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SYRIAN ARAB REPUBLIC

Technical report: The Pharmaceutical Industry in Syria*

Prepared for the Government of the Syrian Arab Republic
by the United Nations Industrial Development Organization,
acting as executing agency for the United Nations Development Programme

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* This document has not been edited.

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ACKNOWLEDGMENT

The writer expresses his sincere thanks for the co-operation of Mr. M. Koudsi the General Manger of THAMECO, Mr. R. Chamaa, the Technical Manger, Miss F. Bizre, the Production Manager, Mr. B. Haffar, the Planning Manger, Dr. Y. Hiba, Head of Formulated Food Department and all other heads of departments and all those whom the writer had worked with specially in QC, R&D and HPLC laboratories and other departments.

The writer wishes to express his appreciation to Mr Chamaa for allowing facilities and assessment to his office during the period of his stay in THAMECO, also for the valuable information which he provided on the Pharmaceutical Industries in Syria in general and on THAMECO in particular, also for his friendship which helped the writer's stay in Damascus to be more than comfortable.

Thanks are due to the administrative staff of UNDP Office/Damascus especially Dr. K. Alooch.

ABSTRACT

Post title: Instrument Analysis Expert (DP/SYR/86/009/11-17)

Duration : 1 month (June 24 to July 27, 1990, spent in THAMECO, Damascus, mainly in the QC, R&D and HPLC laboratories.

Five lectures/round table discussions, were presented.

The theoretical basis of HPLC was explained and demonstrated through an analysis of one of THAMECO's products. The development of analytical methods relating to a number of the company's products were successfully achieved. Advice was given concerning the filling and packaging of an eye drop preparation.

Recommendations concerning problems faced by THAMECO were made, including:

a) updating its library with relevant reference material

b) updating production equipment through the purchase of modern instruments

c) imposing GLP, GMP and GSP

d) incorporating the above in THAMECO's training programmes.

Recommendations were also made concerning the new THAMECO's facilities at Allepo in general and its QC laboratories in particular, with regard to improving its GMP, GLP, and GSP record.

Concerning the development of the pharmaceutical industry in Syria, present and future plans were discussed, and the writer's conclusions and recommendations were made known.

Attatched are:

- outlines of the five lectures given.
- the list of instruments, apparatus and equipment recommended.
- job descriptions for proposed experts
- contact list for THAMECO

INTRODUCTION

This report relates to the second month of a four months split mission. Project No. DP/SYR/86/009/11-17.

The mission commenced on June 24 and terminated on July 27, 1990. Field work was mainly in THAMECO (28 days) and included a one day brief visit to the newly constructed THAMECO facilities in Allepo.

The original objective of the project was to assist the Government of the Syrian Arab Republic to improve the performance of industry at the sectorial level and to effect the optimal utilization of existing capacity. Furthermore, the project aimed at supporting the country's economic development plan, stressing the need for self-reliance, the utilization of national resources, and the promotion of exports in order to increase foreign exchange earnings.

The assignment was to the General Establishment for Chemical Industries, THAMECO, and was expected to solve and/or execute the following:

a) in house training of lab staff on the use of HPLC and amino acid

b) sampling: selection and preparation of reagents

c) reading and interpretation of results

d) maintenance and calibration of equipment

e) development of analytical methods

f) establishment of laboratory GMP

All these requirements were accomplished and the objectives attained within the time limits set.

I. DEVIATION FROM JOB DESCRIPTION

Upon arrival at THAMECO a meeting was held in the office of Mr. M. Koudsi, the General Manager, attended by Mr R.Chamaa, the Technical Manager, Dr. B.Kabani, the Research and Development Manager, and the writer. All parties agreed that some aspects of the job description required further discussion and explanation, to take the form of a round table discussion in the main auditorium of THAMECO. Such a discussion would allow all those interested in the subject, in addition to those directly concerned, to attend and participate. Staff members of the Faculty of Pharmacy, University of Damascus, 4th year Pharmacy students undergoing summer training at THAMECO, graduate students, the managers and heads of department at DIMAS, were all invited to attend. Attendance was generally between 70 and 100, and every presentation was attended by the managers of THAMECO, together with the company's technical staff.

Each lecture/discussion took around two hours, and was followed by approximately half an hour of questions and open discussion. All the lectures and discussions were presented in Arabic, at the request of the writer's Syrian colleagues, The text of each presentation, again in Arabic, was given to Mr. R. Chamaa for printing and distribution.

