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INTEGRATED DEVELOPMENT OF THE NATIONAL PHARMACEUTICAL INDUSTRY

DU/SYR/92/008/11-09

SYRIAN ARAB REPUBLIC

Technical report: Findings and recommendations*

Prepared for the Government of the Syrian Arab Republic
by the United Nations Industrial Development Organization

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* This document has not been edited.

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INTRODUCTION

The pharmaceutical manufacturing sector in Syria was deregulated in 1989. Since then more than forty small or medium size factories were set up under the national investment law. National standards did not exist in Syria for the design and construction of manufacturing facilities; each factory was created according to the owners' interpretation of GMP.

UNIDO offered the government of Syria a project intended to introduce standards for pharmaceutical production, based on internationally accepted practice.

This project became "Integrated Development of the Pharmaceutical Industry in the Syrian Arab Republic" (DU/SYR/92/008), a joint UNIDO/UNDP/WHO project to strengthen the industry in Syria through the regulatory body and industry.

In the frame of this project a technical mission was undertaken by the UNIDO Technical Consultant during 12-22 January 1997.

The purpose of the mission was to bring up specific recommendations for developing/upgrading/amending pharmaceutical industry policy and legislation.

SUMMARY

The project DU/SYR/92/008 was originated at a time when the private sector of the pharmaceutical manufacturing industry in Syria was created.
Up to that time, the overwhelming majority of all pharmaceutical manufacturing took place in two state-owned factories: Thameco and Dimas.
The traditions of pharmaceutical manufacturing are strong in these companies. The skilled staff is devoted to development in general, and to introduction of internationally accepted procedures for assurance of the quality of products. However, the status of the premises (first of all buildings) reflects the age of the company, and represents the biggest obstacle to comply with GMP guidelines.

The situation in the private sector is different. Being created recently, they had the possibility to build facilities meeting GMP requirements. However, their own interpretation of GMP together with financial constraints resulted in a widely different technical/technological/infra structural level in the private sector.

The economic system of the country is going to change from the centrally planned to the deregulated one.

The pricing of pharmaceutical products is representing the interest of the people and is set and approved by the Ministry of Health. Consequently, there is no margin in the ex-factory prices to cover expenses of proper marketing or costs of new investments which are necessary to comply with GMP.

At present, all pharmaceutical products which are manufactured locally enjoy very effective protection: the same products are banned from import. Further deregulations and approaching to a more open economy will make these measures obsolete. New, internationally accepted means for the protection of the domestic industry must be developed and gradually introduced.

A "survival programme" especially for the small and medium-size private companies and for the state-owned factories seems to be necessary to prepare them for the free completion in Syria and on the international market.

The setting up of a strategy for further privatization in the pharmaceutical industry is essential.

Proper patent legislation will be provoked by international cooperation and commercial relationship. It will also be necessary for the Syrian R&D.

Last but not least at all, the existing legislation and present practice of the chemical industries are to be further developed. Particularly during the registration and control

of products and premises, environmental aspects should be specified.
The introduction of environmental management (ISO 14000) to pharmaceutical companies is necessary and highly recommended. The same is related to the pesticides as well.

The STC wishes to express his thanks to his counterparts who helped his mission in spite of the time constraints due to the Ramadan. The efforts of the Deputy Minister of Health were extremely instrumental in organizing the meetings.

FINDINGS

PRESENT STATUS OF THE PHARMACEUTICAL INDUSTRY

The value of the overall consumption of pharmaceutical finished products of Syria expressed in US dollars can be estimated at about $200 millions. 80-85% of it is produced by local manufacturers, the rest is covered by import.
Prices of pharmaceutical products are regulated by the Ministry of Health.
The structure of pricing is illustrated in Annex III.
It can be stated that the revenue cannot cover the costs of new investments, GMP, marketing and R&D.

All local producers are from Syria and foreign ownership is unknown; THAMECO and DIMAS are state owned companies. All the others belong to the private sector.
(Thameco and Dimas are frequently named as "public companies", which is misleading, due to the fact that they are 100% owned by the Syrian state. In order to avoid misunderstanding, in the present study the expression "state owned" will be used.)

"Production" or "manufacturing" means "formulation", because there is no production of active substances in the country till now. For future development, the backward integration is identified as one of the goals and organic synthesis (based on domestic petrochemical raw materials), fermentation (based on products from agriculture), or extraction of medicinal plants or animal organs may be envisaged as sources of gaining indigenous active substances.

