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DEVELOPMENT OF PHARMACEUTICAL QUALITY CONTROL AND MANUFACTURE

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LIBERIA .

Technical report: Feasibility of establishing a pharmaceutical Quality Control Laboratory*

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

Based on the work of William Hewitt,
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United Nations Industrial Development Organization
Vienna

Contents.

		page
	Summary	4
1	Introduction	7
1.1	Terms of reference	7
1.2	The country	8
2	Medicines legislation	8
3	Import of drugs	9
3.1	The public sector	10
3.1.1	Health facilities	10
3.1.2	Availability of drugs	10
3.1.3	Sources and costs of drugs	10
3.1.4	Handling and storage of drugs	10
3.1.5	The condition of drugs	13
3.2	The private sector	14
3.2.1	Prices of drugs in the private sector	15
3.2.2	Drug depots of the private sector	16
4	Distribution of drugs	16
4.1	The public sector	17
4.2	The mission and industrial health establishments	17
4.3	The private sector	18
5	Pharmaceutical manpower and education	18
6	Drug utilization and misuse	19
7	A proposed medicines policy	20
7.1	Legislation and enforcement	21
7.2	Evaluation and licencing of medicines	23
7.3	Assessment and licencing of manufacturers	24
7.4	Inspection	25
7.5	A laboratory for testing medicines	26
7.5.1	General functions of a pharmaceutical testing laboratory	26

7.5.2	Pharmaceutical testing	27
7.5.3	Laboratory facilities and personnel requirements	28
7.5.4	The laboratory's mandate	29
8	Prospects for pharmaceutical manufacture in Liberia	30
8.1	A tentative programme for public/private sector collaboration	30
8.2	The economics of local production	32
8.3	Proposals concerning pharmaceutical manufacture in Liberia	33
8.4	External quality surveillance of pharmaceutical manufacture	34
9	Pharmaceutical production, - a preliminary cost forecast	34
9.1	Pharmaceutical products that might be manufactured in Liberia	35
9.2	Possible capital costs and production capacities	35
10	Proposed structure for a Pharmacy Administration	35
11	Planning a laboratory for Liberia	36
11.1	The need for phasing of development	40
11.2	Proposed organizational structure and phasing of development	41
12	Estimated operating costs, quality surveillance	41
12.1	Sources of income for the Laboratory and Pharmacy Administration's regulatory role	43
13	Location of the manufacturing/laboratory complex	45
14	Summary of cost forecasts	46
15	Summary of recommendations	46
16	Acknowledgements	48
	References	49

Figure 1	Administrative structure of the Pharmacy Administration	50
Figure 2	Administrative Structure of the Pharmaceutical Quality Control Laboratory	51
Table 1	Analysis of tender data (i)	52
Table 2	Analysis of tender data (ii)	54
Table 3	Analysis of prices of drugs	55
Table 4	Comparison of selected tender prices with overall prices	57
Table 5	Comparison of wholesale prices, Liberia and Britain	58
Table 6	Products that might be manufactured in Liberia	60
Table 7	Manufacture ir Liberia, - pre-feasibility study estimates of capacity and costs	61
Table 8	Staffing and possible salary structure for the Pharmacy Administration	62
Table 9	Phasing of development of the Pharmaceutical Quality Control Laboratory	63
Table 10	Staffing and possible salary structure for the Pharmaceutical Quality Control Laboratory	64
Table 11	Scheme for allocation of costs of analytical services	65
Table 12	Costs of operating the Quality Control Laboratory	66
Table 13	Costs of operating the Pharmacy Administration	67
Annex 1	Licencing of medicines	68
Annex 2	Pre-feasibility study estimates of costs of equipment for pharmaceutical manufacture	80
Annex 3	A proposed intravenous fluids plant	82
Annex 4	A programme for transfer of technology and training	84
Annex 5	Phasing of expenditure on laboratory equipment	86

Summary.

Liberia is at present entirely dependent on imports for all medicines used in the country. Recognising the likelyhood that deteriorated or otherwise substandard drugs would some-times reach the consumer, the Government of Liberia requested assistance from UNIDO for a study regarding the feasibility of establishing a pharmaceutical quality control laboratory. Such a study was undertaken late in 1980. The essential findings are summarized here.

Drugs are imported from numerous sources, mainly in Western and Eastern Europe. Many of these sources are major manufacturers enjoying a high reputation for the quality of their products. However, there are also suppliers who are not well known and some of these appear not to be manufacturers, but wholesalers. Thus, the actual origin of the drugs may not be known to the purchaser. The standard of packing and/or poor physical appearance of some drugs, coupled in some cases with extremely low prices, gives real cause for concern as to quality. Quite apart from their quality, for medicines to be effective and for their potentially harmful side effects to be minimised, it is essential that they be prescribed and used in a rational manner. There is, however, much evidence of widespread uninformed, carefree self-medication often involving the use of potent drugs in Liberia. Despite regulations restricting the availability of such drugs, they are freely available from pharmacies, and some even from street hawkers. This is a problem perhaps of even greater gravity than that of quality. Clearly, the government should aim to have at its disposition a means of effectively regulating both the quality and usage of medicines.

A pharmaceutical quality control laboratory can contribute to the upgrading of the quality of medicines only if it functions within an appropriate legal and administrative framework. Whilst the necessary enabling legislation has been enacted and some progress made in implementation, Liberia has not yet established the required administrative framework. This report outlines a proposed medicines policy and the regulatory and advisory features of a Pharmacy Administration which include :

evaluation and licencing of medicines and their suppliers,

inspection of all places where medicines are sold or handled,

laboratory testing of medicines,

drug information services.

To establish such a Pharmacy Administration, even though there might be substantial aid from donor agencies, would entail

government expenditure on salaries for professional and support staff and general operating services. In present financial circumstances and in the forseeable future, there seems little chance that the government would accord any priority to such a "non productive" project viewed in isolation. The idea has been conceived, however, of a project in which the manufacture of a small range of widely used drugs would be coupled with a laboratory having the dual functions of providing direct quality control services to the manufacturing operation and carrying out the surveillance of imported products within the framework of a Pharmacy Administration. A small medicines tax could provide the financial support needed for operating the regulatory and advisory functions of the Pharmacy Administration that have been described.

The savings that could accrue from a well managed local manufact-uring enterprise may well be more than the medicines tax. However, it is stressed that such a project could only be an economic success with competent management which would ensure aa high enough degree of plant and personnel utilization and would inspire all concerned with an awareness of the need to maintain a reputation for quality.

A tentative structure for the project, which it appears could be supported by the National Investment Commission's Small and Medium Business Department, has been developed. A central body (which might be a public corporation) would assist in production planning and provide certain services to perhaps three or four independent production units. The services provided by the central body would include quality control, engineering maintenance, warehousing and security. It could also procure the raw materials and packaging materials. Its laboratory would provide the analytical services needed by the Pharmacy Administration on an annual fee basis. The individual production units would not be competitors, but would each specialize in defined product ranges, for example, intravenous fluids. tablets, oral rehydration salts and non-sterile liquids.

Premises and also perhaps basic plant might be owned by the central body and leased to the production units. The central body would guarantee a market for basic drugs for the government and perhaps other health services, at realistic prices. In return, the individual production units would undertake to provide the goods in the required quantity, of the required quality, at the agreed time. They would be free to use spare capacity and acquire additional capacity to manufacture more lucrative products for the private sector market subject to the same overall quality control system.

The production units would operate on normal commercial lines but would have the advantage of a guaranteed minimum market. The central body, however, would operate on a minimal profit basis with accumulated profits being diverted towards improving health services, for example, by the provision of mobile dispensaries for the rural areas.

Some minimum production capacities envisaged at this juncture are :

intravenous fluids	150,000 litres
liquid preparations (non sterile)	300,000 litres
tablets	120 million

Pre-feasibility study estimates indicate that the cost of buildings, service installations and plant for the entire manufacturing, warehousing and quality control facilities would be about $1,600,000. Total costs including building of premises for the Pharmacy Administration, additional feasibility studies, transfer of technology including fellow-ships and consultancy have been estimated as about $3,500,000.

More precise estimates have been made for the cost of the quality control operation. The annual running cost of a laboratory having the functions that have been outlined and the scale of operations envisaged is estimated to be about $250,000. The amount payable by the Pharmacy Administration for the examination of about 1000 samples annually in its market surveillance programme would be about $96,000. The total cost of running the regulatory and advisory functions of the Pharmacy Administration has been estimated as about $270,000 annually. Finance for the Pharmacy Administration could be provided by means of fees for Product Licences and Manufacturer's Licences as well as a tax levied on all medicines, imported and locally manufactured. The required sum, $270,000 amounts to just 3% of the expected CIF value of medicines imports for 1981, i.e., 3% of $9,000,000.

It is recommended that a second study be undertaken to develop further the concept of the production/quality control complex so as to assess the real production needs and arrive at true estimates for capital expenditure and thence ex factory costs of the medicines that would be produced. Meanwhile, as soon as the decision to go ahead has been taken, a start should be made on initial recruitment and training of Directors Designate for the Quality Contol Laboratory and Pharmacy Administration.

1. Introduction. Liberia is entirely dependent on imports for medicines used in the government health services, mission and industrial hospitals and in the private sector. These imported medicines arise from numerous sources in many countries. In some cases they are supplied by wholesalers and the actual manufacturer is not known to the purchaser. The possibility of substandard medicines being imported is clear. Moeover, due to the severe climatic conditions sometimes pertaining in Liberia, there is a serious danger that some medicines will deteriorate if not stored under proper conditions.