Lectures presented:

1 a. Good Practices in the Manufacture and Quality Control of Drugs (GMP/WHO)
   b. Certification Scheme on the Quality of Pharmaceutical Products moving in International Commerce (WHO)
   ["f" in job description, Annex No. 1]
   July 8, 1990.
2 Good Laboratory Practices in Governmental Drug Control Laboratories (GLP/WHO), and in Industrial Laboratories.
   [incorporated in "b" and "d" in job description, Annex No.2]
   July 12,1990
3 a. Problems of Storage and their Relationship to the Quality of Drugs.
   b. Good Storage Practices of Drugs (GSP) [Annex No. 3]
   July 15,1990.
4 The Analytical Problem and Quality Control of Drugs
   ["c" in job description, Annex No.4]
   July 18,1990.
5 Scientific methods of taking representative samples including:
   a. Statistical methods
   b. Professional pharmaceutical methods
   [incorporated in "b" in job description, Annex No.5]
   July 22,1990

II. IN HOUSE TRAINING OF LAB STAFF ON USE OF HPLC AND AMINO ACID ANALYSIS

["a" in Job description]

The HPLC instruments available at THAMECO consisted of the following:

- controller model 4030 Pye Unicam
- pump model 4011 Pye Unicam
- oven model 4031 Pye Unicam
- detector model 4020 Pye Unicam
- integrator model 4810 Spectra Physics

Columns

a. Sperisorb 5 ODS Pye Unicam
b. Partisil 10 silica Pye Unicam
c. Partisil ODS Pye Unicam
d. Lishrosorb RP18 10u Pye Unicam

On the first day of the writer's visit to THAMECO it was discovered that the detector of the HPLC instrument was broken owing to a fault in the thyrostore in the electronic unit. The maintenance department of Pye Unicam in Damascus promised to effect the necessary repairs or replacement within one week.

During this period the theoretical basis of chromatography, and HPLC in particular, were explained to the group/ team of HPLC. This group consisted of:

1. Miss H. Sayour, head of the research laboratory
2. Miss R. Nema, laboratory assistant
3. Miss L. Nader, laboratory assistant

Basic practical demonstrations and detailed steps were performed twice in front of the group, who were sometimes joined by 4th year Pharmacy students from the University of Damascus. The group was also supplemented by a number of QC and R&D personnel. These discussions were extremely helpful.

Once the detector was fixed and installed a suitable column was prepared, together with the solvents, and an analysis of "Flaminar cream" carried out.

"Flaminar cream" is a THAMECO product used for the treatment of inflammatory, allergic and pruriginous skin affections. (1 g of the cream contains 0.25 mg fluocinolone acetonide as the active constituent).

Results of the assay were within the accepted range and were repeated and reproduced several times.

The HPLC group headed by Miss Sayour exhibited a satisfactory degree of competence in operating the instrument.

After THAMECO's purchase of the HPLC instrument in 1986 Miss Sayour was trained by the representative of Pye Unicam for three days on its operation. She was given training in the preparation and choice of columns and solvents. These three days of training were supplemented by a week spent at the Pye Unicam training centre in Cambridge, U.K. where Miss Sayour received additional training in GC and HPLC. In 1987 a three day seminar was held at THAMECO, focusing on the training of operatives of the HPLC instrument. Miss Sayour had been an active participant during that seminar.

The writer observed and recommended the following:

a. the HPLC instrument was operated without a voltage stabiliser. When this was pointed out to the group they immediately recognized the importance of obtaining the stabiliser.

b. the electric current was usually turned off causing the programme of the integrator to be immediately erased. To avoid this problem it was deemed necessary that the internal back up batteries be routinely checked, or even better, that the instrument be connected to an UPS.

c. in the case of Miss Sayour being absent another qualified colleague should continue the work. The group therefore needs another qualified university trained pharmacist. The employment of two qualified university graduates would also allow them to discuss problems together. Since the HPLC is one of the few instruments that is constantly in use, in both QC and R & D laboratories it is particularly important that a qualified operative be available at all times. (Notes written in Arabic were distributed to the HPLC group and interested candidates covering the advantages of HPLC techniques, stationary phases, mobile phases, components of the instrument e.g. columns and packaging material, sample injectors, mobile phase pumping systems, detectors and recorders, in addition to covering preparation mechanisms, HPLC hardware components, QC and trouble shooting, quantitive and qualitative analyses of the chromatogram, safety and the do's and don'ts of HPLC technique.

In total about thirty-five hours were spent in the HPLC laboratory.

Amino Acid Analysis:

Dr Y. Hiba, Head of Formulated Food Department, mentioned that when THAMECO signed a contract in 1979 with Nestle Co., the Swiss company, to produce "Cerelac", Nestle did not stipulate that any amino acid analysis be carried

out. When in 1989, this contract expired and the product was renamed "Tamelac", the QC laboratories of the Formulated Food Department carried out analysis of the total nitrogen only, a WHO requirement, using the Kjeldahl method. This same method was also applied to "Thamerice" the second children's preparation THAMECO manufactures, There was no problem in the application of the Kjeldahl method.

At the same time, although there was an Amino Acid Analyzer in the department's QC laboratories (Beckman, Multichrom B, Liquid Column Chromagraph 1255) it had been out of order since 1980. The writer was informed that the instrument was in need of basic repair and maintenance. In addition, Dr. Hiba insisted that his department was not in need of the instrument, being perfectly satisfied with Kjeldahl method and apparatus. There was, in any case, no one in his department who could operate the Amino Acid Analyzer.