All manufacturers belong to the Ministry of Industry (MOI), with the only exception of Dimas which is supervised and controlled by the Ministry of Defence. MOI executes its duty for *state owned companies* through 6 branches: food, sugar, cement, engineering, textile and chemical.
The last, named General Institute for the Chemical Industry, is in charge of the following industries: fertilizer, pesticide, pharmaceutical (Thameco), detergent, plastic, paint, rubber, tires, leather, shoe, pulp/paper.
Private companies are supervised by a separate division of MOI.
Petrochemical industry belongs to the Ministry of Petroleum and Mineral Resources. In addition to the existing two refineries a third one is being planned.
Syria has significant natural gas resources; its further utilization is currently under investigation; the establishment of a petrochemical industry is envisaged, which can justify the expectation of the production raw materials for the pharmaceutical and pesticide industries.
The import of all finished products is carried out exclusively by the state owned General Organization for the Trade of Pharmaceutical Products SAYDALAYA-PHARMEX.
Raw materials and excipients for Thameco and Dimas are imported by the producers themselves through tenders.

Domestic products are protected from external competition; no import permits are given for finished products which are already produced locally.

Distribution is carried out through Pharmex and through other channels as well. Competition between local producers is steadily increasing; state owned companies are severely hampered by rigid regulations and lack of flexibility. (More details are given in the next section.)

Advertising is prohibited in the mass media. Promotion is allowed in scientific literature and through direct contacts with pharmacists, medical doctors, hospitals, universities, pharmacies, etc. by "scientific offices", which are registered in the Ministry of Health.

A patent system for pharmaceuticals is not developed, an effective product protection is lacking. The use of registered trade names and trade marks is exercised.

There is no ongoing research for new chemical entities.
Development of new formulae has recently started.

TECHNO-ECONOMICAL SURROUNDINGS OF THE STATE OWNED COMPANIES

Due to time constraints, the STC had the opportunity to visit only Thameco. Dimas belongs to the Ministry of Defence, so there are certain differences in the structure and relationship between the two companies. However, concerning technical standards and situation on the civil market there is no substantial difference between them, so the findings and recommendations of this study relate to both companies.

The yearly plan for the company containing all important items (products, investments, etc.)is issued by the Ministry of Planning. The product list, including quantities, is based on the request of the Ministry of Health.

Raw materials, excipients and all other auxiliary materials are financed by the companies. Foreign currency payments are made by banks after having been approved by the Ministry of Economy.

Prices are fixed by the Ministry of Health.
Quality of products, supervision of processes, equipment and premises, introduction and maintaining of Good Manufacturing Practices (GMP), registration of new products, also belong to the competence of the Ministry of Health.

Being an industrial company, Thameco belongs to the Ministry of Industry. The interface between them is the General Institute of Chemical Industry. Applications for permission for new investments or new equipment are screened first in the institute. If agreed, the proposal goes through the Ministry of Industry to the Ministry of Planning. If approved, the Ministry of Economy is in charge to provide the necessary funds for the acquisition.

Wages, salaries, and the organization of the company are to be approved by the Ministry of Industry.

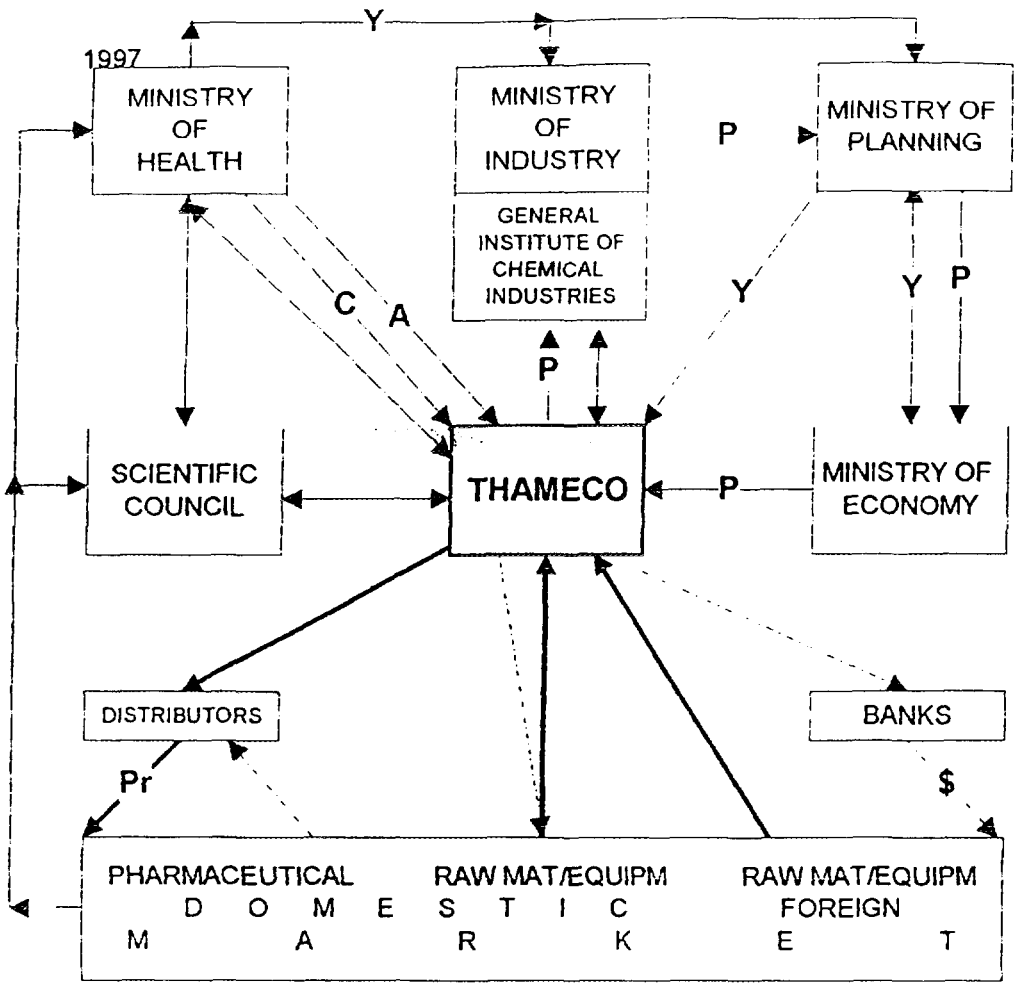
The Scientific Council serves as an intermediate between the Ministry of Health and the companies.

