11.2 Space Requirements for Alternative I and II

The estimated floor space is 3,060 m^2 consisting of the following occupancy (see layout drawing):

- Raw material store : 600 m^2
- Disposable syringe production area (clean room area) : 800 m^2
- Cardboard packing area : 250 m^2
- Sterilizing area : 200 m^2
- Laboratory : 180 m^2
- Quarantine store : 200 m^2
- Final product store : 400 m^2

- Workshop	:	100 m²
- Administration	:	180 m²
- Compressed air and cooling water station	:	150 m²
		3,060 m²

12. STERILIZATION GENERAL

All possible sterilization methods have been discussed and the disadvantages and advantages of every single method has been analyzed. The availability of ethylene oxide in the country and the lower financial investments have been the major arguments for the decision to use the EO-gas sterilizing system. It is the opinion of the Corporation to use 100 % EO-gas for the sterilizing programme.

The Consultant of the UNIDO recommends for the sterilization of disposable articles a sterilization gas mixture of:

90 % Ethylene oxide
10 % $C0_2$

100 % Ethylene oxide gas used in large volume sterilization units is not common practice since the danger of polymerization of the Ethylene oxide gas during the gasing procedure is possible resulting in a non-sterilization effect.

It has been agreed upon that a sterilization system has to be used which guarantees an EO-gas-free exhaust air and no possible contamination of the cooling water, system water (vacuum pump) and the operating area.

13. MACHINERY AND EQUIPMENT

Due to the tight financial situation on the one hand and the urgent necessity to implement a production plant for disposable syringes on the other hand, the UNIDO Consultant proposes the following machinery and equipment for 2 alternative production capacities and syringe sizes:

ALTERNATIVE I

Approx. 85 million syringes per annum (3-shift operation)

2 ml = 43-45 million/annum
5 ml = 40-42 million/annum

Injection moulding machines

2 pcs Injection moulding machines (125 tons)
2 pcs Injection moulding machines (225 tons)

Moulds

1 pc 32-cavity mould for 2 ml cylinder
1 pc 32-cavity mould for 2 ml cylinder
1 pc 32-cavity mould for 5 ml cylinder
1 pc 32-cavity mould for 5 ml cylinder

Printing and assembly

1 pc Printing and assembly machine for 2 ml, 2-piece syringe (with 2 different graduations)
1 pc Printing and assembly machine for 5 ml, 2-piece syringe

Packaging

1 pc Packaging machine for 2 ml and 5 ml
2 pcs Moulds for 2 ml and 5 ml

Sterilizer

EO-gas sterilizing unit, approx. 15 m^3

1 pc Cooling unit for cooling water, approx. 70 kW cooling capacity
1 pc Compressed air system, approx. 3 m^3/min (local supply) with air dryer and microfilter
1 pc Waste material granulator (for recycling of raw material)
2 pcs Raw material container, approx. 0,5 m^3
2 pcs Raw material transport system from raw material containers to injection moulding machines
30 pcs Plastic palettes 1200 x 800 mm
600 pcs Plastic containers 400 x 600 x 320 mm
4 pcs Manual forklifts

Additional equipment for laboratory, clean room, etc. as per ALTERNATIVE II.

ALTERNATIVE II

approx. 130 million syringes per annum (3-shift operation)

1 ml = 41-42 million/annum
2 ml = 43-45 million/annum
5 ml = 22-24 million/annum
10 ml = 20-22 million/annum

Injection moulding machines

2 pcs Injection moulding machines (100 tons)
4 pcs Injection moulding machines (125 tons)
2 pcs Injection moulding machines (150 tons)

Moulds

1 pc 32-cavity mould for 1 ml cylinder
1 pc 32-cavity mould for 1 ml cylinder
1 pc 32-cavity mould for 2 ml cylinder
1 pc 32-cavity mould for 2 ml cylinder
1 pc 16-cavity mould for 2 ml cylinder
1 pc 16-cavity mould for 5 ml cylinder
1 pc 16-cavity mould for 5 ml cylinder
1 pc 16-cavity mould for 10 ml cylinder
1 pc 16-cavity mould for 10 ml cylinder

Printing and assembly

1 pc Printing & assembly machine for 1 ml 3-piece syringe (with 2 different graduations)
1 pc Printing & assembly machine for 2 ml 2-piece syringe (with 2 different graduations)
1 pc Printing & assembly machine for 5 ml & 10 ml 2-piece syringe
4 pcs Elevators for automatic syringe transport to inserting device
4 pcs Inserting devices for automatic inserting of syringes in the packaging machines