III. DEVELOPMENT OF ANALYTICAL METHODS ("e" in job description)

3.1

The Technical Committee of the Ministry of Health recently decided to cease the production of "Betazon Tablets", and produce instead "Metazone Tablets". Each tablet contains 0.5 mg dexamethazone.

The writer gave detailed practical steps on how to prepare a laboratory reference standard of dexamethazone, preparing it himself as example. The spectrophotometric method (UV) for the analysis of the tablets was used and gave satisfactory results.

3.2

Develop an assay method for Vitamin B_1 , in "Vitaplex Capsules" (a multivitamins preparation + Ca pantothenate + Ca glycerophosphate, Each capsule containing 25mg of vitamin B_1 .)

Results were improved by +9% and after modifying spectrophotometric method (visible) and the preparation of the sample for analysis, the results fell within the accepted range.

3.3

Develop an assay of vitamin B_6 in "Nitrosyl-B_6 capsules" (a preparation used for acute and chronic infections of the urinary tract. Each capsule contains 20 mg vitamin B_6 and nitrofurantoin).

Very good results were obtained both volumetrically and spectrophotometrically (visible).

3.4

Develop the assay method of erthromycin in "Erthrovit" (a veterinary preparation used for the prevention and treatment of chronic respiratory diseases, complex syndrome and periods of stress in poultry. Each 500 g powder contain 10.175 mg erthromycin activity together with vitamins).

Results were improved by about +10% to come within the accepted range.

3.5

A minor modification was suggested for the determination of total chlorides in "SMO-4" (an osmo-rehydration salt used for the treatment of dehydration in diarrhoea. Each sachet of 10 g contains 1.75 g sodium chloride and 0.75 g potassium chloride, sodium citrate and glucose). The preparation of the sample for analysis was also modified. The given results were excellent.

3.6

Suggest a modification for the assay of vitamin A in "Tamelac" (an enriched infant milk cereal. Each 100 g of powder contains 1030 IU Vitamin A, other vitamins, mineral salts and iron), and also to suggest a modification for the assay of vitamin A in "Thamerice" (an enriched rice cream for babies. Each 100 g powder contain 750 IU vitamin A, other vitamins, mineral salts and iron).

The developed method was a modification of the Carr-Price method, using glycerol 1,3 - dichlorohydrin (GDH) and anhydrous antimony trichloride $Sbcl_3$. Results were greatly improved to fall within the accepted range.

3.7

Suggested a very simple chemical method to differentiate between unlabelled cylinders of compressed nitrogen and compressed carbon dioxide (in Syria there are no regulations concerning the colour or shape of compressed gas cylinders). The cylinders differentiated by bubbling the gases through calcium hydroxide solution.

3.8

Advised, discussed and recommended that the best method for the assay of gentamcyin (as sulphate) injection in "Negamycin" preparation, each 2 ml ampoule of which contains 80 mg gentamycin sulphate, was the microbiological assay method. THAMECO was convinced by this suggestion and will follow the writer's advice.

3.9

Advised, discussed and recommended that the determination of vitamin B_{12} as a raw material is by UV spectrophotometric analysis, this being by far the most convenient and accurate method. The recommendation was accepted and will be applied,

3.10

"Urotofar" - effervescent granules used in the treatment of rheumatism, gout, gravel, pains and arteriosclerosis. Each 100 g contains 0.048 g theobromine and 4.38 g hexamine.

The writer was informed by the Technical Manager Mr.R. Chamaa that THAMECO was not satisfied with the way its product effervesced. After the licence from Archifar S.P.A., Milan, Italy, expired the manufacturing department attempted to modify its methods of production making minor changes in the quantities of ingredients, Though they claimed to have greatly its effervescing properties, the QC department was unable to reach acceptable results for the determination of theobromine and hexamine, A great deal of time and effort was spent achieving negligible results.

Mrs. W. Abdul Ghani and Mr M. Al-Mahmoud, the analysts who for many years had worked with this product achieving satisfactory results before the modifications in the manufacturing process, failed, after many trials and modified analytical methods, to reach an acceptable formula for the analysis of the preparation.

It was the conclusion of the writer that the modifications to the manufacturing process had rendered all methods of analysis impractical. The person responsible for the modifications to the manufacturing process was not available for comment, having resigned his post at THAMECO. The company was unable to contact him.

The writer suggested that during manufacture of the next batch, in-process quality control should be carried out step by step in order to ascertain just where the fault lay in the manufacturing process.

During discussions with the general technical and production managers concerning this problem, it was decided that this particular preparation was not profitable and that its production should cease.

The ten items above were all carried out under the writer's supervision in the QC laboratories, some of the steps actually being carried out by the writer himself.

3.11

Ramicol eye drops.