The government, being aware of these dangers, requested assistance from UNIDO for a feasibility study having the object of preparing the ground for the establishment of a quality control laboratory which would play its part in protecting the public by detecting sub-standard medicines.

1.1 Terms of reference. The formal terms of reference required the consultant to carry out the following activities :

(i) To assess the pharmaceutical products available in Liberia, their correlation with public health, their prices at national and at international level and the feasibility of establishing a Central Quality Control Laboratory.

(ii) To suggest a suitable location for the laboratory giving details of building requirements and different sections to be established within the laboratory.

(iii) To work out the details of facilities required including number, qualifications and responsibilities of staff, recommended equipment for carrying out analysis including chemical, microbiological and pharmacological evaluation of products along with technical specifications and estimates of cost.

(iv) To formulate a training programme for personnel to run the laboratory.

(v) To prepare a final report, setting out the findings of his mission and his recommendations to the Government on further action that might be taken.

A laboratory cannot be considered in isolation. To have any impact at all on the quality of medicines, it must function within an appropriate legal and administrative framework that enables it to examine the right samples

for the right purpose, to have its work capacity properly utilized and follow-up action to be taken when unsatisfactory medicines are discovered. Such a framework does not yet exist in Liberia. Hence, it became apparent at an early stage of the mission that the terms of reference should be widened so as to include all aspects of quality control by the regulatory authority. Also, as will be explained in section 8 of this report, due to financial constraints, the quality control function had to be considered in the context of an overall programme of development including pharmaceutical processing in Liberia.

For drugs to be effective and free from undue hazard, it is not sufficient only that their quality be assured, it is also necessary that they be used in a rational manner. For this reason, comment will be made on prescribing and self medication.

1.2 The country. Liberia has an area of about 110,000 square kilometres. It is located on the south west coast of the western bulge of the African continent. It has a coastline of about 550 kilometres and in some places extends about 300 kilometres inland. The capital, Monrovia, lies at a latitude of 6° N and a longitude of 11° W. In 1977 it was estimated that the population was about 1.75 million and the literacy rate only 20%, a fact of significance so far as the correct usage of medicines is concerned. The population of Monrovia is around 200,000. The climate is warm and often very humid.

2 Medicines legislation. Chapter 67 of the Public Health Law deals specifically with Pharmacy. This was published in November 1977 and ended with the statement : "This Act shall become effective upon publication". Briefly, the Act regulates the licencing of pharmacists, dispensers, pharmacies, registered medicine stores, wholesalers and manufacturers. All thses terms are defined and certain licence fees are specified.

It is required that every retail pharmacy, every wholesaler and the pharmacies of hospitals having more than 100 beds be under the direct supervision of a licenced pharmacist at all times when pharmaceutical services are being rendered. The Act established the Liberian Pharmacy Board consisting of six members of which four are pharmacists. The purpose of the Board is to assist the Minister on matters concerning the practice of pharmacy, the licencing of pharmacists and dispensers wishing to practise in Liberia.

The Board conducts written examinations for such pharmacists and dispensers which are obligatory regardless of oversees qualifications.

The licencing of individual medicinal products is not specifically prescribed in Chapter 67; however, it does include the statement that "The Board,...,shall regulate and control the sale, distribution, character and standard of drugs, medicines, poisons and therapeutic devices". Section 43.4 of the Act requires that the Liberian Pharmacy Board "Shall promulgate a catalogue based on quality of drugs...which may be imported into the Republic, classified under their generic names, with brand names if any, and names and addresses of manufacturers". Thus, there is in existence a legal basis for the licencing of medicines.

Section 43.1 of the Public Health Law requires the establishment of a Liberian Drug Register which would define categories of drugs and the manner in which they may be legally supplied to consumers. These categories are :

category A	Prescription drugs and medical preparations.
category B	Non-prescription drugs and medical preparations dispensable by licenced pharmacies.
category C	Non-prescription drugs and medical preparations dispensable by registered medicines stores.
category D	Unrestricted drugs and medicalpreparations that may be safely sold in any establishment.

Such a drug register has been established but there is ample evidence that its provisions are not enforced, and indeed are unenforceable in present circumstances.

3. Import of drugs. There is no local manufacture of medicines and so all must be imported. Records of the Ministry of Planning and Economic Affairs show that under the heading "541, Medicinal and Pharmaceutical Products", goods to the value of US $8.3 million approximately were imported in 1978. These were mainly from Europe, with Britain as the main supplier providing 39.6% of the whole. It is therefore logical to make comparisons between the Liberian and British prices of individual items.

3.1 The public sector. The National Medical Supply Depot of the Ministry of Health and Social Welfare is responsible for the supply to the Health Facilities of the Government of Liberia of all their medical needs. The Chief Pharmacist is responsible for the day to day operations of the Depot and reports to an Advisory Committee. The Depot has four active Departments :

Procurement,

Financial Management,

Requisition and Distribution,

Stock Management.

The Depot's constitution provides for a fifth Department, Pharmaceutical Manufacturing and Repackaging of Drugs. However, such a section has not yet been established.

3.1.1 Health facilities. The National Medical Supply Depot provides drugs to the following Government establishments :

hospitals	15
health centres	24
health posts/clinics	227

Additionally, three Mission Hospitals purchase their requirements fron the Depot.

3.1.2 Availability of drugs. A Formulary Committee prepared in 1979 a proposed Drug Formulary. The present catalogue of the National Medical Supply Depot lists nearly 400 drug items in accordance with the formulary. The formulary was prepared taking into consideration the World Health Organization's publication, "The Selection of Essential Drugs",(1). It may be noted that Liberia contributed to the development of the Model List of Drugs that is included in this WHO publication. Thus, there is every reason to suppose that the range of drugs procured by the National Medical Supply Depot corresponds to the true needs of Liberia. Unfortunately, due to financial constraints, drugs are not always available in the quantities needed. It was observed that several commonly used drugs had not been available in the J. F. Kennedy Hospital for a period of around one month.

3.1.3 Sources and costs of drugs. A study of the sources of drugs and their costs was carried out. The writer was priviliged to examine the summary of bids received in

response to a request for quotations for the supply of nearly 300 items in May 1980. In the case of 20 of these items, bids were examined in detail and the conclusions are presented here in table 1. Data on the successful bidders and the proportion of the order they were awarded is summarized in table 2. Although it must be added that due to lack of funds, not all of these items could be ordered, it is not felt that this detracts from the value of the exercise which has thrown light on purchasing policy. Additionally, detailed information on all purchases of a second list of drugs was kindly provided by the National Medical Supply Depot covering a period of almost two years. This data is summarized in table 3. Nine items were common to both lists of 20 drugs and so a comparison of the tender price and the overall (weighted mean*) price is presented in table 4 where also British wholesale prices are shown for comparison.

The results of these studies are now discussed. First, considering the tender, 73 companies made successful bids. Amongst these were many major internationally known companies of North Americal and Western Europe, the state owned corporations of Eastern Europe and China, the non-profit agency, the Intenational Dispensary Association (IDA) of Amsterdam as well as many companies previously unknown to the consultant including a few from his own country. The prices offered for an individual item sometimes ranged tremendously. For example, in the case of metronidazole tablets, 200mg, the highest bid was 93 times that of the lowest ! It was, incidentally, almost 4 times the British wholesale price for the best known branded product. As a guide to the evaluation of prices, in table 1 the following information is given :

lowest price,

highest price,

median price,

IDA price (either its tender bid or catalogue price).

The IDA price is given because this is a non profit foundation, and so its prices may be taken as some indication of what is a realistically low price for a drug of reasonable quality. Perusal of table 1

* Weighted mean price of a specified pack size of an item is obtained by dividing the total cost of all purchases of that pack by the number of packs.

reveals that in 6 cases out of the 20, the lowest bid was not accepted, presumably due to lack of confidence in the bidder. Prices accepted were invariably lower, and usually very much lower than the UK and Liberian wholesale prices.

The total value of bids accepted was, in round figures, US $889,000. The distribution of this sum between the 73 successful bidders is summarized briefly in table 2 from which it will be seen that the individual shares of 45 of these were less than 1% of the whole and totalled only US $140,000 or 15.7% of the whole. (In fact many of these individual shares were less than 0.1%). This is of considerable significance from the point of view of quality control, since some degree of evaluation/ surveillance of products and their suppliers is called for even though the volume of their sales may be quite small. A further 27 suppliers secured 68% of the total, and one supplier, the International Dispensary Association of Amsterdam secured 16.3%.

The reputation of the supplier provides some degree of assurance as to the quality of the product. Indeed, for a country not having its own quality assurance system nor access to a laboratory overseas, this is the only criterion available to it. Suppliers known by repute to the consultant were 26 in all. Their share of the total was about US $400,000 or 45%. Of the other 47 suppliers, there will undoubtedly be some that are very reliable. However, the poorly packaged products of some manufacturers and physically deteriorated tablets and capsules seen in stores, together with the exceptionally low prices sometimes offered, gives cause for real concern. Some observations on the condition of drugs seen in Liberia are presented in section 3.1.5 of this report.

3.1.4 Handling and storage of drugs. The storage area for drugs of the National Medical Supply Depot consists of a warehouse of concrete construction approximately 36 metres long, 15 metres wide and 6 or 7 metres high. It has a smooth cement floor and a corrugated iron roof. There were four individual air conditioning units but only two of these were working. The consultant visited the store on two occasions. The temperature could not be ascertained. On the first occasion the store was distinctly warm, but on the second occasion, early in the morning, it seemed quite cool.

There were shelves for individual packs and small outers. Larger outers were placed on the floor. It was clear that the outer packaging used by some suppliers was inadequate to withstand the rigours of the journey to Monrovia. For example, intravenous fluids originating from two major manufacturers and contained in 500ml and 1 litre plastics containers, had been repacked in open wooden boxes because the original cartons had been severely damaged in transit. Labels on bottles of benzyl benzoate application had deteriorated badly, apparently through exposure to rain.