The economical environment of Thameco is illustrated in Fig.1.

The marketing activity of the company is rather limited; the domestic market is "attacked" by the same or similar products of the private companies who have more effective means than Thameco to promote their products. In consequence of this, certain lines of traditionally accepted and popular products (ointments, creams, suppositories, rehydrating salts) have to be stopped due to lack of orders. Thameco started to respond to this challenge and organized new channels of distribution. As a result, the stopped production lines have been recently restarted.
Unfortunately the response of Thameco to the demands of the market is slow due to the above illustrated rigid bureaucracy in purchasing materials.

Last but not least, the premises of the company are not in compliance with GMP guidelines: the buildings are old, at the time of their erection GMP was unknown.

This is in strong contrast to the skills of the personnel, up-to-date thinking and devotedness to improve conditions by approaching to meet GMP requirements.



Delivery of raw material

Pr — Delivery of product

Flow of money (Syrian Pounds)

$ — Flow of money (foreign currency)

Flow of information

Y — Process of approval of yearly plan

P — Process of approval of purchasing raw materials or equipment

A — Approval of new product, or process

C — Control of quality of product/process/premises

Fig.1

The economical environment of Thameco

LEGISLATION AND CONTROL OF PHARMACEUTICAL PRODUCTS/PRODUCTION

Production, sale, distribution and import of pharmaceutical products are controlled by the Ministry of Health (MOH) and are executed by four directorates headed by the Deputy Minister of Health. Decisions are made by the technical council.

Technical Committee (TC)
The Technical Committee, consisting of representatives of related organizations, universities and leading scientists and professors - headed by the Minister - is making decisions and exercising supervision of this activity. Prices of pharmaceutical products as well as import permits are to be approved by the Technical Committee.
One of the guiding principles is to cover the list of essential drugs by domestic products as much as possible, thus replacing the imports, meanwhile keeping a fair balance among the local producers.

The control procedure is executed by the following organs of MOH:

Directorate of Pharmaceutical Affairs (DPA)
DPA deals with registration/approval/permission of

- **production facilities**
- **new products, such as: pharmaceuticals,**
  paramedicines,
  baby-food,
  sera, vaccines.

(Veterinary products belong to the competence of the Ministry of Agriculture.)

The procedure of registration of drugs is well elaborated and introduced. A computer programme for a data base has been adopted with the assistance of WHO.
For the registration of domestic products, the applicant is requested to provide the information detailed in Annex IV, the information for imported pharmaceutical products is mentioned in Annex V.
"Paramedicinal products" or "domestic chemicals" are not registered, but the permit of production/distribution/sale is obligatory.

Directorate of Drug Quality Control (DQC)
This directorate is in charge of control, monitoring and supervision of pharmaceutical

- **products (s.:above)**
- **production facilities**
- **quality assurance**
- **clinical studies**

The controlling procedure starts by visiting the sites before they start working by the *Evaluation Committee*, consisting of the four Directors of the MOH, the President of the

Syndicate of Pharmacists, the professor of the Faculty of Pharmacy, the Directors of Themeco and Dimas, and headed by the Deputy Minister of Health.
Based on the recommendations of this Committee, the TC gives the permission to start the production.