The writer was asked by Dr. Y. Nahlawy, Head of the Eye Drops Department, for advice concerning the filling and packaging processes of Ramicol Eye Drops, a 4% chloramphenical eye drop preparation. After watching the process closely the writer observed the following:

3.11.1

The filling process was not completed in a satisfactorily asceptic area, there being inadequate exposure to Laminar Flaw

3.11.2

After being automatically filled, bottles were closed manually with metal caps by staff who did not wear gloves, masks are head coverings.

3.11.3

Observation of particulate matters against strong light was completed poorly.

3.11.4

Bottles were neither washed nor sterilized before filling, though a number were exposed to dust.

All the processes criticised were immediately corrected according to the writer's recommendations. The only exception was that bottles were sterilized by heating without being washed.

IV. THE NEW FACILITIES OF THAMECO IN ALLEPO

On July 17, 1990, a one day visit to the new THAMECO facilities at Allepo was arranged. During this visit useful discussions were held with the construction staff, the electrical and civil engineers.

Allepo, Syria's second largest city, lies 360 km north of Damascus. The new plant comprises a total area of 100,000 square metres, of which the actual premises take up 20,000. The plant is located 20 km south of Allepo.

The total cost of the new plant will be approximately SUS 15 million, a figure including a loan from the French government of 18 million French Francs, earmarked for the establishment of a department of large volume parenterals. The total production of this department will be 4 million polyvinyl chloride (pvc) packages, each of 1 litre per year per shift of eight hours. The packages include:

a. Glucose solution
b. Sodium chloride solution
c. A mixture of both these solutions

The activities of the Allepo facilities will be fully co-ordinated with THAMECO's Damascus operation, and the new plant will be the only producer of large volume parenterals in the country.

The new plant is expected to be inaugurated during the first half of 1991.

Since it would, generally speaking, be both difficult and costly to institute acceptable levels of GMP, GLP and GSP at THAMECO's Damascus operation, it is firmly to be hoped that the new facility in Allepo will meet such requirements. To this end the writer strongly recommends that the committee responsible for scrutinizing the new plant should include an expert in GMP, GLP and GSP.

4.1
Observations and comments

4.1.1
The writer observed that the ceilings of the QC laboratories were too high, being of the same height as the manufacturing departments. Not only is this a waste of space, but it makes the air conditioning of the QC labs unnecessarily expensive.

4.1.2
The QC laboratories are situated across a corridor from production areas. Being in such close proximity to areas of production exposes the sensitive instruments necessary in the QC labs to large amounts of vibration. Whatever the precautions taken it would be impossible to fully eradicate the vibrations

caused by the heavy machinery used in production, and such vibrations can have only an adverse effect on the accuracy of the highly sensitive instruments used in the laboratory.

4.1.3
Water and gas pipes as well as electric wires are fixed outside the walls, forming a trap for dirt.

4.1.4
The central store, which should have tightly fitted windows and doors, to guard against incursions of insects, birds, virmin, dust and odour is insufficiently secure.

V. THE DEVELOPMENT OF THE PHARMACEUTICAL INDUSTRY IN SYRIA

Though both THAMECO, and its new plant at Allepo, and the DIMAS factory, are state owned, the government has since 1989 been attempting to encourage the private sector. In its attempt to liberalise restrictions on the private sector the government has issued a number of decrees, among which are:

5.1

Allowing the private sector permission to manufacture preparations which the public sector does not produce.

5.2

Allowing the private sector to enter into licensing agreements with foreign pharmaceutical companies to manufacture drugs, including technology transfer, and permitting the establishment of joint venture and companies.

5.3

On July 18, 1990 an agreement was signed between the Medical Syndicate of Syria (pharmacists, medical doctors and dentists) and ACDIMA / Amman, establishing a new pharmaceutical company to be called PHARCO. Expected to begin production early in 1993, the activities of this joint venture company will include:

5.3.1
The production and marketing of raw materials and medicinal plants.

5.3.2
The production and marketing of dosage forms, both national and under licence.

5.3.3
The encouragement of pharmaceutical research.

The capital of this company is divided between the Syrian Ministry of Health and the Medical Syndicate, who jointly hold 65%, and ACDIMA, which holds 35%. Total capitalization is approximately SUS 20 million.

5.3.4
The Syrian market is divided as follows:

THAMECO..... 40%
DIMAS..... 10%
Private Sector....10%
Imports..... 40%

5.3.5
Under new investment regulations three small private plants were inaugurated and started production in July, 1990. An additional ten private plants are under construction. The writer was told that the government issued too many licences for private plants.

5.3.6
In support of its policy of encouragement to the private sector the government increased the margin of permissible profit allowed to drug stores and pharmacies, and now routinely reviews drug prices.

In the writer's opinion the development of the pharmaceutical industry in Syria should depend on the manufacture of starting raw materials from natural resources such as petroleum products, minerals and medicinal plants. In Homs there already exists a petroleum refinery some of whose products could be used as starting materials or intermediates in the synthesis and production of some pharmaceutical starting raw materials.

