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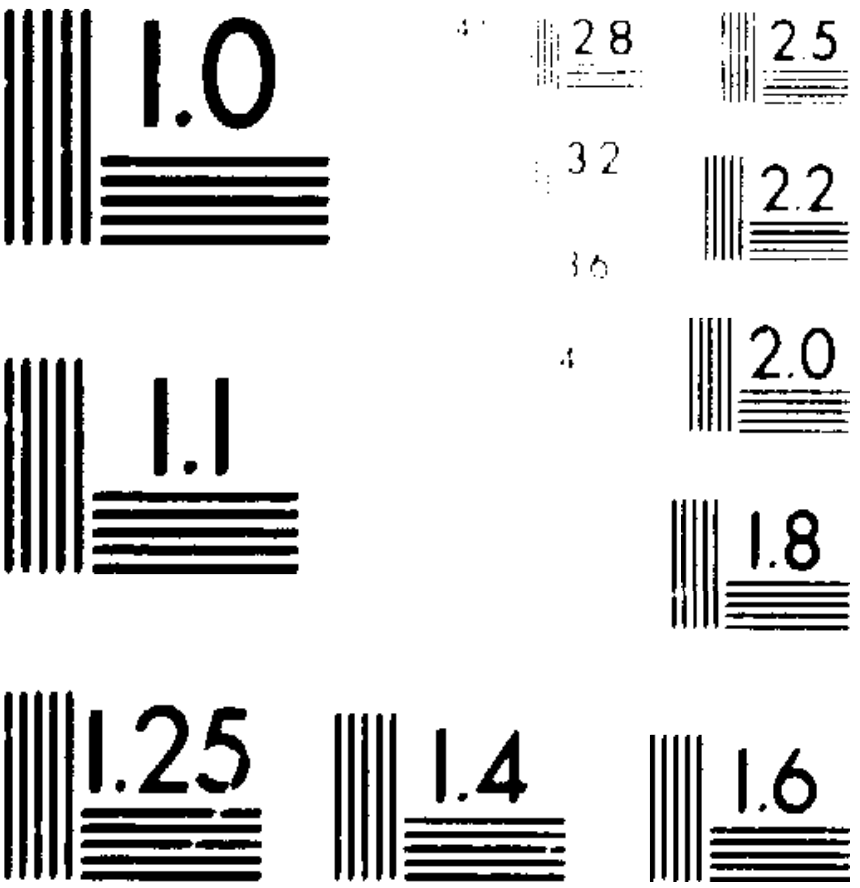

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Barbados.

ASSISTANCE IN THE DEVELOPMENT OF DRUG CONTROL ADMINISTRATION AND ESTABLISHMENT OF QUALITY CONTROL LABORATORY.

SI/BAR/83/801

BARBADOS

Terminal report*

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

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United Nations Industrial Development Organization
Vienna

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SUMMARY

The Government of Barbados has introduced a system of bulk purchasing of pharmaceutical dosage forms so as to economize in the cost of drugs. As a result, several foreign manufacturers, acting in the country through local distributors, tender for the supply of a variety of pharmaceutical products. A serious problem in this system is that drugs with generic names and in the same dosage form are offered with vast variation in prices. The variation may go up to tenfold or even more without any apparent reasons with regard to quality of the dosage forms offered.

The Government has established a Special Benefit Service which enables certain categories of people to avail specified drugs free of charge or at reduced cost. In both cases the balance of the prescription is paid by the Government. Having in mind the limited financial resources of the country, the question is that how drugs of high quality could be chosen within reasonable price when same pharmaceutical dosage forms under common generic name are offered by the tenderers at highly varying prices.

In absence of facilities for drug testing in the country, arrangements were made to send samples abroad for assessment. Unfortunately, because of unusual delays in receiving analytical reports, this arrangement also did not work successfully.

Accordingly, the Government planned for setting up a Drug Quality Control Laboratory within the existing Government Laboratory and requested UNIDO for technical assistance for this purpose in 1983.

The writer was assigned as a quality control expert to Bridgetown for three months under UNIDO expert assistance.

The emphasis of the project has been on determining training needs and equipment for carrying out all physical, chemical and microbiological testing of drugs.

Based on the available documentation, an illustrative list of priority drugs has been compiled. The above list of drugs is given in Annex I. An illustrative list of equipment has also been given which will be required for physical and chemical analysis of the priority drugs.

Procurement of drugs based on Tender Document is described on Page 6. All importers must provide manufacturers quality certificates with the supplies. At the present stage, however, this administrative requirement is the only measure for quality assurance.

One of the aims of mission was to make an assessment of the quality of drugs based on the available data. In absence of availability of any drug certification documents, assessment of the quality of drugs was attempted by merely visiting local public dispensaries and the local manufacturer. This investigatory survey raised doubts as to whether the drugs distributed over the country are of good quality, and whether any deterioration due to improper storage in the tropical climatic conditions has not taken place.

Survey of the existing facilities for the quality control of pharmaceuticals revealed the inadequacies for carrying out desired analytical tests. Laboratory rooms for physical and chemical testing of drugs are available but equipment and reference or standard active substances are lacking. Properly trained staff is also required at different technical levels.

It also appeared that there were no drug control inspection services operating in the country.

Under such inoperative situation it was not possible for the expert to carry out certain duties included in the job description, such as improving the efficiency of the laboratory and training the personnel.

Based on the above findings, recommendations have been made for follow-up in two phases:

1. In Phase I the Government should consider:

The possibility of equipping the dispensaries with air-conditioning units and refrigerators in order to store drugs under prescribed temperature and humidity. The staff should be instructed to keep the drugs listed in Annexes II and III under specified storage conditions.

The Government should,as far as possible, avoid purchasing certain specified drugs in economy-pack containers. The documents mentioned in the Tender Document must be presented by the tenderer at the time of supply of consignments.

It is also advisable to modify the procurement system of drugs until the existing programme for registration is implemented.