After starting the production but prior releasing to the market, samples are taken by the inspectors of DQC and checked by the DCL.
The practice of random sampling is exercised by approximately 400-450 times per month.
Regular and random inspections are carried out following GMP guidelines.
Imported finished products are also controlled by samples taken from the stores of Pharmex and from the pharmacies.
Visits of premises of foreign producers are not yet exercised.
It is worth mentioning that the samples of each batch of certain specific drugs (for example: sera, cardiovascular drugs, eye-drops) are analysed by the laboratories of DCL.
In case of disorders, the Evaluation Committee proposes required measures which may be

- **"freezing the work" (for repeated checking),**
- **stopping the production (to eliminate the problem), or**
- **withdrawing the product from the market.**

<u>Directorate of National Drug Quality Control and Research Laboratories.(DNDQCRL)</u>
(Usually called as: Central Laboratories)
The main tasks of DNDQCRL are:

- **quality control of pharmaceutical projects, starting materials, biological products, medicinal products, raw materials**
- **contributing to bioavailability studies**
- **drug research in the field of manufacturing and quality control**
- **training in the field of drug quality control**
- **participating in local and international workshops**

<u>Directorate for Drug Studies</u> **(DDS)**
In order to make decisions for the selection of new drugs, formulae, to elaborate strategies, or to introduce proper measures in the drug policy, different studies are needed.
It is the responsibility to prepare such studies and arrange the meetings of the TC.

ENVIRONMENTAL LEGISLATION

Status of legislation

In the Presidential Decree XI **in 1991 it was decided to increase the level or authority of the Ministry of Environment by transforming its status into the General Commission for Environmental Affairs (in the present study the generally used expression is: Ministry of Environment) and also to set up the Higher Council for Environmental Safety.**

The *National Investment Law* contains the basic elements of investment policy and conditions of establishing new plants, facilities.

The *Draft Law on Protection of Environment* has been recently approved by the Government. The approval by the National Assembly is in progress.

Present practice

The *Higher Council for Environmental Safety* - headed by the Prime Minister - is consisting of 12 ministries. Its principal tasks and activities are to:

- **set up environmental policy for the country,**
- **monitor its implementation,**
- **approve the Yearly Action Plan for Environmental Protection.**

The *Ministry of Environment* is gradually starting to exercise its duties and to build the necessary organs and facilities.

Ministry of Environment (MOE)

The main tasks of MOE are:

- **to prepare the Yearly Action Plan,**
- **to elaborate the environmental strategy,**
- **to monitor the quality of environment,**
- **to review the legislation,**
- **to raise the awareness in related Ministries,**
- **to approve selection of sites for new plants/ premises,**
- **to approve and monitor processes, technologies, with special attention to industrial wastes,**
- **to build the capacity of the MOE**
- **to follow up international conventions.**

MOE is going to exercise its duties through *seven directorates*, located in seven water basins of the country. Three of them are already working; the other two will start its activities in 1997. (It is worth mentioning that the country is divided into 14 governorates.)

Beside the directorates, MOE assists in the establishment of environmental departments in the governorate and related ministries.

The *Scientific and Environmental Research Center (SERC)* also belongs to the MOE. Its specialized laboratories cooperate with and assist the other labs of the ministry.

A *Monitoring Department* is going to be set up equipped with a "moving lab" (a van equipped with instruments to analyse samples immediately on-site.)

Recommendations and drafts for policy making and legislation are prepared in *special committees* where the related ministries and organizations are represented.

The *Committee for Chemical Safety* is - among others - in charge of the supervision of the chemical industries, however, for the time being, the pharmaceutical industry does not belong to its competence. (All information on environmental management in the pharmaceutical industry is needed and appreciated.)
Concerning formulation of other chemicals, there are two plants producing household chemicals, but till now no formulation of pesticides is going on in Syria. Use, selection, and import of pesticides belong to the competence of a committee in the Ministry of Agriculture. (Information on safe and effective handling and the use of pesticides is also welcome.)

Last, but not least, the work of the MOE is assisted by the *UNDP/World Bank Project: Strengthening National Capacity for Environmental Affairs.*
Main objectives of the project are to:

- **formulate National Conservation Strategy**
- **identify the Environmental Action Plan**
- **build the necessary capabilities**

RECOMMENDATIONS

Future development of the pharmaceutical industry in Syria will be determined by the following factors:

- **Ongoing and a future deregulation process in the industry: approaching/implanting free market economy, competition**
- **steadily increasing requirements on quality assurance**
- **steeply growing importance of environmental management.**

In connection with environmental aspects of handling of agrochemicals, recommendations for the legislation of formulation of pesticides are also mentioned.

1. PRESENT TASKS

1.1 Increase the ability of the state owned companies to participate in the competition of the domestic market.

- **improve the sale/distribution capabilities**
- **deregulate the decision making**
- **more liberal wage policy**
- **deregulate the access to foreign currency**

1.2 Help the state owned companies in their efforts to meet GMP requirements in the existing buildings.

1.3 Strengthen the importance of environmental protection esp. chemical safety in the licensing of new sites, plants, processes.

- **environmental assessment/audits of processes: effluents, exhausts, solid wastes.**
- **waste management**

Training workshops for personnel of all levels

1.4 Steady technical improvement of the facilities of the central laboratories in the MOH.

Especially the whole pharmacological section is to be reconstructed.
Up-to date instrumentation for example, HPLC is needed.