In addition, the country possesses a wealth of medicinal flora, varying in habitat from the Mediterranean coast, mountains, deserts and valleys, with a variety of dry and humid climates. The writer recommends that the government adopts a screening programme covering all of Syria's flora and fauna.

Since there is a clear tendency towards expansion in the medicinal plant market worldwide, a tendency especially noticeable in the Middle East, the establishment and development of a pharmaceutical industry based on exploring the flora of Syria can only aid the development of Syria's pharmaceutical industry generally.

The writer strongly believes that Syria should develop its pharmaceutical industry by utilizing the nation's natural resources.

The development of the industry is, in addition, encouraged by the cooperation between it and other Arab pharmaceutical industries such as that of Egypt. The sharing of exchange visits, missions and of research results, such as those on bio-availability, can only serve to enhance the development of Syria's own pharmaceutical industry.

RECOMMENDATIONS

1. There must be very close co-operation and a strong relationship between UNIDO and THAMECO.

2. UNIDO should support THAMECO with technical assistance and in executing trustfund pharmaceutical projects. Since one of THAMECO's major problems is its lack of hard currency, UNDP/ UNIDO should endeavour to help THAMECO solve this problem.

3. THAMECO' s library should be provided with up to date periodicals, journals and text books covering all fields of pharmacy, including different Pharmacopoeias e.g. British, United States, European and International. Subscription to international pharmaceutical periodicals and journals is essential.

4. THAMECO must update its QC laboratories by purchasing modern instruments and apparatus since those presently in use are inadequate for advanced methods of analysis.

   Some equipment must be purchased over the next two years, the remainder to be bought within 2 - 5 years, depending on THAMECO's budget and priorities. After five years the THAMECO QC laboratories must be fully equipped with state of the art instruments and apparatus. Annex No.6, a list of instruments, covers chemical, physical, instrumental, microbiological, pharmacological, medicinal plant and natural product units need.

   Although the QC labs are both spacious and clean, THAMECO Damascus follows few if any of the requirements of GMP, GLP and GSP. It is to be hoped that this situation will be avoided in the Allepo branch of THAMECO.

5. Whilst equipping QC laboratories with the requisite, up to date instruments and apparatus, a specialised staff must be trained in their use and operation. The staff should be University graduates, and should receive training in the training centres of the companies from which the equipment and apparatus is bought. Additionally, they must be given the opportunity to visit the QC laboratories of the leading international pharmaceutical industries to observe and learn the systems of QC. Such visits should cover a period of between one and two weeks. Those whose knowledge of languages would be inadequate to benefit from such visits must visit relevant industries in the Arab world, e.g. Egypt.

   Fortunately a protocol signed between Egypt and Syria in Cairo on July 16, 1990 provides for mutual co-operation in the field of pharmaceuticals. It covers mutual recognition for the registration of drugs in both countries, co-operation in manufacturing raw materiales, QC and the specifications of pharmaceutical preparations and training. Some pharmacy students from Damascus University have already traveled to Egypt for summer training in

the Egyptian pharmaceutical industries.

In addition, the General Manager of THAMECO, Mr M. Koudsi, has already visited a number of pharmaceutical industries in Egypt and Alexandria as a member of the Syrian delegation that executed the protocol. THAMECO should take advantage of this protocol, arranging visits to branches of the Egyptian pharmaceutical industries, especially for those whose knowledge of foreign languages would render visits to other countries of minimal value.

6. The majority of production equipment is very old fashioned, some 75% of such equipment being over fifteen years old, even in departments such as the Formulated Food, the only department of its kind in the country. The modernization of production equipment is urgently needed.

7. THAMECO has nine study missions (fellowships) studying abroad, either in the Soviet Union or Eastern Europe. Yet THAMECO's staff still needs highly qualified candidates in all specializations. Presently there are only two members of the THAMECO staff holding Ph.Ds. THAMECO should arrange with staff from the Faculties of Pharmacy, Medicine and Veterinary Medicine, help in directing research and in solving problems.Such help could be arranged either contractually or through weekly visits. It would have the additional benefit of strengthening the ties between academia and industry that can only be useful in developing Syria's pharmaceutical industry.

Foreign experts should also be encouraged to visit THAMECO in order to give advice and help towards the solution of problems that might arise, though owing to language difficulties it is likely that such visits would cover a period of no more than one week.

8. A maintenance department should be established and staffed with qualified electronic engineers, in order to maintain and repair the instruments and apparatus necessary in the QC labs. When outside help is required to repair a machine, such help may take weeks to arrive, though the actual repair may take only five minutes as in the case of the HPLC instrument. This specialised unit could be incorporated in the main maintenance department of THAMECO.