The Chief Pharmacist has made proposals for improvement of the building by installation of a suspended ceiling so as to avoid the heating effect of the sun's rays on the metal roof; and also the replacement of the existing air conditioners by one central air conditioner. Funds have not yet been made available for implementation of these proposals. Although the facilities are not at present satisfactory, it is suggested that some improvements could be achieved by sorting and segregating the obviously unsatisfactory, and restacking the apparently satisfactory products in such a manner as to avoid further exposure to unhygienic conditions.

The stock room of the pharmacy of J.F. Kennedy Hospital was air conditioned and storage conditions appeared to be reasonably satisfactory.

3.1.5 The condition of drugs. On visiting storage depots, the majority of drugs that were seen appeared, on visual inspection, to be satisfactory. The comments that follow, therefore, refer to a substantial minority that on visual inspection alone, appeared to be of doubtful integrity.

At the National Medical Supply Depot the following were observed:

Intravenous fluids, - some rectangular plastics bottles were mis-shapen, suggesting exposure to excessive heat during rough handling, - labels were in Spanish only, in contravention of regulations of the Pharmacy Board of Liberia. Other containers had variable quantities of liquid in them and some were obviously leaking, - application of pressure resulted in a fine jet of liquid being ejected. The main danger is probably from the not-so-obviously leaking containers that may have become bacteriologically contaminated.

Thioridazine tablets 50mg. Two batches from the same manufacturer were seen. These were not sugar coated. One batch had a satisfactory polished appearance, the other was powdery, - a clear case of inconsistency in standards.

Amobarbital capsules 200mg. The lid of the can was rusty. The capsules were packed in a polythene bag within the can. Some of them had become badly discoloured.

The thioridazine tablets and amobarbital capsules were from the same manufacturer whose standard of packaging was generally rather poor.

Propranolol tablets 40mg. The name of the product was wrongly spelled on the label as "propanolol". One is bound to wonder as to the degree of control in manufacture and packing operations when such an error can occur.

Ascorbic acid tablets 200mg. Tablets were light brown in colour.

Several products were seen that had either passed or were close to their nominal expiry dates. In view of the adverse conditions sometimes pertaining in the store, it seemed likely that many of these would be substandard.

In the J. F. Kennedy Hospital Pharmacy, the following examples of substandard drugs were seen :

Ethambutol tablets 400mg. These were of brown speckled appearance. They had been supplied by one of the non-profit procurement agencies. The actual manufacturer was not named on the label nor was the date of production or an expiry date given.

Calcium lactate tablets. These were crumbling, - not a serious fault from the patient's point of view in this particular case. However, this product was of a manufacturer whose standards of packaging was generally rather poor and has been mentioned earlier in connection with thioridazine tablets and amobarbital capsules.

3.2 <u>The private sector</u>. There are three major importers of drugs. They are :

Clave's Pharmaceutical Inc.,

Glaxo Liberia Limited,

Mohan's Medical (Liberia) Limited.

Clave's Pharmaceutical Inc. purchases drugs from about 54 suppliers and also some surgical items and cosmetics. Under the same ownership are five retail pharmacies of which three are in Monrovia and two in the provinces. Imported products are sold by the Wholesale Division to Government Institutions, the industrial hospitals and clinics, the Clave's Pharmacy Group and other retail outlets.

Glaxo Liberia Limited has in the past acted as a general importer of pharmaceuticals. However, present policy is to deal only in products of the Glaxo Group of companies.

Mohan's Medical (Liberia) Limited purchases drugs from 29 main suppliers as well as surgical items and some generic drugs from other sources. The company also has two retail outlets. The company's catalogue lists about 600 medicinal items.

The exact value of medicines imported by these three companies is not known. However, from informal comments made by managements, it seems that the total might be around US $2½ million.

In addition to the main importers, at least a further 13 of the mainly retail pharmacies import drugs and have in some cases, sole agencies of well known international companies. The consultant visited six of the smaller importers

The general impression of the import business was that a good proportion of drugs arose from reliable sources. There were also however, many apparently worthless medicines, for example, a "fortified blood tonic" of European origin, specially packed for the African market. Perhaps of greatest cause for concern are the generic drugs obtained from little-known companies. They are what may be termed "serious drugs", for example antibiotics and other prescription only items. Their quality is of much greater importance than that of a "blood tonic".

3.2.1 Prices of drugs in the private sector. Wholesale prices in Liberia for a selected range of drugs have been compared with British wholesale prices. British prices were chosen as a basis for comparison for two main reasons. Britain is the largest single supplier of drugs to Liberia (see section 3 of this report). British prices are probably amongst the lowest in Western Europe. Wholesale British prices have been

taken from the Chemist and Druggist Price List for December 1980. These are the prices normally paid by retail pharmacies in Britain for drugs that are to be supplied to patients under the National Health Service scheme. In table 5 a comparison is made of the prices of 16 generic drugs and/or their brand versions, as well as four branded drugs having two or more active components.

From table 5 it may be seen that of the 23 comparisons, the Liberian and UK prices are about the same in 5 cases (plus or minus 10%). The Liberian price is less in 9 cases and substantially greater in 8 cases. It may be noted that the prices of products of Hoffman Laroche, which have been imported from Switzerland are generally high. The same products sold in Britain are made by the British subsidiary for the home market only. With the exception of these Swiss products, wholesale prices in Liberia seem quite reasonable by European standards.

Since the vast majority of drugs imported for the private sector are of Western European origin (reflecting the public's preferences) the comparison with Western European prices is logical. It is nevertheless, pertinent to note that in certain countries having a substantial drug industry and strong government control, prices are very much lower. Examples are Egypt, India and Turkey. In Sri Lanka too, even though pharmaceutical industry is not well developed, prices are low since all imports are by the State Pharmaceuticals Corporation, a government monopoly.

As regards retail prices, in both Britain and Liberia the retailer normally adds 50%.

3.2.2 Drug depots of the private sector. The depots of two of the major importers were visited. In both cases those parts of the premises in which drugs were stored were air-conditioned and the temperature seemed to be satisfactory. Products were stocked in an orderly manner.

4. Distribution of drugs. Drugs reach the consumer through three legitimate routes. These are :

The public sector, - government hospitals and health centres etc.

The mission and industrial hospitals, clinics etc.

The private sector, - retail pharmacies, registered medicines stores and other outlets as authorised by law for certain simple medicines.

4.1 The public sector. The Health Facilities of the Government of Liberia that are supplied with drugs by the National Medical Supply Depot include :

Hospitals	15
Health centres	24
Health posts/clinics	227

4.2 The mission and industrial health establishments. There are several missions and industrial/mining enterprises throughout the country that have established hospitals and other health facilities. These include the Catholic Hospital in Monrovia, the ELWA Hospital on the outskirts of Monrovia, the Bong Mines Hospital, Lamco Health Services and the Firestone Medical Services. Some idea of the scale of the facilities of the industrial health services may be gained from a consideration of the Firestone operations. The Firestone Rubber Plantation employs about 15,000 persons but its health services cater for the needs of a total of 70,000 employees and their dependents, - about 4% of the entire population of Liberia. In addition to the Medical Centre, which is in fact a hospital, there are two Regional Health Centres equipped to carry out minor surgical operations, and 42 clinics. The depot of the main Medical Centre carries on average a stock of drugs valued at $125,000. Annual consumption of intravenous fluids was said to be not less than $60,000 per annum. Many of the drugs were purchased locally and brands seen on shelves in the depot reflected the same variety of sources as had been seen in retail pharmacies and government establishments.

It is understood that Lamco health facilities are on an even bigger scale than those of Firestone. Their annual consumption of drugs is said to amount to about 2.5 to 3 million US dollars annually, i.e. about 30% of Liberia's entire drug bill.

4.3 The private sector. The Pharmacy Board of Liberia has published a directory of Pharmacies and Medicines Stores. The edition dated November 1980 shows that there are 32 pharmacies, of which only 4 are located outside Monrovia. Of 91 registerd medicines stores, 11 are in Monrovia and 80 arelocated throughout all counties and territories of the country. In the cases of only 3 of the Monrovia pharmacies and one provincial pharmacy, pharmacists had not been appointed at the time of publication of the register. Thus, in this respect, good progress has been made towards implementation of legal requirements. However, pharmacists are not always in attendance when pharmaceutical services are rendered.

5 Pharmaceutical manpower and education. The Directory of Pharmacies and Medicines Stores published by the Pharmacy Board of Liberia in November 1980 showed that there were 38 pharmacists registered in Liberia, of which 10 were Liberian nationals. There were over 90 registered dispensers.

There has been under consideration for several years a proposal to establish a School of Pharmacy in Liberia which might also serve neighbouring countries. A study carried out in 1979 indicated that there was no possibility of Liberia producing more pharmacists than it needs. However, the study did not go so far as to estimate the cost of training of pharmacists, nor did it establish that the pharmacists graduating could be absorbed. (It is necessary to distinguish between a country's needs and what it can afford to pay for).

In the opinion of the writer, the idea of training high calibre pharmacy technicians to meet the real needs of general practice pharmacy, particularly in the rural areas, has much to commend it, since there are many aspects of the training of graduate pharmacists that have little relevence to the every day problems of a pharmaceutical dispensing service. However, such a policy appears not to be favoured in Liberia. It is suggested, therefore, that pharmaceutical education in Liberia, when it is established, should be to general degree standard only and should be orientated particularly towards general practice pharmacy, i.e. hospital and retail pharmacy. The syllabus might be devised in collaboration with an overseas school so as to facilitate recognition of the general degree course as satisfying the requirements of the overseas School in part fulfillment of its

conditions for enrolment for further studies leading to an honours degree. Liberian graduates would then be able to proceed to study specialised subjects such as pharmaceutical technology, quality control or microbiology which would be relevent to the hoped for developments in manufacture and quality control.