2. In Phase II the National Quality Control Laboratory should be strengthened by the required additional equipment and training. Initially, the laboratory would be equipped to carry out only physical and chemical tests of drug dosage forms and active substances involved. To establish microbiological and biological quality control sectors does not seem to be realistic at the moment and therefore, it should be deferred for the time being.

Registration of drugs is a pre-requisite but it will not fulfil its purpose adequately until the laboratory can start working smoothly and efficiently.

The establishment of inspection services is also recommended for which a specific training programme should be formulated and carried out.

INTRODUCTION

Barbados is a small island country in the South-Eastern Caribbean Sea with an area of 431 sq. km and a population of 250,000. About 40% of the total population live in the capital, Bridgetown. Over the past few decades in-depth studies have been carried out in the field of health care.

Some medicines are produced locally, but the pharmaceutical market greatly depends upon imports from extra-regional manufacturers. With the aim to improve the drug supply and to economize in the cost of prescribed drugs in both public and private sectors while ensuring the continuous availability of quality drugs of known therapeutic effectiveness, the Government established the Barbados Drug Service (BDS). The BDS, being a drug management and serive system, has three integrated service components:

a) Formulary System

b) Supply and Inventory System

c) Special Benefit System

Within the Formulary System, the Barbados National Drug Formulary has been edited and periodically revised, which provides information on indications, side-effects and dose ranges. Pricing and drugs covered by the Special Benefit System have also been included.

The Supply and Inventory Service contracts for drugs supply and computes the country's needs for the forthcoming contract period.

The Special Benefit System is designated to provide specified prescription drugs to certain categories of people either free or at reduced cost.

According to background information provided in the job description, the Drug Testing Unit of the Barbados Government Laboratory carries out quality control "to ascertain whether medicines conform with generally accepted standards" and the unit "plays a vital role in attaining quality assurance for all drugs offered on the Barbados market".

The above mentioned information, however, could not be substantiated. At present the existing unit neither carries out quality control nor plays any appreciable role in attaining quality assurance. It should be revitalized to play this role and that is the reason why the Government has secured UNIDO's assistance.

I. FINDINGS

1. Distribution of drugs

Most of the drug requirements are met through imports as there is only one local manufacturer who, incidentally, is also one of the major distributors of imports, representing numerous manufacturers from several countries. Drugs on the market may come from many of the 140 foreign manufacturers operating in the country through about 10 local distributors.x/

Having no warehousing facilities with the government, the imported stocks of drugs are retained in the suppliers' own warehouses and periodically delivered to the dispensaries by the suppliers' transport directly.

Drugs are sold both by public and private dispensaries (pharmacies). The public dispensaries sell only the drugs included in the National Drugs Formulary, and purchased by the government. The private dispensaries, on the other hand sell a variety of non-formulary drugs and also the drugs included in the formulary. The non-formulary drugs, however, are outside the purview of the government control system.

The proposed programme for registration of drugs has not yet been implemented due to inadequate funds and lack of trained staff.

2. Procurement of drugs

In order to bring down expenditure on drugs the Government introduced a system of bulk purchasing in economy-pack containers, subsequently to be repacked in dispensaries into smaller packaging units. In the above system a number of pharmaceutical firms with small international reputation are tendering for the market.

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x/ Barbados National Drug Formulary 1983.

Prices differ considerably amongst different bidders of same product and at time even up to tenfold or more[x/], thus creating serious problems for the Government to place order for the right quality product at most competitive price. Generally, the drugs are purchased out of lower price range offers. The cost of drugs purchased by the Government is about US$ 2,500,000 per year, as compared to about US$ 4,000,000 covered in the private sector.[xx/]

The Government purchases are made on annual basis and only for those drugs which have been selected by the Formulary Committee and published in the Barbados National Drug Formulary. The requirements of the domestic market is estimated, but Government purchases do not always cover the demand in full, the rest being covered by the private sector.

A deadline for the submission of tenders is fixed and the procurement of drugs is based on the Tender Document. The Drug Tender Committee, acting on behalf of the Barbados Drug Service, makes analysis of the tenders received and makes final selection of bidder with guarantee to purchase the amount of drug offered in the tender within a fixed contract period. Since the Government has no storage facilities of its own, the purchased drug is stored by the supplier and delivered to Government owned dispensaries as the demand arises.

The tenderer's only obligation is to fill in and sign the Tender Document and to give a statement that the contracted drugs meet the quality control requirements. The required documentation should theoretically be as follows:

a) in addition to internal manufacturing control, quality control testing of the product is certified by ... (company name and address to be filled in),

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x/ Drug Product List for Contract Period No. 5, July 1983 - June 1984.

xx/ Personal communication from the management of the Barbados Drug Service.

b) the governmental quality assurance assessment authorities in respect of the product ... (name and address to be filled in),

c) the product being tendered is approved for distribution and is sold in the country of origin. Only certified batches actually being so marked will be shipped to Barbados under the contract ... (signature needed),

d) all products shall

- meet the requirements of the legislation of Barbados concerning drugs, their quality and their control,
- meet the requirements of legislation of their country of origin for distribution,
- be formulated and produced in accordance with sound manufacturing practices,
- meet the requirements of the official reference stated, and otherwise shall meet the standards stipulated in B.P., B.P.C., U.S.P. or an acceptable international or official standards,
- meet whatever other specifications are stipulated in the Tender Document,

e) dated and even other products must have a minimum shelf life of not less than 24 months or three quarters of their legal shelf life on the the date of receipt of supplied in Barbados within contract period,

f) invoicing of product to a wholesaler shall be separately carried out by the supplier who will provide a certified copy to the Barbados Drug Service also showing quantity under supply, lot number and date of shipment,

g) documentation which may be requested from a supplier and which the supplier should agree to provide on request includes:

- a certificate of analysis of each product for which an acceptance of offer has been issued;
- a statement on the master formulation as a confidential information for the Formulary Committee.