9. At some time in the future it is necessary for the Ministry of Industry, who have jurisdiction over the pharmaceutical industry, and the Ministry of Health, to co-operate in establishing a training centre covering all aspects of the pharmaceutical industry.

10. In order to follow modern trends in the pharmaceutical industries it is necessary to radically reorganise the administration of THAMECO, establishing data base information and computer systems techniques. This needs to cover production, QC, administrative and documentation departments in both Damascus and Allepo.

11. System of self-inspection, an integral part of QA should be implemented at THAMECO. It is one of the cornerstones of raising the quality of products.

12. The quarantine store, which is presently some distance away from the general store, should be relocated so that all storage will be in one place, thereby minimizing the risks of any mix ups.

It is hoped that THAMECO staff, Damascus, will consider the twelve recommendations above and implement them within the next six months.

The implementation of these recommendations, together with those already mentioned in Chapter V, will aid the development of the pharmaceutical industry in Syria.

Annex No. 1

1.a. Good Practices in the Manufacture and Quality Control of Drugs. (GMP/WHO)

The lecture covered definitions of drug, manufacturing, starting materials, batch, batch number, quarantine, QC, and half-finished product. The duties and qualifications of personnel, specifications of premises, the design, place and maintenance of equipment and sanitary standards were explained.

Details of the manufacturing operations such as cleanliness, contents of equipment and containers, precautions against contamination, manufacturing batch records and the labelling and packaging of finished products were presented.

The importance of QC systems and the principal duties of QC departments and their responsibilities, together with the importance of self-inspection of pharmaceutical industries, were discussed.

1.b. Certification Scheme on the Quality of Pharmaceutical Products moving in International Commerce. (WHO)

The WHO has expressed concern that drugs intended for export are not always subjected to the same control procedures as those intended for the domestic market. In this area, developing countries, lacking the necessary laboratory facilities, are placed at a distinct disadvantage.

The objective of this particular Certificate is to provide a simple administrative mechanism whereby importing countries can:-

- obtain assurance that a given product has been authorized to be placed on the market in the exporting country and, if applicable, obtain information on the reasons for a product not being placed on the market of the exporting country.

- obtain assurance that the manufacturing plant in which the product is made is subject to inspection and conforms to the requirements of GMP recommended by WHO.

- exchange information on the implementation of inspection and controls exercised by the authorities in the exporting country. In the case of serious defects in the exporting or importing country such information and requests for enquiries may also be exchanged.

Certificates may be requested whenever a product is imported. They are of particular value when the manufacturer is unknown to the importing authority and when a drug is to be imported for the first time.

Annex No 2

Good Laboratory Practices in Governmental Drug Control Laboratories (GLP/WHO) and in Industrial Laboratories.

A governmental drug control laboratory is a laboratory maintained by the drug regulatory authority for carrying out the tests and assays required to establish that a drug conforms to the quality specifications claimed for it.

The organizational structure, staffing, system of incoming samples, details of analytical worksheet, specific tests and their evaluation, together with the importance of retention samples, were discussed.

Reageants, including solvents and water, their preparation, storage and containers, were discussed. The role of reference material, the importance of instruments and callibration, and the importance of safety in drug control laboratories were discussed.

A comparison between governmental and industrial QC laboratories was made.

Annex No. 3

3. a. Problems of Storage and their Relationship to the Quality of Drugs.

A necessary precondition in regulating the stability of drugs is to standardize their storage conditions. Controlling humidity and temperature is very important. All premises, areas and facilities connected with storage should comply with prescribed standards to protect the material from potentially harmful influences.

Storage areas, their sanitation, the process of receiving the incoming material, stock rotation and control (first in, first out) especially concerning expiry dated materials, were discussed.

3. b. Good Storage Practicis of Drugs (GSP)

Glossary of terms used e. g. storage, material, finished products, primary packaging material, printed packaging material, was presented. Qualifications of personnel, specifications of premises and facilities, and special storage conditions, were copiously explained.

Annex No.4

The Analytical Problem and Quality Control of Drugs.

Statistical analysis and interpretation of data together with the importance and significance of figures, were explained in detail. The difference between accuracy and precision, also the difference between determinatory and intermediate errors, was explained.

Mathematical examples were given to explain the difference between the absolute and relative error, also the average and standard deviation. Examples were presented concerning rejection quotients and confidence limits, according to the Dean and Dixon table.

The method of choice i.e. how does the analyst select the best method for the problem at hand? was discussed, giving detailed examples.

Annex No. 5

Scientific Methods of Taking Representative Samples.

5. a. Statistical methods
5. b. Professional pharmaceutical methods

Different methods of sampling were presented, how to use the table of random numbers together with the common techniques for obtaining a good sample from powdered material by "Coning and Quartering."

Sampling of finished pharmaceutical products, sterile products, capsules and tablets, was discussed, giving examples with emphasis on the importance of sample intervals.

Instruments and tools used in sampling were demonstrated with the help of visual aids.