Packaging

1 pc Packaging machine for 1 ml & 2 ml
1 pc Packaging machine for 5 ml & 10 ml
4 pcs Moulds for 1 ml, 2 ml, 5 ml and 10 ml

Sterilizing

EO-gas sterilizing unit, approx. 30 m^3

Accessories

1 set Cooling unit for cooling water
approx. 200 kW cooling capacity

1 set Compressed air system, approx. 5-8 m^3/min (local supply)
air dryer & microfilter

2 pcs Waste material granulators
(for recycling of raw material)

2 pcs Raw material container, approx. 1.5 m^3

2 sets Raw material transport systems from raw material containers to injection moulding machines

80 pcs Plastic palettes 1200 x 800 mm

1600 pcs Plastic containers 400 x 600 x 320 mm

6 pcs Manual forklifts

Laboratory

a) Chemical laboratory equipment and furniture
b) Bacteriological, seriological laboratory equipment and furniture
c) Pyrogen laboratory equipment and furniture

Clean room equipment

Air conditioning system with 12-15 circulations of the air per hour and an overpressure of 10-15 mm water column.

Room temperature	: 20 - 22 °C
Rel. Humidity	: 50 %

Engineering

Complete engineering works for planning, delivery, construction, start-up, performance test runs and handing over, including establishment of the technical documentation and manual instructions.

Erection, start-up and performance test runs supervision

Supervision of the erection and installation works, start-up of the machinery and equipment as well as the enforcement of the performance tests.

Training of personnel

Training of main personnel abroad.
On the job training of the operating personnel.

14. PERSONNEL

14.1 General

According to the Corporation, the availability of management and technically skilled personnel is guaranteed.

Approximately 25 students from the local Polytechnicum in Yerewan, skilled in plastic engineering, are available per annum.

Furthermore, plastic production companies in and around Yerewan have skilled and semi-skilled operating personnel.

Since the Corporation itself has a biotechnical Institute and several chemical companies, personnel for laboratories are available for the quality control and final production control.

The injection syringes line will work in 3 production shifts.

The main personnel connected with production and quality control must be trained abroad. Approximately 3 Ma/mo training at the supplier's premises distributed in 6 specialities (moulding, printing and assembling, packing, sterilizing, quality control and production services).

14.2 Personnel Requirements for Alternative II

a) Management

Plant manager	1
Chief engineer	1
Assistant	1
Accountant	1
Sales manager	1
	5 people

b) Supervisory and clerical staff

Secretary	1
Typist	1
Personnel clerk	1
Receptionist-Telephonist	1
Sales representative	1
Cost clerk/invoice clerk	1
Store keeper	2
Handling staff	2
Laboratory staff	5
	15 people

c) Production and maintenance staff

JOB DESCRIPTION	SHIFT 1	2	3	TOTAL
Shift leader	1	1	1	3
Raw material handling	2	1	1	4
Inj. moulding dept.	2	1	1	4
Printing & assembly	2	1	1	4
Packing staff	5	5	5	15
Sterilizer	1	-	-	1
Maintenance staff	2	1	1	4
Electrician	1	1	1	3
Product handling staff	2	2	2	6
Mould maker	1	-	-	1
				45

15. TIME SCHEDULE FOR IMPLEMENTATION

The implementation of Phase I and, if financially possible, also Phase II could be completed within 16-18 months from the effective date of the contract up to the commercial operation of the manufacturing plant.

It had been assumed that the locally constructed building and the manufacturing machines will be available within 12-14 months starting from the effective date of the contract.

The above indicated schedule includes the following acitivities:

- Selection and purchase of equipment
- Delivery of equipment
- Installation of equipment and systems
- Completion of civil works
- Training of the personnel
- Testing and running of equipment
- Handing over, guarantee tests and production operations

16. COST ESTIMATES

16.1 Investment Estimation

for an installation capable to produce 85 million disposable syringes per annum (Alternative I):

	Costs in US$ (1000)
Injection moulding machines and moulds, including spare parts for 2 years operation	1,100 - 1,300
Printing and assembly machines, inserting devices, etc., including spare parts for 2 years operation	700 - 850
Packaging machines including spare parts for 2 years operation	250 - 280
Sterilizing unit including spare parts for 2 years operation	600 - 670
	2,650 - 3,100
Accessories (according to technical specification)	100 - 130
Clean room air condition system	200 - 220
Laboratory equipment	450 - 500
Engineering costs	160 - 180
Supervision of erection and start-up costs	250 - 270
Personnel training costs	100 - 120
	1,260 - 1,420
TOTAL PROJECT COSTS	**3,910 - 4,520**