According to the author's information suppliers do not deliver the above-mentioned documents regularly and the author was unable to have access to this documentation during his assignment.

The Tender Document for the Supply of Drugs covers the documentation required for registration purposes to a certain extent. The essential difference between the above two documentations, however, is that a supplier who wishes to register a drug is obliged to submit comprehensive documentation needed, while he is not under obligation to provide even part of the documentation during contracting for the supply of drugs. Contracting for the supply of drugs, thus in reality means merely registration of suppliers rather than registration of drugs.

3. Legislation of drugs

Legislation of drugs is described in "The Laws of Barbados Subsidiary Legislation" 1978, Vol. I, Cap. 44 entitled, "Health Services (Control of Drugs) Regulations" 1970. As it is stated there, each drug manufactured should be submitted to an analyst for such analyses and assay as the local authority may require. The drugs are allowed for sale after submitting the report of the analyses to the local authority.

According to information collected by the author the above-mentioned rule is not applied, especially in case of foreign suppliers.

The Chapter 44 also states that the specification for drugs should be according to B.P., B.P.C., Martindale Extra Pharmacopoeia, U.S.P., I.P., B.N.F. or the Canadian Formulary. If the specification for a drug differs from the above pharmacopoeias the specification given in B.P. should be considered to be standard for that drug.

In the author's opinion Martindale Extra Pharmacopoeia should not be considered as standard for drugs because it does not give the quality control test procedures to be used. B.P. appears to be the most appropriate standard for locally produced drug dosage forms while in the case of imported drugs B.P. and U.S.P. both should be considered as equivalent.

The legislation act mentioned previously does not include details on the registration of drugs. It neither contains any regulations concerning the importation of drugs nor regarding activities of suppliers on the local market. The act also provides no legislative basis for the activity of a national drug quality control laboratory.

The drug legislation in Barbados deals only with drugs manufactured locally and as such it is not comprehensive in character. The majority of drugs distributed in the country being of imported origin, the legislation should be modified and in the first instance to include procedure for compulsary registration for all suppliers. The scope of the activity of drug quality control laboratory should also be included.

The legislation act mentioned earlier provides the duties of inspectors. Inspectors may enter any place where drugs are manufactured, handled, stored or sold. They may examine drugs, take samples for analysis and examine documents and records.

At present no inspectors are operating in the field at all due to lack of properly trained staff and in absence of facilities to test the samples. Although, according to the legislation, the samples may be sent abroad (to Jamaica) for testing but this is not being carried cut efficiently and regularly.

4. Quality Control Laboratory

The Drug Quality Control Laboratory is part of the Government's Laboratory of the Ministry of Agriculture, and is subsidized by the Ministry of Health.

The laboratory is housed in a modern two-storey building constructed few years ago. The drug quality control section is on the first floor. (See its lay-out in Annex V.)

The laboratory consists of:

- two large typical laboratory rooms,
- one large instrumental analysis room,
- one large balance room,
- two rooms for administrative purposes, and
- a library located on the second floor/providing services to the entire Government's laboratory.

All the rooms are air-conditioned and regular control of humidity in the instrumental analysis room is maintained.

Equipment Available	Approximate age (years)
- spectrophotometers UV and IR	10
- atomic absorption apparatus	10
- high pressure liquid chromatograph	3
- gas liquid chromatograph	10
- tablet disintegration testing unit (according to B.P.)	10 (out of order)
- tablet disintegration testing unit (according to U.S.P. XX)	newly purchased
- dissolution testing unit (according to U.S.P. XX)	recently purchased
- pH meter	3 (out of order)
- thin layer and paper chromatography equipment	
- muffle furnace	
- centrifuge	
- balances	
- refrigerator	

Most of the available equipment is either old fashioned or out of order and requires replacement especially with regard to instrumental analysis.

Non-availability of reference standards is also a serious handicap in carrying out analyses of drug.

Staff

- graduate level: one staff graduate in pharmacy with Ph.D. in pharmacokinetics; appointed as acting Government Analyst and manages the entire Government's Laboratory.
- skilled worker (analyst): no staff is available.

In the present state, the laboratory is not capable of carrying out quality control of drugs due to inadequate equipment and non-availability of reference substances. In special cases drugs are sent abroad for quality control evaluation but on an extremely limited scale as the annual budget for quality control is only US$ 5.000, while the cost of single dissolution test and the determination of active ingredients is over US$ 300.

The main characteristics of the existing facilities of the quality control unit are as follows:

a) There are sufficient size rooms available to establish physical and chemical quality control sections.

b) The introduction of physical and chemical quality control requires training of personnel both at graduate and skilled workers levels.

c) Most of the equipment for physical and chemical quality control is to be rehabilitated or replaced.

d) The total floor space in the laboratory is not adequate for a full fledged quality control unit.

5. Assessment of the quality of drugs

Drugs for the open market are supplied only through private sector which is not obliged to provide any drug quality documentation. As it was previously mentioned, the Government actually carries out registration of suppliers while contracting for supply, in most cases, is done without proper documentation described in the Tender Document. The only possibility to assess the quality of drugs therefore was based on visiting local manufacturers and public dispensaries. The author has, however, ascertained the conditions of production, storage and dispensing in the country in considerable details.

5.1 Manufacturer's level

Carlisle Laboratories (with Collins Ltd., a sister company, as distributors) is the only local private manufacturer of pharmaceuticals and one of the major distributors who represents several foreign manufacturers. The firm employs about 27 persons and operates at 60 - 70 per cent of its production capacity. In accordance with the latest contract period[x/] Carlisle Laboratories supply the local market with several drugs, among which about 30 are amongst the most important group of drugs listed in Annex I. Products made by Carlisle Lab.[xx/] are listed in Annex IV. Collins Ltd. acts as distributor and exports drugs to neighbouring countries as well.

The production is based wholly on imported raw materials. There are no indications as to the standards of the quality of imported raw materials but even if they meet highest standards, the production conditions in any case do not meet the GMP requirements.