Annex No. 6

LIST OF EQUIPMENT, INSTRUMENTS AND APPARATUS

(Chemical, Physical and Insrumental Units)

No.	General
1	Microbalance (five place) and balance table.
3	Analytical balance
3	Laboratory balance (top loading)
1	Refrigerator (with freezer compartment)
1	Water distillation still (10 litres/hour)
1	Water deionizing equipment (10 litres/ hour)
1	Drying oven
1	Vacuum oven
1	Oil vacuum pump (rotary)
10	Water vacuum pump
1	Muffle furnace
6	Heating Plates with magnetic stirrers
3	Mechanical stirrers
3	Vacuum rotary evaporator
10	Drying piston
6	Water bath (electrical)
3	Automatic titrimeter
1	Kjeldahl apparatus and micro
1	Mechanical shaker with adjustable rate of shaking (wrist action)
1	Centrifuge (table model)
1	Electric melting point apparatus
1	Electric freezing point apparatus
1	Equipment for TLC including - spreader

-spotting equipment
-developing chambers
-spraying bottles
-UV viewing lamps
-densitometer

1	Equipment for paper chromatography
1	Laboratory centrifuge (floor model)
6	Columns for chromatography
1	Ultrasonic cleaner
1	Vortex mixtures
5	Heating mantles for flasks (assorted sizes)
6	Variable transformers
1	Micrometer calipers
1	Glove box
1	Sieves with shaker (set)
1	Microscope
3	Blender
12	Apparatus for limit test for arsenic (B.P. & U.S.P.)
1	Platinum crucible and dish
3	Vibrospatula
1	Karl -Fisher titrator
3	Azeotropic distillation set
1	Solvent recovery apparatus

No.	Major (Instrumental)
1	IR spectrophotometer (recording, grating and acessories).
1	UV/Visible recording spectrophotometer, computer controlled.
1	UV/Visible spectrophotometer
1	Visible spectrophotometer (spectronic type)
1	Gas chromatograph
1	HPLC chromatograph and accessories
1	Polarimeter (manual)
1	Photocelectric polarimeter
1	Refractometer
1	pH-meter with electrodes
1	Antionic and cationic selective electrodes (set)
1	Disintegration test equipment
1	Dissolution test equipment
3	Oxygen flask combustion apparatus
2	Hydrometer
1	Viscometer
1	Ice machine
1	Solvent recovery apparatus
1	Atomic Absorption spectrometer
1	Flame photometer

1	Osmometer
1	Fluorometer (filter)
1	Hardness tester
1	Dehumidifier
1	Electrophoresis apparatus
1	Friability tester

Microbiological Unit

No	
1	Autoclave
1	Bacteriological microscope
2	Incubator
1	Centrifuge with refrigeration
1	Membrane filter assembly for sterility tests
1	Colony counter with magnifier
1	Laminar Flow bench
1	Hot-air sterilizer
1	Spectrophotometer, visible (simple model)
1	Nephelometer and turbidimeter
1	Refregerator
1	Deep-freezer
1	Large-plate microbiological assay equipment, including zone reader and recorder
1	pH-meter with electrodes
3	Blender
5	Zone magnifier for petri dishes
1	Zone projectors for large plates
1	Cleaning machines for glassware, especially one for cleaning pipettes
2	Water bath (thermostatically controlled)
1	Mechanical shaker with adjustable rate of shaking (wrist action)
6	Anaerobic jar

Pharmacological Unit

No	
1	Isolated organ bath
1	Polygraph
1	Artificial respiratory pump (large and small animals)
1	Physiograph with strain guage transducer
3	Mercury manometers (large and small)
1	Operation table (large animals)
1	Operation table (small animals)
1	Slow infusion pump
1	Electric balance

1	Centrifuge-small bench
1	Mecbanical shaker with adjustable rat of shaking
1	Photoelectric colorimeter
1	Hot air oven
1	Incubator
1	Temperature recording apparatus for pyrogern testing for rabbitts
1	Microscope
1	Stop watch
3	Anaesthetic boxes for cats and rabbits
1	Small animals weighing cages
1	Balance
1	Refrigerator
1	Guillotine
12	Syringes (different volumes)
	Polyethylene tubes

Medicinal Plants and Natural Products Unit

No	
1	Blance
1	Hammer mill with sieving arrangments
3	Percolator (glass)
3	Percolator (stainless steel)
1	Circulation pump
1	Vacuum pump
1	pH-meter with electrodes
1	Centrifuge table model
6	Contineous extraction apparatus (Soxhlet apparatus)
1	Vacuum oven
1	Muffle furnace
1	Microscope
1	Nuclear magnetic resonance (NMR)

Annexes Nos. 7, 8, 9 and 10

THAMECO is urgently in need of the following experts:

Annex No. 7

Job Description

Post title : Senior Computer Expert

Duration : 1 month

Duties : The expert must be capable of establishing an intergrated programme to serve the following:

a. establish a data base of the raw materials as well as finished pharmaceutical products, to include their names, suppliers, date of purchase, details of QA, manufacturing steps, name of quality controller etc.

b. establish a data base of information covering both suppliers and customers to aid proper purchase and scientific advertisement.

c. establish an electronic desk top publishing operation for the continuous supply of tailored, informative, as well as advertizing, materials.