6 Drug utilization and misuse. Three factors combine to facilitate the misuse of drugs in Liberia. These are :

The absence of an effective regulatory authority,

The ready availability of potent drugs.

The paucity of professional and sub-professional health personnel to prescribe drugs correctly or to advise on their correct usage.

There is ample evidence of widespread uninformed, carefree self medication, often involving the use of potent drugs. Tetracycline, for example, is one of the drugs that may be purchased from street hawkers in the market area of Monrovia.

It is understood that "prescriptions" may be written by nurses, medical students, dressers etc. and that these may be quite lacking in specific information as to nature, strength and dosage.

It was observed that pharmacists and dispensers play a part in reducing to some extent the ill-advised use of drugs. This is to be commended and the further development of this role should be encouraged. However, there is much room for improvement.

It appears that topical corticosteroids may be purchased without prescription. Dipyrone and chloramphenicol are freely available. It is pertinent to quote from "The Extra Pharmacopoeia, Martindale" on the dangers and limitations of these two drugs :

> "Dipyrone. Toxic effects, as for amidopyrine, i.e. The risk of agranulocytosis in patients taking (dipyrone) is sufficiently great as to render this drug unsuitable for use. Onset of agranulocytosis may be sudden and unpredictable. ..... Of 960 patients treated with amidopyrine there were 11 cases of agranulocytosis. Uses, its use is justified only in serious or life threatening situations where no alternative antipyretic is available or suitable."

"Chloramphenicol. Toxic effects, the most serious toxic effect of chloramphenicol is its depression of the bone marrow which can take two forms. (The first is not reproduced here). The second and apparently unrelated form of bone marrow toxicity is severe, irreversible and often fatal aplastic anaemia which is reported to have an incidence of 1 in 20,000 to 1 in 100,000. Uses. The liability of chloramphenicol to provoke life threatening toxic effects, particularly bone marrow aplasia, severely limits its clinical usefulness. It should never be given for minor infections and regular blood estimations should be made during treatment. Typhoid fever and similar salmonellal infections are the prime indications for the use of chloramphenicol ....".

Possible methods of controlling such drugs are suggested in section 7.1 of this report.

7 A proposed medicines policy. The ultimate objectives of any realistic medicines policy must include the following :

(i) Medicines must be effective. i.e. of proven therapeutic value and proper pharmaceutical quality.

(ii) Medicines must be free from undue hazards and side effects in relation to the severity of the condition that is to be treated.

(iii) Medicines must be used in a rational manner so that they may achieve their potential beneficial effects and that undue hazards/ side effects may be minimised.

(iv) Medicines must be available to all who need them at a realistic cost, whether to the government or the individual patient.

To make progress towards achieving these objectives, a comprehensive administrative machinery is needed. This machinery must function to regulate commerce in medicines; to provide information on medicines and their uses/hazards, as is appropriate for the health professions and the general public; and to ensure that medicines are available, properly presented to the patient/consumer, are of the required quality and a realistic price. The term "realistic price" is

intended to convey the idea of a price that takes into consideration the legitimate interests of both vendor and purchaser. A price has to be paid for quality and it is, therefore, not necessarily in the interests of the patient to use the cheapest drugs.

The necessary administrative machine will ne referred to henceforth as the "Pharmacy Administration". The main branches of the Pharmacy Administration that are relevent to the present study are :

Legal and enforcement section, including an inspectorate.

Medicines evaluation and licencing section.

Drug information services section.

Medical supplies procurement section.

Pharmaceutical testing laboratory.

7.1 Legislation and enforcement. In section 2 of this report, mention has been made of the Liberian Drug Register which defines legal categories of drugs, the retail outlets from which they may be supplied and the manner in which they may be obtained, e.g., whether a prescription written by a registered medical practitioner is required. Prerequisites for the successful application of such a regulatory system are that the country has adequate professional and sub-professional health manpower to operate it and that the regulatory authority has an effective means of monitoring compliance. Only four pharmacies serve the estimated 1½ million people who live outside Monrovia, i.e., outside Monrovia there are only four private sector establishments that may legally supply "drugs and medical appliances" of categories A and B. The Ministry of Health and Social Welfare has no means of monitoring commerce in these areas. Clearly, until such time as the present regulations can be enforced, they should be suspended and replaced by some system that endeavours to offer some degree of protection to the public yet permits them to obtain legally the medicines that they need.

Of fundamental importance for the success of any scheme that may be devised, is a sense of responsibility and self-discipline on the part of the participating health personnel. To devise a scheme appropriate to the circumstances pertaining in Liberia will not be an easy task. Perhaps the World Health Organization could offer assistance based on experience gained in other

developing countries. The foundation would then be laid for the more rational and less dangerous use of drugs. One specific proposal only will be made here on this topic, that is the establishment of a "hospital use only" category of medicine. This might be the logical classification for oral chloramphenicol products. Dipyrone, if its use is to be sanctioned at all, should clearly be restricted to this category.

Concerning the quality of drugs, adequate standards are readily available in the many National and Regional Pharmacopoeias and the International Pharmacopoeia. (see also section 7.5.2). Standards for products not described in such pharmacopoeias, - the many proprietary medicines, should eventually be laid down in a specification forming part of the Product Licence (see section 7.2). Meanwhile, general standards may be related to the label declaration of content. The recognition of pharmacopoeial or general standards may be embodied in the legislation together with a code of practices for the handling and storage of drugs which may be based on the World Health Organization's publications :

Good Practices in the Manufacture and Quality Control of Drugs (2)

Quality Assurance in Pharmaceutical Supply Systems (3)

With such standards and codes given legal status, the inspectorate (see section 7.4) and the quality control laboratory (see section 7.5) would then have reference points by which to determine whether there had been a transgression of the law. Legislation should prescribe the action that may be taken by the Pharmacy Administration. It should define penalties and make provision for the confiscation of, or recall from the market of drugs found to be sufficiently defective as to warrant such action.

It is recommended that a Legal and Enforcement Section be established at an early stage in the development of a Pharmacy Administration. Ideally, it would be headed by a person having qualifications in both pharmacy and law. Its functions would be to review existing legislation and prepare draft revisions when circumstances appeared to warrant any change, to plan and participate in inspections and sampling of medicines, and to take appropriate action when products or pharmaceutical practices failed to meet the required standards.

7.2 Evaluation and licencing of medicines. The thorough evaluation of medicines is a major task which it would be unrealistic for any small nation to undertake alone. However, a workable evaluation and licencing system can be established at modest cost by taking into consideration the decisions of licencing authorities in the major pharmaceutical manufacturing countries. The licencing authority of the country of the drug's origin can be asked to provide a "free sale certificate", i.e. a document stating that the products has been approved for sale in the country that is offering to export it. It would then remain for the Liberian authority to ensure that the product as offered for sale in Liberia was adequately packaged to withstand local climatic conditions, and that labels, cartons, package inserts and any other promotional literature included the same indications for use, warnings of side effects and contra-indications as appeared on/with the product as offered in the country of origin. (There is evidence that this is not always the case and that export literature gives more indications for use and less warnings and contra-indications).

Based on experience in another small developing country, a simple scheme for the evaluation of medicines and their manufacturers, and for licencing, is proposed for Liberia. Its essential features would be applied in three phases of which the first gives a useful measure of control, and, because of its simplicity, can be implemented during a period of as little as one year.

The three phases are :

(i) Initial screening of all products currently marketed, based on an evaluation of a minimum level of data that is already available to the importer. When the result of the evaluation is satisfactory, an "Interim Product Licence" having a validity of three years is issued.

(ii) Screening of manufacturers based on information given by the applicant in accordance with a questionaire, as well as any other information available to the licencing authority. A "Manufacturer's Licence" would be granted to those applicants providing satisfactory answers and believed to be operating in accordance with a code of "Good Manufacturing Practices". (see also section 7.3).

(iii) Rescreening of all products on the basis of more detailed information supplied by the manufacturer/importer in answer to a questionaire, issue of a full Product Licence.

Fees for licences may be charged to applicants, that are commensurate with the work involved in processing the various forms of application. A proposed scheme, showing the necessary documentation for Phase 1, Interim Product Licencing is presented in annex 1 to this report. Phase 2 is also outlined, however, Phase 3 would be more appropriately considered when a start has been made on implementation of Phase 1. Policy on licencing fees is discussed briefly in section 12.1 of this report.

7.3 Assessment and licencing of manufacturers. There are tremendous differences between manufacturers in their levels of technical competence and in their integrity. These differences will not necessarily be revealed by the laboratory examination of an occasional sample of their products, An importing country is, therefore, faced with some difficulty in assessing which suppliers are genuine and reputable manufacturers. The importing country may reasonably assume that the major internationally known companies and state owned corporations have the required technical competence. Although sometimes allegations are made that such manufacturers export substandard drugs to countries not having the means to test them, it seems to this consultant rather unlikely that companies of these groups would risk their reputation by exporting seriously defective drugs. Of the not-so-well-known manufacturers there are, undoubtedly, many very reliable producers of generic drugs, whose prices may be attractive although not the cheapest. There are also those suppliers who may be manufacturers, but are perhaps also merchants, buying generic drugs in bulk from whatever source happens to be cheap and available, and packing them under their own label. A fourth class is the non-profit procurement agencies that cater for the needs of developing countries in supplying drugs for government and other non-commercial health services. Such agencies secure favourable prices by purchasing on a large scale. Some of their products are of the major manufacturers. Often, but unfortunately not invariably, the name of the manufacturer is made known to the purchaser.