2. STRATEGIC TASKS

2.1 Price policy

First priority: sufficient drugs in good quality at an "available" price for the people of Syria.

In most countries "available" means: cheap.
However, prices - beside production and marketing costs - must also cover investments, developments, first of all GMP related expenses as well. Without constant development in quality and technology, the companies will lose (or never reach) competitiveness.
The survival of the pharmaceutical industry is essential not only for them (and their employees!), but also for the country, because without a strong domestic production, the prices were significantly higher.
After all, the domestic pharmaceutical industry is Syrian, and as such it represents value, let it be state owned or private.

2.2 Policy of protection of domestic products/producers

At present, all Syrian products enjoy the ban on import of competitive products. The number of locally produced competitive products is limited by the Technical Committee. The competition between companies is balanced by the TC.
By proceeding to a more open economy, all these measures must be eliminated - gradually of course.
Every country is protecting its own industry, the Syrian Government will not be an exception either; but proper and internationally accepted methods must be introduced.

2.3 "Survival programme" for the small and medium size companies

Companies of the private sector differ - among others - in size, product range, technical level, marketing skill, and GMP compliance. By approaching GATT they will gradually be swallowed by the international competition. A strategy of survival would be very instrumental in finding ways of how to face the challenges of the international competition.

2.4 The same is related to the state owned sector (Thameco and Dimas) as well.

2.5 Privatization policy

The following options are to be considered:

- **invitation of foreign capitals, if yes:**
  - **only in licence cooperations, or also in**
  - **new joint ventures, or**
  - **ownership in existing private companies, or even at**
  - **Thameco and/or Dimas**
  - **advantages and burdens of private ownership**
  - **attraction of foreign capital without ownership**
  - **participation of domestic private capital in the state owned companies**
  - **investment policy without further privatization.**

2.6 Patent policy

The importance of patents will increase in parallel with the liberalization of the economy, especially when Syria will join GATT. The introduction of an internationally accepted patent legislation will be the background for cooperation with foreign partners but it will also help the domestic research and development aiming at new products and processes.

2.7 Programme on the introduction of environmental management in the pharmaceutical industry.

Environmental policy of a certain organization comprises the intentions and principles of action of the organization regarding environmental impacts.
The environmental management system assures that the company will continue to meet requirements.
The programme should contain all basic elements of environmental protection: waste management, chemical safety, prevention and response in chemical accidents, reduction of emissions, pollution control, working safety and occupational health, introduction of ISO 14000.
Assistance of related international organizations (UNIDO, UNDP, FAO, UNEP, World Bank) may be considered.

2.8 Legislation on the management of chemicals in Syria. Harmonization of the Syrian legislation with OECD Instruments

In order to prevent chemical accidents and to reduce risks of human or environmental damages, a comprised legislation dealing with chemical substances is necessary. Considering present commercial relationship of Syria with foreign countries, the harmonization with OECD (Organization for Economic Cooperation and Development) decisions and recommendations seem to be practical. However, due to their global influence, regulations and practices of EPA (Environmental Agency of the USA) are worth to consider.
This programme should make recommendations on the following issues:

- **levels of legislation (acts, laws, decrees, standards)**
- **measures for the handling of toxic chemical**
- **drugs***
- **pesticides****
- **carcinogenic substances**
- **import/export of hazardous chemicals**
- **prevention of accidents, emergency preparedness**
- **exchange of data on chemicals**

*** see: 2.7**
****see: 3**

3. FORMULATION OF PESTICIDES

The high growth of population of the country makes the development of agriculture essential to satisfy the increasing demand on food. To improve the yields of food crops the importance of pesticides is growing.
In order to reduce production costs in the agriculture, the substitution of the import of the most widely used and/or most expensive finished products by locally formulated pesticides seem to be inevitable. Discussions on licences with two foreign countries are already in progress.
Considering the present trend of the transformation of the Syrian economy towards free market system and privatization, the appearance of small to medium size formulators can also be forecasted.

Due to the chemical substances and auxiliary materials, formulation represents certain risks to the environment, especially if the small or medium size companies are lacking the essential expertise.

The introduction of local formulation must not surprise the Government; on the contrary: the whole process must be initiated and controlled by a well-harmonized cooperation of the related ministries (MOA, MOI, MOE, MOH). The implementation of the following measures is recommended:

31. Programme to establish and promote domestic formulation of pesticides.
31.1 Assessment of present and forecasted production of food crops and cash crops. Identification of priority crops.
31.2 Present and forecasted use of pesticides.
31.3 Identification of new, environmental friendly pesticides, Integrated Pest Management, use of biopesticides.
31.4 Selection of candidates for local formulation.
31.5 Forms and measures of governmental support for local formulators.

32. Programme of the introduction of safe handling of pesticides.
32.1 Safe and effective use of pesticides.
32.2 Safe handling of pesticides during their formulation.
32.3 Safe handling of pesticides during their packing, storage and transport.
32.4 Quality Control of Pesticides.