The Quality Control Laboratory is located far from GLP, is extremely poorly equipped and is merely capable of carrying out very simple, in-production

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x/ Drug Product List for Contract Period No. 5, July 1983 - June 1984

xx/ Catalo e of Medical Products of Carlisle Laboratories

analytical evaluations. There is no possibility to perform full quality control of raw materials, finished products, containers and to study the stability behaviour of drugs. According to explanation by the manufacturer, finished products are sent for evaluation to a laboratory in the United Kingdom. Upon receipt, the certificates of the analyses are submitted to the Barbados Drug Service, which permits the products to be distributed and sold after scrutiny of the certificates.

Storage conditions in the manufacturer's warehouse are unsatisfactory. Containers, raw materials and dosage forms are all stored in the same area with no air-conditioning and with no control of temperature and humidity. There is no provision to keep drugs in a cool place for materials requiring such storage.

Without any documentary evidence, especially with regard to the results of quality tests, it cannot be stated with full confidence that drugs produced locally are of proper quality. On the contrary, the quality becomes subject to doubts in view of the fact that production facilities are not of acceptable standards. Even if it is assumed that quality drugs have been actually manufactured, there is no certainty that they will retain the quality upon storage under inadequate warehousing. Same is the case with drugs from foreign manufacturers which are being stored in the same warehouse.

In order to ensure required qualities in the drug supplies, it is essential for the Government to establish inspection services and to install facilities to control the quality of drugs before they reach dispensaries.

5.2 Dispensaries' level

There are 15 public and about 50 private dispensaries, some located at various hospitals and clinical centres. Several private dispensaries are typical drug-stores selling a variety of other merchandise. The writer has visited only public dispensaries in Bridgetown as well as in rural areas. As

explained earlier, the dispensaries receive supplies of drugs directly from distributors by their own means of transport. The Barbados Drug Service records only requirements and expenses.

Professional staff of the dispensaries are qualified after completing a two years training in pharmacy at the Barbados Community College. They undergo a supervised "intership" for further six months before given independent charge of a dispensary.

Storage facilities are not available in every dispensary and even where the stores are provided these are not maintained at required temperature and humidity. Generally, the drugs are stored at temperature and humidity undesirable for certain drugs bearing specific storage conditions on their labels with respect to temperature and humidity.

The labels on the containers of drugs often do not provide full information required. They may not indicate either manufacturing date or expiry date or even lot number. Both dates, however, are inscribed on the containers of drugs sensitive to humidity, temperature or light, but still not indicating necessary information relating to storage conditions.

Generally, drugs marketed by well-known world manufacturers are more properly labelled. Precaution taken by one producer of high repute, against deteriorative high humidity, by providing the containers of tablets with humidity absorbing substance, deserves mention of appreciation and ethics.

It is doubtful, however, that imported drugs always come from reputable manufacturers; for instance, an injectable drug in ampoules was found with recommendation on the label to be stored in humidity not higher than 50%, an obviously irrelevant precaution.

Large containers are opened in dispensaries many times exposing the drug to high atmospheric moisture. It was observed that certain stocks of tablets had actually developed visible discoloration or undesirable odour due to deterioration caused by moisture.

Several kinds of tablets and capsules are re-packed from the large containers to small plastic bottles without ascertaining that the bottles meet the U.S.P. requirements for clasure airtightness and the walls impermeability to moisture. The bottles, colourless or amber, both are imported and although declaration on packing boxes claims that the bottles are airtight, no additional certification was provided with regard to conditions of usage. It was also noted that light-sensitive tablets re-packed in colourless bottles are stored without protection from day-light.

Each dispensary visited was equipped with a refrigerator of small size but, unfortunately, even the available limited refrigerated space was not used in full.

The author had no opportunity to visit private dispensaries. Nevertheless, according to the information obtained, the situation is not much different there either.

Inspection of dispensaries clearly showed improper storage conditions of pharmaceuticals. The conditions of storage greatly influence the quality of drugs. It should be realized that temperature of about 30°C and humidity of about 90% r.h. prevailing in the store are similar to the conditions employed to evaluate stability of pharmaceuticals in accelerated conditions.

If there is no instruction on the label of a drug as to how it is to be stored, it is supplier's responsibility to ensure that the drug will remain stable within the given expiry date under the climatic conditions of the destined country. But if there is a statement on a label to keep the drug in a cool and dry place, it is dispenser's duty to store the drug according to recommendation. The supplier is responsible for the quality of drugs only to the extent of original container but if the drug has been re-packed, the dispenser is responsible for subsequent quality.

The following steps should be undertaken in order to improve the situation:

a) providing the dispensaries with necessary facilities in order to store drugs at proper temperature and humidity,

b) providing the dispensaries with containers meeting the U.S.P. requirements,

c) educating the staff on importance of keeping the drugs according to instructions given on labels,

d) developing inspection services to control dispensaries,

e) establishing a quality control laboratory in order to control quality of drugs and containers used for re-packing,

f) implementing the registration of drugs in order to maintain control on the manufacturers, suppliers and supplies.

6. Illustrative List of Priority Drugs

Drugs purchased in relatively large quantities are of special concern for the Government because of a) high volume of expenditure; b) are often tendered by several suppliers, with great differences in price; c) some of them belong to the category of benefit drugs for which the Government bears partial cost to the consumer.

The drugs purchased in large quantities include drugs like diuretics, antihypertensives, antidiabetics, antiepileptics and cardiovasculars. In conformity with the Government's decision, the drugs belonging to the above groups, as well as some other drugs for which the demand is high, have been given priority. The list of priority drugs has been based on documents[x/] from the last three years, which illustrate the country's demand and specify the quantities purchased by the Government.