In the assessment of overseas manufacturers, the Liberian Pharmacy Administration may seek the help of the regulatory authority in the country of the drug's origin, by requesting a statement certifying that the intending supplier is the actual manufacturer of the product in question and operates under the surveillance of that regulatory authority. As in the case of evaluation and licencing of medicines, a simple scheme for the assessment and licencing of manufacturers is presented in annex 1 to this report.

7.4 Inspection. The present law, Chapter 67 of the Public Health Law, makes provision for the inspection of "licenced establishments", i.e. those establishments of the private sector that are licenced for wholesale and retail dealings in medicines or for their manufacture. It does not make provision for the inspection of establishments in the public sector. In fact, there is not at present an inspectorate constituted to carry out these duties.

It is recommended that powers be extended so as to permit surveillance over all premises (private and public sectors, industrial and mission health services etc.) and give the right to enter premises where there is reason to believe that medicines are being stored or handled illegally, and to apprehend street hawkers of medicines. It is the consultant's general finding in many countries, that the qualities of competence and self discipline are equally likely to be lacking in the public and private sectors, hence the need for a uniform standard of surveillance.

The presently existing legally constituted establishments that would need to be inspected is summarized :

Public sector	266
Private sector	123 retail or retail/wholesale 4 purely wholesale
Mission hospitals	
Industrial health complexes	

Additionally there should be surveillance of the handling of medicines arriving at seaports and airports. There is need for a permanent inspectorate which would be responsible for planning the inspection programme, maintaining records of observations, and initiating any follow up action that might be necessitated as a result of an inspection.

The inspectorate should consist of pharmacists having at least three years post-graduate experience which would include time spent in retail and/or wholesale pharmacy.

Actual inspections of the legally operating private sector establishments should be carried out by a small ad hoc team which would include at least one member of the permanent inspectorate as well as other pharmacists who might be nominated by the Pharmacy Board or the Pharmaceutical Association. When pharmaceutical manufacture is started in Liberia, this too should be subject to independent surveillance. However, the inspection of pharmaceutical plant and operations requires long experience of pharmaceutical manufacture and quality control procedures in industry. It is suggested that the most economically effective way of achieving that surveillance would be to request the services of some overseas organization such as the inspectorate of one of the European national regulatory authorities. This is discussed further in section 8.4 of this report.

7.5 A laboratory for testing medicines. In order to ascertain whether medicines conform to "generally acceptable standards", access to laboratory testing facilities is essential. That access may, in principle at least, be either through the establishment of a competent local (national) laboratory, or by the use of a reputable overseas commercial laboratory. The advantages and convenience of having a national laboratory are self evident. However, the cost of testing is substantial, and only if a national laboratory is conducted in an efficient and business-like manner, is it likely to compare favourably on economic grounds with the "best buys" from overseas commercial laboratories. The fees charged by such commercial laboratories provide a useful reference point in assessing the viability of a National Laboratory Project and so examples will be quoted in this study.

7.5.1 General functions of a pharmaceutical testing laboratory. Samples may be submitted to a pharmaceutical testing laboratory from a variety of sources for a variety of purposes other than what is the prime purpose of the present study, i.e. the assurance of quality of medicines to the consumer. Thus, in a public or governmental laboratory, samples maybe submitted by the police, customs

authority or the courts to establish the identity or nature of a material. This might include the identification of narcotics. The quality control function itself may be broken down thus :

Samples taken by the government inspectorate in accordance with a planned sampling programme.

Samples taken by the government inspectorate because there is some specific reason to suspect the quality.

Samples submitted by the medicines licencing authority when considering an application for the marketing of a product.

Samples submitted by hospitals or government medical depots to verify the fitness of the product for use after it has passed its nominal shelf life.

The laboratory might also provide a quality control service to manufacturing industry in the routine examination of products.

A pharmaceutical testing laboratory in pharmaceutical industry will be called upon to carry out several routine tasks as a service to that industry such as the control of water at various stages of its treatment for use in pharmaceutical processing and as boiler water. Control of liquid and gaseous effluents as well as control of the environment for manufacturing processes are important functions of the industrial pharmaceutical testing laboratory.

7.5.2 Pharmaceutical testing. Samples of medicines are tested in pharmaceutical laboratories for conformity with acceptable standards. In the case of a regulatory laboratory, those acceptable standards are generally as laid down in a pharmacopoeia. When a product is not described in a pharmacopoeia, then it may be examined for conformity with a specification that has been provided by the manufacturer along with written standard methods of analysis, and has been accepted by the registration authority at the time of granting a Product Licence. Alternatively, until such time as full (as distinct from interim) Product Licences can be issued, samples may be examined in accordance with logical requirements based on the label declaration of content and general standards for the particular dosage form, e.g. the general pharmacopoeial requirements for injectable products.

Specified and implicit standards generally include the following classes of requirement :

A description of appearance with which compliance may be mandatory.

Test for identity.

Tests for defined impurities that might arise from the manufacturing process or as a result of deterioration.

An assay for strength or potency.

Additionally, depending on the nature of the product, there may be tests such as :

Variation of weight or content of active ingredient in tablets, capsules and other unit dosage forms.

Test that a tablet disintegrates within a specified time under controlled conditions, or alternatively, liberates a defined minimum proportion of the active ingredient(s) under controlled conditions, (the dissolution test).

Tests that products for injection or for application to the eye are sterile.

Tests that products for intravenous injection are free from pyrogens, i.e. substances that would cause an unacceptable rise in body temperature.

Tests that products are not unduly toxic.

7.5.3 Laboratory facilities and personnel requirements. To carry out the above mentioned classes of test, a laboratory is usually divided into sections having appropriate equipment and suitably qualified and experienced professional personnel. Typically, these sections would include :

chemical analysis section,

physical instrumentation section,

sterility and general microbiology section,

microbiological assay section,

pharmacology section.

The chemical and physical instrumentation sections may be combined together under the direction of a single section head. Similarly, sterility and general microbiology may be combined with microbiological assay and perhaps also

with the pharmacology section in a small laboratory. The pharmacology section would normally carry out only a limited range of routine tests such as pyrogen testing and freedom from undue toxicity. Pharmacopoeial monographs for some products such as insulin, digitalis etc. require biological tests involving small animals. Such tests are more efficiently carried out in specialist laboratories in which they become a routine. The economics of the control of biologicals is discussed in section 11 of this report. However, in contrast to such biological testing, the microbiological potency testing of antibiotics is a routine which can and should be established in all but the simplest of pharmaceutical quality control laboratories.

Professional staff of the laboratory would in general be graduates in pharmacy but perhaps also in chemistry or microbiology. Senior personnel have usually had post graduate training either by academic courses or on-the-job training to fit them for their specialization.

7.5.4 The laboratory's mandate. The examination of some samples might present a substantial work load to a laboratory and yet be of relatively little value to the recipient of the report. Examination of samples can be a costly business and should not be undertaken unnecessarily. To enable the laboratory to carry out its role effectively and efficiently, it is necessary that it should have defined terms of reference. These would define the manner of taking of a sample and its submission to the laboratory and would require the purpose of the analysis to be declared. A fee should be charged that would be commensurate with the effort involved. In this way the examination of samples to no really useful purpose would be minimised and the laboratory would be able to avoid the situation where the wrong test has been applied to the wrong sample for lack of background information being provided along with the request for analysis.

For surveillance of products on the market, complete control by testing every batch of every product is both impracticable and unnecessary. Samples for testing should be taken in accordance with a programme agreed in the Pharmacy Administration by all parties concerned. In this way, effort could be directed to the examination of those products known to be liable to deterioration, or in which failure to conform to standards could have

unfortunate consequences. The programme would ensure that some products from all suppliers (manufacturers) were examined from time to time and the results made known to the supplier whether satisfactory or unsatisfactory. In this way the suppliers would be made aware that surveillance was real. A sampling programme should be designed so as to ensure the examination of several similar samples at the same time, thus enabling the laboratory to work efficiently.

8 Prospects for pharmaceutical manufacture in Liberia. During recent years there has been some expression of interest by the private sector in the establishment of plant for pharmaceutical processing in Liberia. Hitherto, government reaction has been that manufacture should not precede the establishment of a national pharmaceutical quality control laboratory.

It became evident at an early stage of the present study that prospects of the government according priority to the establishment of a "non productive" organization such as a Pharmacy Administration and associated Quality Control Laboratory were, in the forseeable future, quite negligible. Arising from discussions with officers of the Ministry of Health and Social Welfare, the National Investment Commission, as well as UNIDO/UNDP permanent staff officers in Liberia and the West Africa Region, a concept of parallel development of production and quality control was evolved. The concept envisages an overall programme in which production and quality control offer mutual support. At this stage the concept is of necessity loosely defined. It may be developed further through studies that would aim to establish a realistic basis for collaboration between the private and public sectors in providing quality drugs for the country's health services.

8.1 A tentative programme for public/private sector collaboration. The programme envisaged comprises the following main points :

(i) The establishment of a central body (that might be a public corporation) having strictly defined terms of reference. Essentially these would be to procure, or to arrange for the local manufacture of a limited range of drugs in small independent production units. This range, which would be reviewed from time to time, would include only those drugs that are regularly

purchased in large quantities and/or there is reason to suppose could be with advantage manufactured locally.