16.2 Investment Estimation

for an installation capable to produce 130 million disposable syringes per annum (Alternative II):

	Costs in US$ (1000)
Injection moulding machines and moulds, including spare parts for 2 years operation	1,900 - 2,100
Printing and assembly machines, inserting devices, etc., including spare parts for 2 years operation	1,200 - 1,400
Packaging machines including spare parts for 2 years operation	500 - 600
Sterilizing unit including spare parts for 2 years operation	800 - 900
	4,400 - 5,000
Accessories (according to technical specification)	140 - 160
Clean room air condition system	200 - 220
Laboratory equipment	450 - 500
Engineering costs	320 - 360
Supervision of erection and start-up costs	550 - 580
Personnel training costs	100 - 120
	1,760 - 1,940
TOTAL PROJECT COSTS	**6,160 - 6,940**

17. RECOMMENDATIONS OF THE UNIDO CONSULTANT

Taking into consideration the discussions with the specialists of the Company ARMBIOTECHNOLOGIA in Armenia and the background information received by the UNIDO-staff in Vienna with respect to the financial aspects of the project, the Consultant suggests the following to implement a production plant for disposable syringes and hypodermic needles:

a) The distribution rate of various syringe sizes in use in European countries is specified in paragraph 5. According to this distribution, approx. 70 % of the total number of disposable syringes used are in the range of 2 ml and 5 ml size syringes.

The Consultant therefore recommends to start with a producton line for disposable syringes for 2 ml and 5 ml only.

In order to achieve a high factor of utilization of the proposed machinery and equipment to be purchased, the ratio should be 50 % 2 ml and 50 % 5 ml.

With the number of machinery proposed by the Consultant in paragraph 13, Alternative I, a production capacity of approx. 80 million syringes per annum (3 shift operation) can be achieved.

The investment costs for the machinery and equipment necessary amounts to approx. US $ 3 - 3.2 million, excluding laboratory equipment and clean room equipment (see cost estimates).

It is of course advisable to appoint a main contractor for handling the whole project and on the other hand to have a responsible partner for the performance of the production plant and the quality of the product.

Reputed companies charge usually the following rates for their services:

Engineering, know-how, documentation, etc.	:	approx. 6 - 8 % of total project costs
Supervision of erection, start-up and performance test	:	approx. 10 - 12 % of total project costs
Training of personnel abroad and on the job during start-up of the plant	:	approx. 3 - 4 % of total project costs

b) The existing factory building can be used for the proposed production of disposable syringes. The building has of course to be completed and adapted to the requirements of a disposable medical article plant and finally to the recommendations of the main contractor responsible for the execution. The Consultant suggests to occupy the first floor of the building for the first phase of the project, the manufacturing plant, and the ground floor for the service machinery and equipment (cooling unit, air conditioning system, compressed air system), and storage areas for raw material and final products, etc. (see drawing). The sterilizing unit has to be, due to safety reasons, in an extra single floor building (see drawing). It is not allowed to locate EO-sterilizers in multistoried buildings. Therefore, a new building in accordance with the instructions given by the supplier has to be erected.

   The Consultant further recommends to construct production areas large enough for additional machines and equipment necessary for a future increase of the production capacity (see layout drawing and machinery and equipment according to Alternative II).

c) Clean rooms for the manufacturing of disposable syringes according to GMP or FDA standard should correspond to Class 10,000 as per US Federal Standard 209d. It is the opinion of the Consultant that a Class between 10,000 and 100,000 is sufficient for the production of disposable syringes. The Consultant therefore recommends to purchase necessary building elements locally and only the air conditioning/treatment equipment abroad, if necessary.

   - Wall and ceiling elements with coated steel panel
   - Integrated lighting (400 - 600 lux) and air channels in ceiling panels (including air filter)
   - floor covers, electrostatically conductive
   - round corners for easy cleaning and disinfection
   - air lock system
   - changing and washing facilities, etc.

   Further details are outlined in paragraph 6, article "Condition of the production area".

d) As already mentioned in paragraph 8 "Product Characteristics" it is the opinion of the Consultant and the Corporation "Armbiotechnologia" that two-part disposable syringes consisting of syringe cylinders and syringe plunger should be used for the syringe sizes of 2 ml, 5 ml, 10 ml and 20 ml. The syringe cylinder should be made of homopolymeric polypropylene modified with a special sliding agent (3 - 5 %) (imported) and the syringe plunger be made of high-density polyethylene due to colour contrasting reasons (easy identification of the plunger position during syringe preparation by the consumer/doctor).