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x/ 1. Tendered Contract No. 3, October 1981 - June 1982

2. Drug Product List for Contract Period No. 4, July 1982 - June 1983

3. Drug Product List for Contract Period No. 5, July 1983 - June 1984

As it has been mentioned, the government sector does not always meet the demand for a given drug in full, the balance country requirements fulfilled by the private sector. Since the drugs for which the demand is highest are offered by several suppliers at widely different prices, the Government is interested in organising a drug quality control of its own. The task of such a laboratory would be, first of all, testing the quality of those drugs for which the demand is highest, in order to enable an appropriate selection of suppliers.

Bearing the above in mind, an illustrative list of priority drugs has been made to include those drugs for which the demand is highest and which are simultaneously offered by several suppliers. The list is given in Annex I.

It is evident from the documents on which the list is based, that there is considerably high demand for a large variety of tablets, and capsules pharmaceutical dosage forms. Injectable drugs and other dosage forms are needed in rather low quantities. Accordingly, the entries made in Annex I cover mainly tablets and capsules.

The drugs specified in Annex I numerically cover 7% of drug formulations purchased by the Government. Because of actual volume of consumption, however, the major part of financial resources is spent on them. It is evident from the documents that the drugs included in Annex I are offered by several suppliers, often as many as ten or more, all differing considerably in prices, even as much as tenfold or more. It seems that the suppliers are taking full advantage of the fact that the country has no facilities of its own for carrying out quality comparison of drug offered through the tenders.

To ensure that the drugs offered on the market are of proper quality, two essential measures should be simultaneously undertaken:

a) registration of drugs,

b) development of quality control.

Registration itself will certainly decrease the number of suppliers, but it must be accompanied by introduction of quality control which will enable to assess and compare the quality of the drugs offered.

The steps proposed above could cover at first the drugs listed in Annex I. It would require to institute only physical and chemical analyses as the tablets and capsules, the great majority of the dosage forms included in the list, do not require biological evaluation.

Microbiological and biological quality control of injectable drugs would be expensive to be implemented at the present stage. Nevertheless, injectable drugs and antibiotics could be partly covered by the quality control in terms of chemical and physical evaluations and instrumental analyses.

II. RECOMMENDATIONS

1. Immediate action (Phase I)

IMPROVEMENT OF DRUGS STORAGE CONDITIONS

Warehouses. The Government should influence local suppliers to improve storage conditions. It is not acceptable that drugs, raw materials and containers all are stored in the same space without any control of temperature and humidity. Stores should have separate, air-conditioned space with possibility of three separate storages with temperature ranges:

not higher than 8°C,

from 8°C - 15°C,

20°C - 25°C with controlled humidity.

Dispensaries. The Government should take steps to ensure the storage of different drugs according to instructions on labels. It is necessary to equip the dispensaries with air-conditioners and adequate size refrigerators. All drugs

requiring storage in a cool pace should be kept in temperature not higher than 15°C and drugs requiring storage in a cold place should be stored only in refrigerators.

The Government should influence private dispensaries to adopt similar measures to improve the storage conditions.

The staff in the dispensaries should pay more attention to proper storage of pharmaceuticals. They should be induced to fully utilize existing facilities in order to protect drugs requiring special care due to their unstable nature.

The staff should be oriented towards the necessity to repack light sensitive drugs only in light-resistant containers and to protect them from light during storage. Airtight containers should be used in case when a drug requires protection from atmospheric humidity. The containers should be purchased after ensuring that they meet the U.S.P. requirements concerning airtightness and moisture permeability.

The drugs listed in Annexes II and III include tablets and capsules, under generic names of active substances, which are of great importance for the country. Most of these drugs require special care during storage due to their susceptibility to moisture or light. The lists have been delivered to the Barbados Community College with suggestion to educate the students in this important aspect. It is recommended to deliver the lists to public and private dispensaries also for their benefit and reference purposes.

Economy - pack containers. It is recommended to purchase drugs in economy-pack containers always with suitable dessicant substance inside the containers.

Tablets and capsules more sensitive to humidity should be avoided from purchasing in economy-pack containers as far as possible.

The Government should review its policy of purchasing oral dosage forms in economy-pack containers basing the decision merely on lower price because the possibility of higher rate of deterioration and loss in the economy-pack may offset the savings made during purchases.

2. Long-term action (Phase II)

QUALITY CONTROL LABORATORY

It is recommended to strengthen the activities of Quality Control Laboratory at the earliest.

Role of the laboratory

a) Quality evaluation of active substances and dosage forms submitted for registration purposes.

b) Quality evaluation of drug dosage forms imported into the country.

c) Quality evaluation of samples of drug dosage forms drawn from suppliers' warehouses or dispensaries.

d) Quality evaluation of containers used for repacking.

e) Stability behaviour studies of drug dosage forms.

f) Training of students from Barbados Community College in order to inculcate the required proficiency in undertaking jobs in dispensaries and the laboratory.

Training needs

At least 3 staff graduated in pharmacy or in chemistry qualified from local university should be trained in analytical chemistry relating to quality control of drugs and dosage forms. They should be given both the theoretical basis as well as practical training in physical and chemical analytical procedures described in pharmacopoeias. The duration of training should be for at least 12 months in a suitable institution abroad.

Apart from 3 graduate persons, the laboratory will require at least 4 laboratory assistants. Those who have passed the Barbados Community College

would be acceptable after training in basic chemical and physical quality control of drugs. They should be trained through special courses for laboratory assistants in drug quality control. Another possibility is to train them directly at the drug quality control laboratories.

The above trained manpower is the pre-requisite for the laboratory to start operation. This staff would be able to train additional personnel according to growing future needs.