(ii) The central body would support local production by guaranteeing a market for basic drugs for the health services at realistic prices. It would give guidance in production programming and assistance in procurement of raw materials. (As a public body it would probably qualify for assistance in procurement by organizations such as the non-profit International Dispensary Association of Amsterdam). In addition to supplying drugs to the Government health services, the central body could supply other non-profit services such as the mission and industrial hospitals and to similar bodies in neighbouring countries.

(iii) A production/services complex is envisaged in which the central body would provide a complete quality control service to several independent manufacturers of specific ranges of pharmaceutical products. For example, the following separate privately managed production operations might be conducted :

intravenous fluids and water for injections,

tablets and capsules,

liquid preparations not required to be sterile,

powders packed in sachets, e.g. oral rehydration salts.

It would be logical for all production units to be sited within a single compound and sharing general services such as engineering maintenance, fire fighting, security etc. in addition to quality control. The premises, and also plant might be owned by the central body and leased to the individual private manufacturers.

(iv) Preliminary discussions with representatives of the National Investment Commission (NIC) in Monrovia indicate that capital financing for such a venture might come initially from the NIC (which currently has funds that may be used for the support of small industries only, hence the emphasis on small separate production units).

A small levy on all medicines (imported and locally produced) could provide on-going support for the Pharmacy Administration and the laboratory services that it would utilize. On the basis of 1979 figures for imports, a levy of only 1% would provide an income of US $80,000 per annum. Quality control, engineering maintenance and other services to be provided by the central body would be paid for at a realistically economic rate by the participating individual manufacturers.

(v) The privately managed production units would undertake to produce pharmaceuticals in accordance with a programme to be agreed with the central body, and that these would be delivered promptly, in the required quantities and be of the required quality. With the possible exception of the intravenous fluid producing unit, they would be free to use spare capacity and/or acquire additional capacity to manufacture more lucrative products for the private sector. However, such production should still be subject to the same quality control surveillance.

8.2 The economics of local production. To reduce the financial burden of the drug bill on a health service, the local production of a range of widely used pharma-ceuticals seems an attractive proposition. Apart from the potential savings there are other advantages, - the drugs can be relatively recently manufactured when they reach the consumer, and therefore perhaps be in better condition, - expertise is introduced into the country and employment is created in the pharmaceutical operation itself as well as in ancillary industries, e.g. in the production of containers and packaging materials.

However, before embarking on such a venture, it is necessary to recognise the potential difficulties. The cost of locally produced drugs can compare favourably with that of generics imported from reliable sources, but only in a competently managed operation in which production levels are such as to provide for a high degree of utilization of plant and staff capacity. It is essential to inspire confidence in the quality of the products and to maintain that confidence. Failure to do so would be likely to restrict sales to a great extent to the "captive market", i.e. in Liberia, the National

Medical Supply Depot. The consequent drop in sales would lead to higher production costs and possible financial failure. Thus, in the proposed scheme, great emphasis is placed on the quality control function. Provided that all parties concerned are aware of the pitfalls and recognise that strict quality control is to their advantage, then prospects for success seem good.

A range of products is envisaged in which many are not particularly liable to deterioration. This provides a further safeguard for the reputation of the organization, particularly in the early years of its operation. This tentative range of products is shown in Table 6.

8.3 Proposals concerning pharmaceutical manufacture in Liberia. It is proposed that a detailed study be undertaken with the following objectives :

(i) To assess the range of products that might be produced economically in Liberia and the likely demand for these in the public, industrial and mining, and mission health services, as well as in the health services of neighbouring countries.

(ii) To assess the material facilities needed for their production and distribution, i.e. site selection, buildings for manufacture, warehousing, quality control, offices and ancillary accomodation for personnel, basic engineering services, equipment for manufacture and quality control, laboratory and office furnishings and office equipment and their costs.

(iii) To assess the personnel required for the success -ful operation of the project, the training programme and expert guidance that would be needed for start-up and early years after establishment and the cost of such training and guidance.

(iv) To postulate an annual production programme specifying quantities and batch sizes of individual products, estimate the costs of raw materials, packaging materials and process -ing costs based on the capital investment, running costs including salaries/wages. Estimate the necessary investment in working capital (mainly capital tied up in raw and in-process materials). From this data to estimate the ex-factory cost of each product

for the time when full production capacity has been attained.

A study such as proposed above would, in fact, be an extension of the present study in which detailed proposals have been made concerning all aspects of the quality control operation other than the laboratory building and its furnishings. The study could be carried out by a small team being drawn from, or having access to the required disciplines including pharmaceut-ical production and quality control, engineering, architecture and economics, so as to provide a realistic-ally considered view of all aspects of the proposed project.

8.4 External quality surveillance of pharmaceutical manufacture. Despite being planned to have an effective internal quality control system, that system can only be as good as the people who operate it. Absence of any apparent errors over a number of years could lead to over confidence and an unwarranted sense of security. Staff may change and the replacements be less aware of quality assurance than their predecessors. It is desirable, therefore, that operations of manufacture and quality control should be reviewed periodically by an independent assessor.

In countries having a large or even a moderate sized industry, this surveillance would normally be the respons-ibility of the Pharmacy Administration. However, in a country having such limited production facilities as are proposed for Liberia, it would be quite impracticable and uneconomic to have even one person trained to carry out this task. Accordingly, it is proposed that outside assistance be sought in this matter. An annual review or "quality control audit" should be carried out. This might be carried out by overseas commercial consultants. Alternatively, the regulatory authority of some other government might be prepared to do the job. The Govern-ment of Liberia might approach the European Inspection Convention to explore this possibility. This is, in any case, a service that would have to be paid for and so the Pharmacy Administration should make appropriate provision in its budget.

9 Pharmaceutical production, - a preliminary cost forecast. In section 8.3 of this report it has been proposed that a feasibility study be commissioned regarding the establish-ment of pharmaceutical manufacture in Liberia. The results of such a study would indicate the potential work load from the manufacturing enterprises on a quality control laboratory. This would provide a basis for

realistic estimation of costs of testing and thence to costs of the entire quality control operation, and of the Pharmacy Administration. In the meantime, it is instructive, and can give some guidance to decision makers, to present the results of a preliminery estimate of possible costs and means of financing.

9.1 Pharmaceutical products that might be manufactured in Liberia. Consideration could be given to the manufacture of the items listed in table 6. These have been selected for one or more of the following reasons :

(i) They are used in large quantities in Primary Health Care.

(ii) They are bulky and so substantial economies in transportation costs might accrue.

(iii) The manuafacturing processes are, in general, straightforward. However, an exception to this generalization is the manufacture of intravenous fluids for which the process must be strictly controlled.

9.2 Possible capital costs and production capacities. Based on experience in another developing country in 1978, some indication of capital investment costs and production capacities may be gleaned. Table 7 presents these indications for fixed capital investment. These would be updated in a feasibility study to take into consider -ation the actual production capacities selected, and estimated building and equipment costs for, say, 1982. Additionally, costs of transfer of technology, training programmes and working capital are major items to be considered.

The basis for the figures quoted in table 7 is shown in annex 2 to this report. In the case of the proposed intravenous fluid plant, more detail is presented in annex 3 based on the experience of the International Dispensary Association of Amsterdam which is currently establishing such a plant in Vientiane for the Government of Laos.

10 Proposed structure for a Pharmacy Administration. The main branches of a Pharmacy Administration relevent to the present study were defined in section 7 of this report. In the structure proposed for Liberia, because of economic constraints, the quality control laboratory would not be

an integral part of the Pharmacy Administration but would be part of an independent body as envisaged in sections 3 and 3.1 of this report, and would be under contract to provide analytical services to the Pharmacy Administration. Such a system is not without precedent; in Britain, for example, testing of medicines for the regulatory authority is undertaken by the Pharmaceutical Society (the professional body of pharmacists) in laboratories specially established for this purpose in Edinburgh.

The proposed structure is shown diagramatically in figure 1. The descriptive title "Pharmacy Administration" will continue to be used in this report, although the Government may wish to give it some other name such as "Directorate of Pharmacy", indicative of its status. It is suggested that its Director should report directly to the Minister of Health. He or she would be supported and advised by the existing Pharmacy Board and may at the same time hold office on that Board. The functions and staffing of the various sections could be as follows :

(i) Legal and enforcement section. Its functions would be to review and update legislation as required, to define circumstances in which recall of product batches from the market would be warranted, to define circumstances in which withdrawal of a product from the market would be justified, to define penalties for transgression of Pharmacy Laws. It would include an inspect-orate which would plan the surveillance programme and participate in it as indicated in section 7.1 and keep records of all inspections. The head of the section would be supported by two pharmacists initially but further expansion of the team would be expected within a few years time. For inspection duties outside Monrovia, one vehicle and a driver should be allocated. Travel within Monrovia could be more economically provided for by a daily allowance for taxi fares.

(ii) Medicines evaluation and licencing section. To prepare (in conjunction with a consultant) a detailed programme for evaluation of medicines currently being imported into Liberia, or which it might be proposed to import or manufacture in Liberia. To evaluate medicines in accordance with that programme and issue licences for those that are approved, authorizing their marketing.

To prepare a detailed programme for the evaluation of overseas manufacturers/suppliers of medicines, to evaluate them in accordance with that plan and issue licences to those that are approved, thus permitting the import of their products subject to the granting of an Interim or Full Product Licence. To issue licences for pharmaceutical personnel and premises as is currently done under the direction of the Pharmacy Board.

The head of the section would be a pharmacist preferably having a special interest in pharma -cology. He would be supported by one other pharmacist.

(iii) Drug information section. To promote aware -ness of the correct usage of drugs and the hazards of their misuse. One pharmacist, preferably having a special interest in pharma -cology would be appointed to this section. He would collect data from various sources including the World Health Organization through its regular publications, and would issue bulletins to physicians, pharmacists and other health personnel at appropriate levels. He would arrange for publicity on drug use and misuse through media such as radio, television etc.