Due to technical reasons (precision of moulding) it is advisable to produce 1 ml syringes with plungers made of polyethylene and an additional rubber sealing ring. These disposable syringes are called three-piece syringes and are mainly used for tuberculin and insulin injections.

Many years of experience have shown that for tuberculin and insulin injections 80 - 90 % of the patients can use the standard two-piece 2 ml syringe with a special graduation. It is therefore recommended to produce the 2 ml syringe with two different graduations.

e) For the production of disposable syringes it is most important to have accurate moulded products (cylinder, plunger) with respect to measurements and dimensions.

Therefore it is most important to purchase first class injection moulding machines and moulds. Microprocessor-controlled injection moulding machines together with hot runner moulds ensure exact products and reproducible machine settings, when changing the mould from one size of syringe to another.

f) As soon as the tight financial situation relaxes, it is recommendable to implement a production plant for hypodermic disposable needles. For the installation of the needle tube manufacturing line a separate building respectively separate floor in a multistoried building has to be used due to the contamination of the environs with very fine metal dust (grinding process, etc.). It is therefore necessary to install efficient dedusting equipment and airfilters.

The assembly of the needles with the plastic hub and the protection cover as well as the injection moulding can be carried out in the same clean room area as the production of the disposable syringes. For economic reasons the production capacity of such a hypodermic needle production line should not be less than 150 to 200 million pieces per annum (3-shift operation). The following main machinery and equipment are necessary for the production:

- Metal strip forming & welding machine
- Tube drawing and derodding machine
- Sinking machine
- Tube straightening, polishing and cleaning device
- Cutting machine
- Tip grinding machine
- Ultrasonic cleaning device
- Inspection equipment
- Injection moulding machine
- Mould for hubs and protection covers
- Assembly machine
- Packaging machine
- Sterilizer
- Accessories

The investment costs for such a production plant amounts to approx. US$ 5 -6 million depending on the exact production capacity and of course on the number of different needle sizes.

The basic machinery should be capable to produce the following needle sizes with at least three different lengths:

20 G	10 %
21 G	55 %
23 G	20 %
25 G	15 %

g) Production Quality Control

The production quality control should be carried out regularly and the results must be recorded and presented upon request.

Batch tests must be performed on every homogenous production unit that has identical properties and characteristics in all parts.

The batch test is intended to ensure that the quality of the disposable syringes meets this standard in every phase of the production including sterilization and packaging:

The batch test comprises:

- Test of the defined measurements
- Test of the seal and the lettering
- Visual check of faults
- Check of dimensional accuracy of the connecting zone
- Test of thightness between the outside cone and the cannula. The cone connection is stressed for 30 seconds with water at a pressure of 3 bar. The test can be also conducted with air under water instead of with water.
- Test of the tightness between piston and the cylinder with water. Disposable syringes up to 10 ml are tested with 3 bar, 20 ml with 2 bar. The duration of the test is 30 seconds. The necessary pressure is achieved by loading weight onto the piston as follows:

Syringe ml	1,0	2,0	5,0	10,0	20,0
Weight kg	1,2	2,0	3,7	5,9	7,0

The cone or the cannula must be tightly closed.

- Test of the transparency of the disposable syringe cylinder. An aqueous solution is charged for the test.

- Biological test (sterility, free from pyrogens)

The number of disposable syringes required for the batch test amounts to at least 1 % of each batch for the tests according to the method mentioned above.

18. CONCLUSION

As outlined in the description of the general situation found by the Consultant in Armenia, the activities of his mission were quite different from those specified in the UNIDO Job Description.

In addition to the basic project implementation studies according to the Job Description, the Consultant was confronted with very advanced project details, such as technical and commercial offers of reputed companies, layouts, etc. These documents and data had been obtained by the Corporation since beginning of this year.

Therefore, the Consultant was requested by the Corporation to elaborate exact technical specifications for machinery and equipment and to evaluate project prices on the basis of project capacities defined by the local Ministry of Health.

Due to the opinion of the Consultant, the elaborated data and prices should enable the Corporation to compare them with offers already available and offers to be obtained in the near future as well as to select the most suitable supplier.

Considering that according to local authorities the donated disposable articles, such as disposable syringes, hypodermic needles, etc. received during the worldwide charity programme on the occasion of the earthquake catastrophe in Armenia, are used up soon, the implementation of a manufacturing plant for the production of disposable syringes and by hypodermic needles should be started as soon as possible.

19. LAYOUT OF THE PRODUCTION PLANT

Attached to this report is a detailed layout drawing showing a proposal for the position of the production machines, devices and equipment.