Qualifications: A background in pharmacy, science or chemical engineering, At least 5 years experience in a pharmaceutical or chemical company, including experience of administrative computerization.

Language : English, A knowledge of Arabic would be a great advantage.

Annex No. 8

Job description

Post title : Senior pharmaceutical microbiologist

Duration : 1 month

Duties : The expert will be expected to:-

a- demonstrate experience in the design of heat stabilizers, including large volume pnrenterals.

b- be familiar with a range of industrial equipment, taking special account the various types of container that may be used.

c- possess experience in systems for the validation of sterilization processes in general, and those relevant to the sterilization of large bottled fluids in particular. The candidate must also possess a knowledge of the range of validation instruments covering physical and biological perameters.

d. have experience with in-procecs documentation and to be familiar with final product QC methodology and the co-ordinative procedures between production and the QC process.

e. experience with sterile supply approaches and systems would be an advantage.

Qualifications: Should be educucated to M.S. standard as a minimum, have considerable experience as a pharmaceutical microbiologist and possess at least seven years experience working with sterilization.

Language :English, a knowledge of Arabic would be great advantage.

Annex No. 9

Job description

Post title : Senior Expert in Instrumental Analysis

Duration : 2 months

Duties : The expert will be expected

a. to develop methods of analysis based on modern techniques (optical, electrical, chromotographic etc.)

b. develop methods of analyses through functional group analysis.

c. to predict stability and expiration dates.
d. establish the GMP rules in general and GLP in particular.
e. establish systems of self-inspection.
f. to train QC and R&D staff concerning the previously mentioned points.

Qualifications: A senior pharmaceutical chemist holding either an M.S. or Ph.D. A minimum of ten years experience in the field of instrumentation, and a thorough knowledge of GMP and GLP requirements is necesrary.
Languag : English, a knowledge of Arabic would be a great advantage.

Annex No, 10
Job description
Post title : Senior Expert in Tablet Coating
Duration : 1 month
Duties : The candidate will be expected to possess
a. experience in sugar coating
b. experience in film coating
c. experience in sustain release coating
d. the ability to train staff and to use:
- pan coating
- dry coating (dry cota and bi-cota)
- air supervision coating
- spray coating
e. experience in the QC of coated tablets, including the control of colour, appearance, tablet size, coating, friability, imprinting, in vitro and vivo testing, stability testing of the coated tablets and the bio-availability during the early stages of development and periodically during their routine production.

Qualifications: A snior pharmacist with at least seven years experience in tablet coating.
Language :English, a knowledge of Arabic would be a great advantage.

Annex No. 11
Contact list in THAMECO. (List of people met.)

Mr Maged Koudsi, B.S.Pharm.	General Manager.
Mr Riad Chamaa, B.S.Pharm.	Technical Manager.
Miss Fadia Bizre, B.S.Pharm.	Production Manager.
Dr. Bassam Kabani, Ph.D	R&D Manager.
Mr. Bassam Haffer, B.A	Planning Manager.
Dr. Yousef Hiba, Ph.D	Head of Formulated Foods Dept.
Mr. Yasser Nahlawy, B.S. Pharm.	Head of Eye Drops Dept.

Miss. Nahida Andoura, B.S. Pharm.	Head of Documentation and in-process control
Miss. Hanan Sayour, B.S. Pharm.	Head of Research Lab.
Miss. Sayour's team	
Mrs. Maysoon Ramadan, B.S. Biochem.	Head of QC Lab. for Raw Materials
Mrs. Wafaa Abdul-Ghani,B.S.Pharm.	QC Lab Analyst for dosage forms.
Mr. Mohamed Al Mohnuud, Dip.General Chem.	Assistent Chemical Engineer.

EXPLANATORY NOTES

1.	THAMECO	The Arabian Medical Company
2.	DIMAS	The General Establishment of Blood and Pharmaceutical Industries Company
3.	GMP	Good Practices in the Manufacture and Quality Control of Drugs
4.	WHO	World Health Organization
5.	GLP	Good Laboratory Practices in Governmental drug Control Laboratories
6.	GSP	Good Storage Practices of Drugs
7.	HPLC	High Performance Liquid Chromatography
8.	QC	Quality Control
9.	R&D	Research and Development
10.	GC	Gas Chromatography
11.	UPS	Uninterrupted Power Supply
12.	UV	Ultra Violet
13.	IR	Infra Red
14.	QA	Quality Assurance
15.	ACDIMA	The Arab Company for Drug Industries and Medical Appliances

one US dollar = 11.25 Syrian pounds "LS"