(iv) Procurement and distribution. This section would be the presently existing National Medical Supply Depot. Its functions would be basically unchanged.

(v) Registry and secretarial pool. Apart from the Director's personal secretary, it is suggested that typing and secretarial services be provided by a pool and that all documentation relating to licences, inspections and disciplinary action etc. be kept in a Registry. The head of the legal and enforcement section might also be nominated as responsible for the Registry. A secretarial staff of five is suggested for the pool.

The relationship between the Pharmacy Administration and a proposed pharmaceutical production/testing body (as described in section 8.1 of this report) is also shown in figure 1 by the dashed arrows numbered (1) to (4).

These represent :

(1) Samples that might be tested in connection with the evaluation of an application for a product licence. (Not a routine requirement).

(2) Samples submitted in accordance with a planned sampling programme of market surveillance or taken exceptionally by the inspectorate for specific reasons.

(3) Samples examined as a service to the procurement office to provide guidance in the selection of sources of supply.

(4) Products manufactured for the public health service.

Fees would be payable by the Pharmacy Administration for the services (1) to (3) as well as for the products (4).

Proposals for staffing of the Pharmacy Administration and possible salary costs are presented in table 8. A training programme would be necessary to enable professional personnel to gain experience in the various aspects of pharmaceutical regulatory affairs. A suitable programme is outlined in annex 4 to this report.

11 Planning a laboratory for Liberia. In planning the facilities and staffing of a laboratory for Liberia, consideration has been given to its primary function, i.e. control of the proposed manufacturing programme and surveillance of drugs on the market and health services, in particular, the list of about 400 items normally stocked by the National Medical Supply Depot. Of these 400, only 18 items are "biologicals" the term given to immunolcgicals, gland products such as insulin and blood products. The testing of biologicals generally involves biological assay using small animals, often in large numbers. Such testing is expensive. To illustrate how expensive, a comparison is given of typical prices charged for these tests by commercial laboratories in Britain :

(i) A "pharmaceutical", - tetracycline capsules; full tests in accordance with the monograph of the British Pharmacopoeia, (this includes a microbiological potency test).
Fee £40.00 ($96)

(ii) A "biological", - insulin; potency test only, in accordance with the monograph of the British Pharmacopoeia.
Fee £250.00 ($600).

Biologicals form a very small part of total medicinal imports. Figures obtained from the statistical records of the Ministry of Planning and Economic Affairs showed the total value of biologicals imported in 1978 to be $53,240 only, or less than 1% of total medicinal imports. It seems therefore, that the most economically practicable way of ensuring their quality would be to purchase only from reputable sources and ensure that storage and handling conditions in Liberia were such as to minimise deterioration. For this reason, the level of capability that is proposed for biological testing is minimal. For the control of intravenous fluid production, it is proposed that the Limulus amoebocyte lysate (LAL) test be used rather than the rabbit test for pyrogens.

To assess the facilities needed for the chemical, physical and microbiological testing of the pharmaceutical products stocked by the National Medical Supply Depot, a detailed study of the relevent pharmacopoeial monographs has been carried out. Similarly, the monographs of raw materials (active ingredients and excipients) needed in the manuf-acture of the range of products proposed for local prod-uction have been studied. Arising from these studies, detailed lists have been drawn up showing the necessary laboratory general equipment and instrumentation, chemical reagents, microbiological media, standard reference substances and microbiological cultures. Policy has been to include almost every item needed for full pharm-acopoeial tests on the range of products considered. Some additional items are included based on general knowledge of the type of miscellaneous tasks that the laboratory might be called upon to undertake.

The result is an overall plan for a laboratory with quite comprehensive facilities for chemical, physical and microbiological testing. A programme for phased develop-ment is presented in section 11.2 in which the acquisition of physical facilities would proceed at a pace concordant with the development the personnel training programme.

The cost of chemical reagents, microbiological media etc. is small compared with the overall cost of the laboratory. It is suggested therefore that virtually all these should be purchased in the first phase so that a situation does not arise whereby a test cannot be carried out for the lack of a reagent costing as little as $5. There would be some logical exceptions, thus reagents for use only in gas/liquid chromatography should be purchased only when the decision to acquire the

instrumentation has been taken in the later stages of development.

Although the material facilities proposed are quite comprehensive, only items which it is believed can be justified economically have been included. An atomic absorption spectrophotometer has not been included; the initial cost of the instrument is high and it is expensive to operate due to the high cost and relatively short lives of the many lamps that are needed for different elements. This is an instrument which can be justified only when there will be a heavy work load for it.

11.1 The need for phasing of development. When an analyst reports that a sample conforms to the required specif-ication, his decision is very rarely questioned. In contrast, when his report is unfavourable, it is quite common for doubt to be cast on its validity. In a manufacturing operation, production pharmacists often genuinely find it hard to believe that their product is outside specification. In other situations, the recipient of the unfavourable report may just hope, without reasonable grounds, that the analyst is in error and so demand a retest or a second opinion.

It is a serious matter for the analyst to be found wrong since it jeopardises his reputation. The wise analyst therefore makes every effort to safeguard his reputation and that of his laboratory by checking and rechecking that his results are valid before issuing an unfavourable report. It is, of course, equally undesirable to issue a favourable report on a substandard sample.

To avoid the possibility of error, it is necessary to establish a discipline within the laboratory whereby it is ensured, for example, that the performance of balances and other instruments is regularly verified as being within acceptable limits, that reference standards and reference solutions are correctly calibrated. It must be verified that sterility tests give neither false positive not false negative responses. It is necessary to establish the statistical confidence limits for potency estimates in the microbiological assay of antibiotics and also to recognise the potential sources of error that are not revealed by the statistical tests. Many other examples could be quoted. In other words, the analyst must take nothing for granted if he is to avoid errors. An internal system of quality control for the operations of the laboratory itself must be established.

Designing such a system together with the necessary documentation is the first step. Ensuring that staff of the laboratory are aware of the necessity to observe the requirements of the system and are competent to carry them out is the second step. Finally, the Head of the Department must have sufficient confidence in his senior support staff to delegate responsibility. It is for these reasons particularly, that in a developing country where appropriately qualified and experienced staff may not be available initially in the required numbers, development of the laboratory should be phased and proceed at an appropriately moderate pace.

11.2 Proposed organizational structure and phasing of development. The structure and phasing that is proposed here aims to first establish a basic capability for a useful degree of control of products on the market, as well as control of the proposed manufacturing facilities for tablets and non-sterile liquids. This would be achieved in phases 1 and 2 dealing with general chemical/physical and microbiological assay respectively.

Phases 3 and 4 relate to specific production activities, i.e. oral rehydration salts and intravenous fluids respectively. The laboratory is further developed to a level at which it could provide a quite comprehensive service by the addition of infra red spectrophotometry and gas/liquid chromatography in phases 5 and 6 respectively. Also in phase 6, facilities for a limited range of routine pharmacological tests may be added.

The development of the laboratory is shown in table 9 which summarizes estimated costs of equipment and materials as well as personnel requirements for each phase. A more detailed statement on phasing of expenditure on equipment is given in annex 5. The organizational structure envisaged is shown in figure 2, although it is to be expected that there would be indistinct divisions of work between the sub-sections. A possible scale for staff salaries is given in table 10.

A programme for transfer of technology and further training would ensure that expertise and administrative skills would be developed alongside physical facilities. The programme, which is presented in annex 4, assumes that the scientific personnel are of bachelor degree status and without specialized experience in pharmaceutical analysis.

12 Estimated operating costs, quality surveillance. In this section, estimates are prepared of the costs of operating the quality control laboratory and costs of those sections of the Pharmacy Administration other than the

already functioning procurement section (The National Medical Supply Depot). These estimates are based on certain assumptions of which a major factor is the postulated production capacities of the various manu -facturing units that have been indicated in table 7. Breaking down these individual capacities into batch sizes that are related to proposed plant capacity, it is readily estimated that there would be 1690 batches per year. Additionally, it is supposed that the Pharmacy Administration would submit four samples on average on each of 240 working days, i.e. 960 samples per year in an agreed market surveillance programme. The procurement section might also submit another 800 samples for evaluation prior to selection for purchase, "buying samples". As a service to the manufacturing complex, the laboratory might also be called upon to examine boiler waters daily (240 samples) and effluent weekly (50 samples). Samples may vary very substantially in the amount of analytical effort entailed in their examination. Accordingly, for costing purposes a number of "cost units" has been allocated to the various types of sample. This is some -what arbitrary but has a logical basis that may be illustrated by a few examples.

Intravenous fluids, which require chemical, sterility and pyrogen yests, have been allocated the rather high figure of 180 units. Oral rehydration salts, for which the analysis would be a very repetitive routine involving only chemical/physical tests, have been allocated 60 units. Samples from the Pharmacy Administration's market surveillance programme, because they will be varied and less amenable to routine treatment, have been allocated 200 units.

If one production batch corresponded to only one sample, the total estimated samples per annum would be :

$$1690 + 960 + 800 + 240 + 50 = 3740$$

or about 16 samples daily for each of 240 working days on average. In fact, for each production batch there will be more than one test on average. This will be due to the examination of raw materials, packaging materials, intermediates as well as in-process controls. Some of these tests will be very simple, such as the determination of pH or refractive index. Rather than attempt to evaluate this in detail, an additional number of cost units has been added and is described as "cost units other services". This amounts to an extra 50% for all product groups other than intravenous fluids, in which case it

is only 33 % due to the already high costing for the batch analysis. The costing system is summarized in table 11 from which it can be seen that the "cost units other services" represent an additional 46% charge for the analytical services to production. This may be equated roughly to an effective increase of 780 samples as a service to the manufacturing units, thus bringing the effective total to 4520 samples per annum. The proposed staffing of the laboratory (section 11.2) includes ten "bench workers", thus the work load would correspond to about 10 samples per bench worker per week. This should be well within their capacity.