33. Assistance of related international organizations (UNIDO, UNDP, FAO, UNEP, World Bank) may be considered.

ANNEXES

ANNEX I

JOB DESCRIPTION

JOB DESCRIPTION
DU/SYR/92/008/11-09

Post Title: STC on pharmaceutical industry legislation/policy

Duration: 0.5 m/m

Date required: 15 November 1996

Duty Station: Damascus

Purpose of mission: In close co-operation with the WHO consultant on drug and pharmacy legislation, STC should make a coordinated effort to bring up specific recommendations for developing/upgrading/amending pharmaceutical industry legislation/policy.

Duties: The expert should perform the following duties:

1. Based on the existing drug and pharmacy legislation and the recommendations of the STC of WHO on the same subject, the consultant should assess current existing pharmaceutical industry legislation or industry legislation in general which may be relevant to the pharmaceutical industry.

2. To make specific recommendations on how to amend or upgrade the existing legislation mentioned in para 1 above.

3. To give specific recommendations on an integrated pharmaceutical industry policy which would appropriately respond to the requirements of the drug and pharmacy legislation.

4. To make specific recommendations for pharmaceutical industry legislation based on the industry policy mentioned in para 3 above.

5. To prepare a report in cooperation with the STC of WHO on the above based on which the government would be able to prepare an immediate and medium term action plant to establish the required pharmaceutical industry legislation.

Qualifications: Industrial pharmacist, chemist with managerial working experience in pharmaceutical industry and experience in the preparation of pharmaceutical industry legislation/policy. International experience and specifically experience in developing countries is required.

Language: English

Background Information: The Tripartite Review Meeting for project DU/SYR/92/008 held on 30 March 1996 confirmed the continued relevance of the project concept and design to the priorities of the Government. However, it was agreed that national capabilities in developing standards should be strengthened. The Ministry of Health, Ministry of Industry and the National Standards Board should closely cooperate in this capacity building exercise. It is also important to review the legal framework of the national drug policy. These activities should be integrated into the efforts to revise the national drug policy as indicated in the project document.

The national drug policy was formulated in 1990 but since then several major developments occurred such as the global trend of changing towards transition and market economies as well as the impact of GATT Uruguay Round's agreements. In light of these changes it seems to be important to revise the national drug policy. It requires:

a) Collecting all available legislative documentation for technical review and updating;

b) Revision of policy implementation using the suggested global indicators;

c) Based on the above, the necessary revision of the national drug policy will be made to reflect the national objectives up to the year 2001.

ANNEX II

LIST OF ORGANIZATIONS VISITED, PERSONS CONTACTED

Annex II

LIST OF ORGANIZATIONS VISITED, PERSONS CONTACTED

VISITS

Date of visit	Site of visit
1. 9 January 1997	UNIDO/Vienna (Briefing)
2. 13 January 1997	UNDP/Damascus
3. 13 January 1997	Ministry of Health (MOH) Deputy Minister Directorate of Quality Control
4. 14 January 1997	MOH Minister
5. 14 January 1997	UNIPHARMA Universal Pharmaceutical Industries
6. 15 January 1997	UNDP
7. 15 January 1997	Ministry of Environment (MOE)
8. 15 January 1997	Association of Syrian Pharmacists (and Producers)
9. 15 January 1997	MOH (Technical Committee)
10.16 January 1997	THAMECO The Arabian Medical Company
11.18 January 1997	MOH Dir. of Pharmaceutical Affairs
12.19 January 1997	MOH Deputy Minister
13.20 January 1997	MOE
14.20 January 1997	Ministry of Industry General Institute for Chemical Industry
15.21 January 1997	MOH
16.27 January 1997	UNIDO/Vienna (Debriefing)

PERSONS

Prof.Dr. M. Iyad El-Chatti	Minister	MOH
Dr. Kaukab Al Dayeh	Deputy Minister National Project Director	MOH
Ms. Nadja Kozak	Project Officer	UNDP
Mr. Abdallah Dardari	National Programme Officer	UNDP
Ms. Souheila Hakim	Director (Pharmaceutical Affairs)	MOH
Ms. Souad Ghoon	Director (Drug Quality Control)	MOH
Mr. Ousama Katrieh	Director (Directorate for Studies)	MOH
Mr. Habib Abboud	Director (Directorate of Central Labs)	MOH

Mr. Zeid Al-Hariri	Director General	Min. of Indust. GECI
Ms. Rajwa Gbeily	General Manager	Thameco
Ms. Najwa Nabulsi	Head of Secretariat	Thameco
Mr. Bachar Charouf	Head of Dept.	Thameco
Mr. Imad Maatouk	Deputy Chairman	Unipharma
Mr. Nidal Hussami	Q.A. Manager	Unipharma
Prof.Dr. Ahmad Samur Alnouri	President	ASP*
Dr.Bashir Bardan	General Director	Pharmex
Dr. Mamoun Fahham	National Project Director (UNDP)	MOE
Mr. Yahia Awidah	National Project Coordinator (UNDP)	MOE
Ms. Abir Zeno	Project Officer	MOE
Prof.Dr. Mahmod Salih Soliman	General Director	SERC**
Ms. Samar Ezmishli	Reporter	SANA***