Equipment needs (illustrative list)

1. Spectrophotometer UV - visible, 190 - 600 nm wavelength (preferably with recorder)
2. Spectrophotometer IR, 4,000 - 450 cm^{-1} wavelength (preferably with recorder)
3. Polarograph
4. Karl Fischer moisture determination apparatus
5. Potentiometric titration unit for non-aqueous titration
6. PH - meter, pH range 0 - 14, digital readout, glass and calomel eletrodes
7. Column chromatography equipment according to U.S.P. specification
8. Polarimeter (digital readout)
9. Disintegration testing unit according to B.P. specification
10. Distilled - water unit, output about 5 l./hour
11. Standard sieves according to U.S.P. specification (1 set with mechanical shaker)
12. Melting point determination apparatus, range 0^{o} - $400^{o}C$, digital
13. Water - bath, electrically heated, six places
14. Electric shakers for flasks
15. Hot air oven for drying at $105^{o}C$
16. Vacuum oven with pump for drying at a pressure of 5 mm. Hg
17. Magnetic stirrers with hot plate

U.S.P. and B.P. Reference Substances

Books: the latest editions of the British Pharmacopoeia, the European Pharmacopoeia, the International Pharmacopoeia, the Code of Federal Regulations (quality control of antibiotics only)

The list mentioned above includes adequate equipment required for the laboratory to start operations. List of additional equipment required for subsequent expansion of analytical activities is given below:

1. Colorimeter
2. Polarizing microscope
3. Gas liquid chromatograph with recorder
4. Climatic chamber with constant temperature 37°C and relative humidity 75%
5. Hardness tester for tablets
6. Friability tester for tablets
7. Lamp for visual inspection of injectable drugs

The listed equipment will enable the laboratory to carry out full physical and chemical quality control of tablets and capsules, the most essential drugs for the country as identified in Annex I.

It is not recommended to implement microbiological and biological quality control for the time being. The expenses for additional equipment and training and cost of operation would not be feasible at the present stage, especially considering the fact that injectable drugs imported in the country are extremely low in quantities. There is also neither necessity nor possibility to develop microbiological assays for antibiotics. If the Code of Federal Regulations permits chemical and physical assays, this will be quite feasible in the presently recommended set-up of the laboratory.

It is recommended that for the time being the microbiological and biological tests like sterility tests, pyrogen tests, depressor tests, toxicity tests, if and when required, should be carried out by contracting such services abroad.

Future prospects

The next stage in expanding the scope of laboratory activities would be to initiate conducting sterility tests on parenteral products. It would require:

a) Two staff graduated from the Barbados Community College and additionally trained in microbiology, including sterility test techniques and standard procedures

b) One additional room, air-conditioned and with provision for installing filters for incoming air.

c) Equipment:

1. Laminar air-flc box
2. Autoclave
3. Incubators, water-heated with thermostat control
4. Hot air ovens
5. Necessary glassware for sterility tests

REGISTRATION OF DRUGS

It is recommended to the Government to implement the existing programme for registration of drugs as soon as possible. Applications for approval should be submitted to a Registration Service which could be developed within the Barbados Drug Service. The drugs accepted by the service only would be permitted by the Drug Tender Committee for purchasing purposes.

Drugs purchased by the Government and by the local private market, both should be covered by the registration rules and procedures.

The applicants should submit the following documents for each drug applied for registration:

a) A certificate of analysis of active substance with a clear statement as to the quality standards the substance meets;

a sample of the substance should also be submitted in sufficient quantity for carrying out full quality control;

the certificate should describe the identity, lot number, date of manufacture, date of quality control, release, name and address of manufacturer and name of person responsible for carrying out the tests.

b) A certificate of analysis of drug dosage form with a clear statement as to the quality standards the dosage form meets; if it does not conform to any pharmacopoeial or other recognized standards, full description of the analytical procedures and specifications should be provided;

a sample of the dosage form should also be submitted in sufficient quantity for carrying out full quality control;

the certificate should contain the product history data as described in Point a).

c) A certificate from the responsible health authorities of the country of origin that the drug is approved for distribution and sale in the country of origin.

d) Information on the countries to which the drug is exported; the export should be confirmed either by the importing country's representatives in the country of origin or by the responsible health authorities of the importing country.

e) Data on stability test: long-term storage test, severe-condition test, accelerated stability test.

Certification of stability tests should fully describe the kind of container used for packing. The data on stability tests can be accepted only if the container used during stability tests is the same as of the sample submitted for registration of the drug. If a drug does not require storage at lower temperature, the stability tests data should certify that the drug is not susceptible to higher temperature and the limit thereof.

In each case shelf-life should be clearly stated in the certificate and printed on the immediate label of the container.

f) Statement on complete information on formulation procedure of injectable drugs for the confidential records of the Registration Service and the Quality Control Laboratory should be provided. Even if the injectable drug meets the official standards, full analytical procedures should be delivered in order to confirm that additional substances, included in the drug, are also tested.

g) Declaration that flavouring and colouring agents added to oral dosage forms are officially approved for pharmaceutical purposes.

h) Results of bio-availability tests.

i) Results of acute and long-term toxicity studies.

j) Results of clinical trials carried out with the formulation.

PROCUREMENT SYSTEM OF DRUGS

Until the registration of drugs is implemented effectively the Drug Tender Committee must be provided with the documents described in the Tender Document, by the suppliers.

After the implementation, certificates a) and b) described previously should be attached with a sample of dosage form for quality test. Certificate b) should include a clear statement that the active substance used for the dosage form is the same as declared in the certificate a) (the same number of batch in both certificates).

Particular attention should be paid to containers. Containers presented for contracting purposes should be the same as registered, otherwise additional results of stability tests should be submitted.

INSPECTION SERVICES

To establish an effective quality control network within the country, inspection services should be implemented by the Government. The implementation is absolutely necessary due to effective role the inspectors would play in all steps previously recommended.

Four persons should be trained abroad in courses for pharmaceutical inspectors. Those who have passed the Barbados Community College would be adequately qualified for this training.