* Association of Syrian Pharmacists
** Scientific & Environmental Research Center
*** Syrian Arab News Agency

ANNEX III

Price Structure of Pharmaceutical Products

Annex III

Price Structure of Pharmaceutical Products

Name of product : "X" tablet
Unit : package containing 50 tablets
Packaging : plastic bottle in paper box

Costs			
Active substance:		S.P.	23.85
Excipients			2.50
bottle+cup			3.65*
label			0.30
manufacturing			10.00**
cartoon, leaflet			1.90
Direct cost of production:		S.P.	42.20
Reserve for losses (5%)			2.11
Total cost of production		S.P.	44.30
Storage	5%		
Marketing	5%		
advertisement			
scient. office			
Profit	20%		
Total overhead (incl.profit)	30%	S.P.	13.30
Ex-factory price		S.P.	57.60
Margin for retailers			11.40***
Public price in pharmacies:		S.P.	69.00

*for vial:	3.50	**per tablet:	0.20
glass bottle:	6.00	coated tabl:	0.40
plastic bottle	3.00	if hormones:	0.50
blister:	0.15	ampoule	2.00

**margins

pieces per pack.	margin % on ex-fact. price prescore.	OTC
<10	30	36
10-20	20	24
20-100	15	18
100<	8	8

ANNEX IV

DATA REQUESTED FOR THE REGISTRATION OF LOCALLY PRODUCED DRUGS

Annex IV

DATA REQUESTED FOR THE REGISTRATION OF LOCALLY PRODUCED DRUGS

The registration file for new drug applications is to be submitted to the Directorate of Pharmaceutical Affairs of the Ministry of Health and must follow the form issued by the MOH. The summary of the requested data is as follows:

General data: Data on the company
Name(s) of product (to be registered, produced)
Date of study(ies), names of participants

Specific data: formula(e), packaging
indication
similar products,

Properties: mechanism of action
pharmacokinetics
pharmacodynamics
indication(s)
contraindication(s)
side effect(s)
precaution, warning
drug-food interaction
dosage, administration
over-dosage treatment
copy of instruction for use, labels, packaging

Active substance (raw material):
name(s), composition
physical data, description
chemical, physico-chemical data
analytical methods

Excipients: same as for active substances process of manufacturing:
Description of technology
quality control
in-process control

Finished product: analytical procedures

Description of final appearance of the product:
surface, outside, inside of the box,
content of the box etc.

Data of packaging materials

Suggested protocols for investigations:
bioavailability
bioequivalence
etc.

Suggested price, proforma invoice

ANNEX V

REQUIREMENTS FOR THE REGISTRATION OF IMPORTED DRUGS

GENERAL ORGANIZATION FOR THE TRADE OF PHARMACEUTICAL PRODUCTS

SAYDALAYA

INSTRUCTION N° (105) DATED 30/7/90

FOR THE REGISTRATION OF HUMAN PHARMACEUTICAL PRODUCTS

In virtue of the Technical Committee's decision taken in its session N° 832 dated 8/10/85 and its session N° 948 dated 17/12/89 for the introduction of your products into Syrian markets you are kindly requested to observe the following instructions when submitting an application for the registration of new products:

1) **Application for registration should be addressed to the General Organization For the Trade of Pharmaceutical Products (SAYDALAYA/PHARMEX).**

   a) **On original Certificate of Origin issued by the Health Authority entitled to issue such certificates duly legalized by Ministry of Foreign Affairs of your country and by Syrian Embassy or acting Embassy in your country testifying that the pharmaceutical preparation required to be registered is manufactured and sold or used in country of origin. This Certificate to be worded according to the enclosed model of the Certificate of Origin adopted by the World Health Organization. This certificate should be accompanied by its certified translation into Arabic by a sworn translator legalized by Ministry of Justice and Ministry of Foreign Affairs.**

   b) **A document displaying the composition of the product with all its active ingredients and excipients and its conservation elements, colouring, flavouring, odorents and all other composition components along with packing and packaging materials. This document should be signed by the technical manager or the production manager of the plant.**

   c) **A document showing the method of analysis of all the components of the preparation and its stability study signed by the manager of the analysis laboratory of the plant.**

   d) **A certificate of analysis for all the samples submitted for consideration.**

   e) **Samples for pharmaceutical active substances and reference standards.**
   Starting Materials for the active ingredient.
   Primary reference standards for the active ingredients.

   f) **Some copies of the study made on the preparation, in English and French comprising mainly:**

1. **PRECLINICAL STUDIES:**

Chemistry:

- **Active Substance**
- **Pharmacology**
- **Toxicology (Animal)**
- **Drug Formulation Analysis**
- **Formulation for Route**

Pharmaceutical Form:

- **Dosage Schedule**

Drug Interaction:

- **Health subject**
- **I11 subject**

Drug biological Interaction:

- **Health subject**
- **I11 subject**

2. **CLINICAL STUDIES:**

Protocol

- **Therapeutic Effects**
- **Pharmacodynamic Effects**
- **Pharmacokinetics**
- **Drug Monitoring**
- **Clinical Pharmacology**

Phase I	**24 - 30 months**
Phase II	**12 - 24 months**
Phase III	**12 -24 months**
Phase IV	**12 - 26 months**

A fifty (V) phase with unlimited period
Metabolism biotransformation
Toxicology (Human)
Excretion in Urine and bile.

Acute
Chronic
Isolation of metabolites
Laver
Protein Binding
Enzymatic Systems (Liver)
Single dose, repeated dose

Study of metabolites after administration I.V.P.O. (Cold product, Radio labelled product)
Excretion in Urine and bile

Toxicity

- Haematological (Leucopenia, Agranulocytosis, Thrombocytopenia, and hemolyticanemia

- Teratogenesis in Animal and in the Human (normal dose and large doses) in pregnancy through different period).

Immunological studies.

g) **A duly legalized document indicating the name of the manufacturer of active ingredients to be attached to studies carried out these active ingredients as required in paragraph (f).**

h) **Price quotation for the submitted product, preferably on CANDF basis.**

I) **A certificate showing the public seeling price of the preparation in country of origin duly legalized by the bodies referred to in paragraph (a) above.**

j) **The application for registration as well as the documents set out in item (1) should be put in an envelope of featuring the statement (Registration of new products) and sent to General Organization For the Trade of Pharmaceutical Products (SAYDALAYA/PHARMEX) through registered airmail. The number and date of this circular should as well be written down on the envelope.**

2) **A cheque for the amount of US$ 150,- to order the General Organization of Pharmaceutical Products (SAYDALAYA/PHARMEX) as evaluation fee for each preparation, i.e. for each (pharmaceutical for dosage, packing) accompanied by a letter indicating the names of preparations submitted for evaluation.**

3) **Tenderer shall furnish 30 samples of the preparation submitted for registration**

in its form destined for sale. He shall as well, when requested, furnish additional samples of preparation in case tests are carried out thereof.

4) When the preparation is accepted by the Technical Committee and when it is to be registered at the Ministry of Health, a sum of US$ 250,- shall be paid through a cheque to order General Organization For the Trade of Pharmaceutical Products (SAYDALAYA/PHARMEX) as registration fee.

5) The Certificate of Origin shall remain valid for 5 days starting from registration date of product in Syria. The submission of this certificate of origin should be automatically renewed every five years or as needed per enclosed model and dully legalized with no payment of any fees.

These companies having products registered in Syria since more than 5 years should furnish within one year as from this circular's date new Certificates of Origin for their preparations duly legalized and worded as per enclosed model prepared by the worlds Health Organization.

This registration allows the import of the preparation through periodical orders or through tender calls. But companies desiring to register same of their products for tenders only should get these products registered before offering them against tenders otherwise they will not be accepted.

Registration of products for tender purposes is made strictly as required above to the exception of paragraph (I and g) of item (1) relating to prices. These prices are not required to be submitted for this registration since they are to be made in offers submitted against tenders.

The application for this registration and the related documents should be put in an envelope featuring the statement (Registration of Pharmaceutical Products for Tenders) and sent to General Organization For the Trade of Pharmaceutical Products (SAYDALAYA/PHARMEX) through registered airmail. The number and date of this circular should as well be written down on the envelope.

GENERAL DIRECTOR

ANNEX VI.

COMMENTS OF THE PROJECT MANAGER

Government intervention and regulations are variable in the nature of goods concerned. In a developing country, the Government - through the industrial policy for the pharmaceutical sector - will support national industry. The industrial policy in the pharmaceutical sector should focus on the importance of innovations and the way in which purchasing decisions are made for pharmaceutical products; this will facilitate innovative competition and price competition. However, it is easy to understand that there is a trade-off between price competition and innovative competition. Whatever the mechanisms are, the more intense price competition is, the less intense innovative competition will be.

The role of the Government is to achieve the best combination or at least the optimal combination of these policies. In order to improve quality, to develop good manufacturing practices, to keep abreast with international development in the pharmaceutical sector, the Government should provide incentives to the industry in order to cope successfully with competition and supply of pharmaceutical products of consistently high quality.

In order to achieve this quality, the facilities and processes should comply with the requirements of good manufacturing practice. The regulations and the legislation in the pharmaceutical sector should facilitate the development of industry in this direction as the UNIDO consultant suggested.

Z. Csizer
Project Manager
18 March 1997