The role of inspectors can be clearly visualized in the light of their duties detailed below:

While visiting suppliers' warehouses the inspectors should inspect and ensure that:

a) drugs stocked are only those which have been registered,

b) stocks present are only of those origin which have been actually procured, by ascertaining that the number of batch is same as that under contract. The inspector should also audit the records and verify the certificates as required under the recommendation pertaining to procurement of drugs, and should take a double sample of drug for analytical evaluation,

c) drugs registered, but not under contract should correspond with the analytical certificates; if there are doubts with regard to quality, a double sample should be taken for analytical tests,

d) drugs are stored in accordance with recommendations,

e) all outer and inner containers are properly labelled and inscribed with the name of the product, batch number, date of manufacture, date of expiry, storage conditions, name of the manufacturer and the country of origin,

f) the batch number is identical on the containers, in the invoice and certificates of quality control,

g) labels of the individual containers have not been spoiled during transport.

While visiting dispensaries the inspectors would be obliged to ensure that:

a) drugs are only those which have been registered (concerns private dispensaries),

b) drugs are stored according to recommendations on the labels,

c) containers used for re-packing are those which have been tested and approved by the laboratory,

d) drugs are not kept beyond the limit of expiry date,

e) drugs are properly labelled.

In case of doubtful circumstances a sample of dosage form should be drawn for analytical evaluation.

ANNEX I

ILLUSTRATIVE LIST OF PRIORITY DRUGS*

GENERIC NOMENCLATURE	DOSAGE FORM	STRENGTH	REQUIREMENTS (000's) Contract Period 3	4	5
2. Analgesics, Antipyretics, Nonsteriodal Anti-inflammatory Drugs and Drugs Used to Treat Gout					
2.1 Non-opioids					
acetylsalicylic acid	tablet	300 mg	125	162.5	1,125
allopurinol	tablet	100 mg	10	49	50
diclofenac	tablet	25 mg (sodium salt)	7	95	180
paracetamol	tablet	500 mg	680	1,150	1,300
phenylbutazone	tablet	100 mg	375	450	450
5. Antiepileptics					
carbamazepine	tablet	100 mg, 200 mg	31.8	54.4	61
phenyltoin	capsule	100 mg (sodium salt)	150	100	170
primidone	tablet	250 mg	24	60	20
6. Antiinfective Drugs					
6.3 Antibacterial drugs					
6.3.1 Penicillins					
amoxicilline	capsule	250 mg	250	550	400
ampicillin	powder for injection in vial	250 mg, 500 mg (sodium salt)	7.6	7.4	6.7
phenoxymethylpenicillin	tablet	250 mg (potassium salt)	-	206	130

* The grouping system of the drugs employed in this list is in conformity to one used in Model List of Essential Drugs: WHO, 1983

GENERIC NOMENCLATURE	DOSAGE FORM	STRENGTH	REQUIREMENTS (000's) Contract Period		
			3	4	5
6.3.2 Other antibacterial drugs					
cefradine	capsule	500 mg	4.8	20	20
erythromycin	tablet	250 mg (stearate)	20	55	40
metronidazole	tablet	200 mg	5	12.5	62.5
sulfamethoxazole + trimethoprim	tablet	400 mg / 80 mg	130	125	200
tetracycline	capsule	250 mg (hydrochloride)	90	720	59
6.5 Antifungal drugs					
griseofulvin	tablet	125 mg / 250 mg	16	55.25	22.5
nystatin	pessary	100 000 IU	10	18	180
9. Antiparkinsonism Drugs					
benztropine	tablet	2 mg (mesylate)	325	300	300
10. Blood, Drugs affecting the					
10.1 Antianaemia drugs					
ferrous salt	tablet	equivalent to 65 mg iron (sulfate or fumarate)	60	190	25
ferrous salt + folic acid	tablet	65 mg / 200 mg	25	212.5	125
folic acid	tablet	5 mg	150	36	100
12. Cardiovascular Drugs					
12.1 Antianginal drugs					
dipyridamole	tablet	25 mg	1	70	80

GENERIC NOMENCLATURE	DOSAGE FORM	STRENGTH	REQUIREMENTS (000's) Contract Period		
			3	4	5
glyceryl trinitrate	tablet	0.5 mg (sublingual)	30	50	20
isoxsuprine	tablet	10 mg (hydrochloride)	10	40	15
12.2 Antiarrhytmic drugs					
propranolol	tablet	10 mg 40 mg 80 mg (hydrochloride)	215	135	323
12.3 Antihypertensive drugs					
guanethidine	tablet	10 mg 25 mg (monosulfate)	100	186	25
hydralazine	tablet	25 mg 50 mg (hydrochloride)	145	153	245
methyldopa	tablet	250 mg	600	500	200
metoprolol	tablet	50 mg 100 mg (tartrate)	32	167.5	80
reserpine	tablet	0.25 mg	24	75	24
reserpine + clopamid + dihydroergocristine	tablet	0.1 mg 5 mg 0.5 mg	40	300	350
12.4 Cardiac glycosides					
digoxin	tablet	0.125 mg 0.25 mg	63	348	180

GENERIC NOMENCLATURE	DOSAGE FORM	STRENGTH	REQUIREMENTS (000's) Contract Period 3	4	5
16. Diuretics					
bendrofluazide	tablet	5 mg	750	1,700	1,750
chlortalidone	tablet	50 mg 100 mg	5	33	-
furosemide	tablet	40 mg	200	237.5	300
spironolactone	tablet	25 mg 100 mg	-	36	20
triamterene + hydrochlorothiazide	tablet	50 mg 25 mg	15	50	140
17. Gastrointestinal Drugs					
17.1 Antacids and other antiulcer drugs					
aluminium hydroxide + magnesium hydroxide + simethicone	tablet	300 mg 100 mg 25 mg	48	200	275
cimetidine	tablet	600 mg	50	80	45
17.2 *Antiemetic drugs*					
metoclopramide	tablet	10 mg (hydrochloride)	10	30	16
prochlorperazine	tablet	5 mg (dimaleate)	11.5	95.5	25
17.4 Antispasmodic drugs					
propantheline	tablet	15 mg (bromide)	10	10	20

GENERIC NOMENCLATURE	DOSAGE FORM	STRENGTH	REQUIREMENTS (000's) Contract Period		
			3	4	5
17.6 Diarrhoea, drugs used in					
17.6.1 Antidiarrhoeal (symptomatic) drugs					
diphenoxylate + atropine	tablet	2.5 mg (hydrochloride) 0.025 mg (sulfate)	60	70	30
18. Hormones					
18.1 Adrenal hormones and synthetic substitutes					
betamethasone	tablet	0.5 mg	3	10	18
prednisolone	tablet	5 mg	25	120	120
18.3 Estrogens					
estrogens conjugated	tablet	0.3 mg 0.625 mg 1.25 mg 2.5 mg	-	-	63
18.4 Insulins and other antidiabetic agents					
insulin (different kinds)	injection	100 IU/ml in 10-ml vial	0.642	7.65	8.8
chlorpropamide	tablet	250 mg	950	240	500
glibenclamide	tablet	5 mg	50	125	325
metformin	tablet	500 mg (hydrochloride)	350	600	400
18.8 Thyroid hormones and antithyroid drugs					
carbimazol	tablet	5 mg	87.5	137.5	112.5
levothyroxine	tablet	0.1 mg (sodium salt)	25	700	45

GENERIC NOMENCLATURE	DOSAGE FORM	STRENGTH	REQUIREMENTS (000's) Contract Period 3	4	5
21. Ophtalmological Preparations					
21.6 Systemic preparations					
acetazolamide	tablet	250 mg	500	15	12
24. Psychotherapeutic Drugs					
amitryptyline	tablet	10 mg 25 mg (hydrochloride)	140	90	57
chlordiazepoxide	capsule	5 mg 10 mg 25 mg (hydrochloride)	44	4	8.5
chlorpromazine	tablet	25 mg 50 mg 100 mg (hydrochloride)	423	425	408
diazepam	tablet	2 mg 5 mg 10 mg	200	340	190
fluphenazine	tablet	1 mg (hydrochloride)	1.5	10	4
haloperidol	tablet	1.5 mg	160	220	150
lithium carbonate	capsule	300 mg	60	130	55
lorazepam	tablet	1 mg	10	50	17.5
nitrazepam	tablet	5 mg	75	85	155
perphenazine	tablet	4 mg	3	5	10
phenobarbitone	tablet	15 mg 30 mg 60 mg	177	93	132
thioridazine	tablet	10 mg 25 mg 50 mg 100 mg (hydrochloride)	40	27	20

GENERIC NOMENCLATURE	DOSAGE FORM	STRENGTH	REQUIREMENTS (000's) Contract Period 3	4	5
trifluorperazine	tablet	1 mg 5 mg (hydrochloride)	150	305	350
25. Respiratory Tract, Drugs Acting on the					
25.1 Antiasthmatic drugs					
salbutamol	tablet	4 mg (sulfate)	137.5	325	250
triprolidine + pseudoephedrine	tablet	2.5 mg 60 mg (hydrochloride)	10	11	80
26. Solutions Correcting Water, Eletrolyte and Acid-base Disturbances					
26.1 Oral					
potassium chloride	tablet to be solved	600 mg	290	550	285
27. Vitamins and Minerals					
ascorbic acid	tablet	50 mg	275	120	210
vitamin multi:	tablet		487.5	600	450
ascorbic acid		50 mg			
cyanocobalamin		3 mcg			
nicotinamide		20 mg			
pyridoxine		1 mg (hydrochloride)			
riboflavin		3 mg			
thiamine		10 mg (hydrochloride)			

GENERIC NOMENCLATURE	DOSAGE FORM	STRENGTH	REQUIREMENTS (000's) Contract Period		
			3	4	5
vitamin multi with minerals:	tablet		250	900	500
ascorbic acid		100 mg			
cyanocobalamin		3 mcg			
dexpanthenol		2 mg			
ergocalciferol		400 IU			
folic acid		2 mg			
nicotinamide		20 mg			
pyridoxine		3 mg (hydrochloride)			
retinol		6000 IU			
riboflavin		3 mg			
thiamine		3 mg (hydrochloride)			
calcium carbonate		500 mg			
copper		0.5 mg			
ferrous fumarate		200 mg			
fluorine		15 mcg (sodium fluoride)			
iodine		75 mcg (sodium iodide)			
magnesium		3 mg (magnesium oxide)			
manganese		0.5 mg (manganous sulfate)			
molybdenum		0.1 mg (sodium molybdate)			
potassium		2.5 mg (potassium sulfate)			
zinc		0.5 mg (zinc sulfate)			

ANNEX II

List of active substances
Tablets and capsules of which should be kept in light-resistant containers and protected from day-light

Ascorbic acid

Chlorpromazine

Diazepam

Diphenoxylate + atropine

Furosemide

Gryceryl trinitrate

Haloperidol

Metronidazole

Nitrazepam

Nystatin

Prochlorperazine

Propranolol

Reserpine

Reserpine + clopamide + dihydroergocristine

Salbutamol

Spironolactone

Tetracycline

Thyroxine

Triamterene + hydrochlorothiazide

Triprolidyne + pseudoephedrine

Vitamins multi

Vitamins multi + minerals

ANNEX III

List of active substances
Tablets and capsules of which should be kept in air-tight containers

Ascorbic acid

Acetylsalicylic acid

Amoxicilline

Carbamazepine

Cefradine

Cloxacillin

Diazepam

Digoxin

Erythromycin stearate

Ferrous fumarate

Ferrous fumarate + folic acid

Fluphenazine

Furosemide

Glyceryl trinitrate

Griseofulvin

Haloperidol

Hydralazine

Izoxsuprine

Paracetamol

Phenoxymethylpeniccilin

Perphenazine

Phenylbutazone

Phenytoin

Potassium hudrochloride

Reserpine

Reserpine + clopamide + dihydroergocristine

Spironolactone

Tetracycline

Triamterene + hydrochlorothiazide

Triprolidyne + pseudoephedrine

Vitamins multi

Vitamins multi + minerals

ANNEX IV

Approximate layout of the existing Quality Control Laboratory