The components of annual cost of running the laboratory are shown in table 12 and total $250,770. The allocation of cost units to the various laboratory services was shown in table 11 to total 533,500 cost units. Thus, 533,500 cost units correspond to $250,770 so that one cost unit equals $0.47. If an actual charge of $0.50 were made for each cost unit, the laboratory would operate with a small safety margin. The cost to the Pharmacy Administration for analytical services in connection with the market surveillance programme would then be $96,000 per annum.

It is of interest to note that the estimated charge for the examination of one sample in the market surveillance programme is $100 (200 cost units). This may be compared with the commercial price for the examination of a typical sample, - tetracycline capsules that was quoted in section 11 as $96. It is concluded that this costing system has provided a realistic first estimate. Naturally, it may be revised from time to time as the laboratory develops.

The overall cost of running the Pharmacy Administration, including the analytical services for the market surveillance programme, but excluding the procurement unit, is shown in table 13 and amounts to $273,725 per annum.

12.1 Sources of income for the Laboratory and Pharmacy Administration's Regulatory Role. From the system of costing that is summarized in table 11, the allocation of the laboratory's charges can be estimated as :

Production Units	$138,750
Pharmacy Administration (Regulatory)	$ 96,000
Pharmacy Administration (Procurement)	$ 32,000

It is suggested that the various production units and the two components of the Pharmacy Administration be required to enter into an agreement with the laboratory

to pay an annual minimum fee for which the laboratory would undertake to provide the essential services. Without such guaranteed income, the laboratory could not be an economically viable proposition.

The production units, being run on commercial principles, should have no difficulty in paying for the essential sevices provided that their material facilities and staff are utilized efficiently. The $32,000 or thereabouts for services to the procurement section of the Pharmacy Administration, would represent a very small propo of its regular budget and would be money well spent.

To finance the Regulatory Function of the Pharmacy Administration, it is suggested that a small tax be levied on all medicines, imported and locally produced and that fees be charged for licences issued for products and their manufacturers as has been outlined in sections 7.2 and 7.3 of this report. The actual numbers of products currently marketed in Liberia and the numbers of overseas manufacturers supplying them are not known. The respective figures 3000 and 300 are conservative guesses used for the purpose of estimating possible income from these sources.

Two alternative scales of charges are put forward for consideration :

Scale 1	Interim Product Licence	$15 per annum
	Manufacturer's Licence	$100 for a 3 year period
	Medicines tax on CIF value of imports or ex factory cost of locally produced drugs	2½%
Scale 2	Interim Product Licence	$40 per annum
	Manufacturer's Licence	$250 for a 3 year period
	Medicines tax levied as above	1½%

These scales would both yield an estimated $280,000 which slightly exceeds the estimated need. The second scale has, in principle, the advantage that it might discourage applications for licences that were not going to lead to a substantial amount of business. In this way, a multiplicity of products and suppliers might be avoided, thus making quality surveillance of the market more practicable.

It is suggested that prior to the commencement of a licencing programme, a detailed study be carried out

to assess the number of products on the market and the scale of importation of individual products. Experience in another small country indicates that using importer's invoices as a source of information, the data could be analysed in about 4 man-months of work. With such information available, there would be a basis for the assessment of the quantitative effects of the "deterrent" scale 2 for licence fees. Whatever system of financing the regulatory operations may be chosen, the cost is likely to be the same, i.e. an effective increase of up to 3% in the price of medicines. This seems a small price to pay for the degree of protection that would be afforded. In fact, this cost may be more than offset by savings to the public sector arising from the local manufacture which would be part of the overall programme.

13 Location of the manufacturing/laboratory complex. Many factors will have a bearing on the decision as to where the complex should be located. Consideration will have to be given to the following :

(i) Convenience of communications and transportation facilities for raw and packaging materials to the production units.

(ii) Convenience of communications and transportation facilities for finished goods from the production units to the National Medical Supply Depot, and perhaps directly to other medical depots.

(iii) The availability of a source of water of suitable quality. The cost of treatment to obtain water that may be used in pharmaceutical processing will be dependent on its mineral content.

(iv) The availability of electricity.

(v) The general environment and its suitability for pharmaceutical manufacture.

(vi) The climatic conditions and their potential effect on products, manufacturing equipment and instruments.

(vii) The local availability of a potential workforce including semi-skilled and unskilled workers.

Clearly, the selection of a site must be given very care-ful thought. It is suggested, therefore, that this should be considered during the feasibility study that has been proposed, when samples of raw water from potential locations would be examined to assess their suitability.

14. Summary of cost forecasts. Cost estimates arising from this feasibility study are now summarized together with references to the main text, tables or annexes as appropriate. Also, pre-feasibility study estimates are given concerning the proposed manufacturing operations. The cost forecasts are :

(i) Buildings, services, equipment, meterials and furnishings for a Quality Control Laboratory, derived from tables 7 and 9, $373,000

(ii) Buildings, services and furnishings to house a Pharmacy Administration, derived from table 13, $135,000

(iii) Transfer of technology and training programme for the Pharmacy Administration and the Quality Control Laboratory, see annex 4, $380,000

(iv) Detailed study to assess actual production needs and costs of setting up the required facilities and estimation of the required programme for transfer of technology and its cost, allow up to $ 60,000

(v) Buildings, services, equipment and furnishings for a manufacturing complex, excluding the costs of the quality control laboratory which has been given in (i) above, pre-feasibility study estimate derived from table 7, $1,179,000

(vi) Installation of machinery for pharmaceutical manufacturing complex, pre-feasibility study estimate, allow up to $700,000

(vii) Transfer of technology and training programme for the pharmaceutical manufacturing complex, pre-feasibility study estimate, allow up to $600,000

Total of items (i) to (vii) is $3,427,000.

15. Summary of recommendations. In consideration of the economic circumstances currently pertaining in Liberia it was concluded that a programme for the parallel development of basic pharmaceutical processing facilities and a comprehensive national Pharmacy Administration would meet a real need of the health services and be more likely to attract financial support than a project aimed solely at quality control.

The pharmaceutical processing facilities would be utilized to manufacture a limited range of widely used drugs for the government, industrial and mission health services. A manufacturing complex is envisaged in which perhaps four independently operated small specialized production units would share common services such as quality control, engineering maintenance and security. The Quality Control Laboratory would also provide a service to a Pharmacy Administration in connection with its quality surveillance and procurement programmes.

The Pharmacy Administration would concern itself with both the quality and usage of drugs. It would have sufficient personnel to staff its various sections that would be concerned with legislation, medicines evaluation and licencing, inspection, drug information and its dissemination.

To achieve these objectives it is recommended that the government should take the following actions :

(i) Establish a financial basis for the project by seeking aid from donor agencies for the capital costs of further development and implementation in accordance with cost forecasts as summarized in section 14; make provision for running costs by means of licencing fees and a small medicines tax as suggested in section 12.1 of this report.

(ii) Recruit a team to assess actual production needs and prepare an outline design for manufacturing facilities and warehousing including architect's drawings as well as detailed design including fixtures and furnishings for the Quality Control Laboratory and Pharmacy Administration on the basis of the needs defined in the present study. (UNIDO might assist in the recruitment of the team).

(iii) Explore the interest of the private sector in participating in the proposed manufacturing venture and develop a plan for its legal and financial structure.

(iv) Appoint one person having suitable basic qualifications, as Director Designate of the Pharmaceutical Quality Control Laboratory. Similarly, appoint one person as Director Designate, Pharmacy Administration. Arrange further training as outlined in annex 4.

(v) In accordance with the recommendations arising from the study proposed in (ii), appoint contractors to construct and furnish the required plant, laboratories, warehousing and offices.

(vi) Place orders for laboratory equipment and materials that have been specified in separate documents arising from the present study.

(vii) Recruit consultants to assist in the start of operations of the Quality Control Laboratory and Pharmacy Administration as well as a longer term adviser for the Laboratory.

(viii) Recruit additional staff for the Quality Control Laboratory and Pharmacy Administration as has been detailed in tables 8 and 10. Arrange for further training in accordance with annex 4.

(ix) Take any other actions that might be recommended by the team mentioned in section (ii) in connection with the manufacturing project.

16. Acknowledgements. The writer wishes to express his appreciation of the time devoted by H.E. The Minister of Health, Dr. Kate Bryant and Deputy Minister, Mr. J. Ellis in discussions and guidance on the aims of the mission and form of the report. Thanks are due to Dr. Fred Gordon, Mr. Jacob Cisco and their staffs who went to great efforts to present much of the data that helped to build up a picture of the pharmaceutical scene in Liberia and a basis on which to design a programme for pharmaceutical develop -ment. Thanks are also due to the many members of the private sector of pharmacy who gave their time in discussions, to Mr. Juergen von Gyldenfeldt, UNIDO Industrial Economist, for advice on economic aspects of the project, to Mr. Ivan Contreras, UNIDO Senior Industrial Development Field Adviser for guidance during his visit to Monrovia and finally to Mr. John Gordon and Ms. Judith Sims, UNDP Resident Represent -ative and Deputy Resident Representative respectively, for frequent informal discussions which provided valuable background information.

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2. The 22nd report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations, Technical Report Series 418, 1969.

3. The 27th report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations, Technical Report Series 645, 1980.

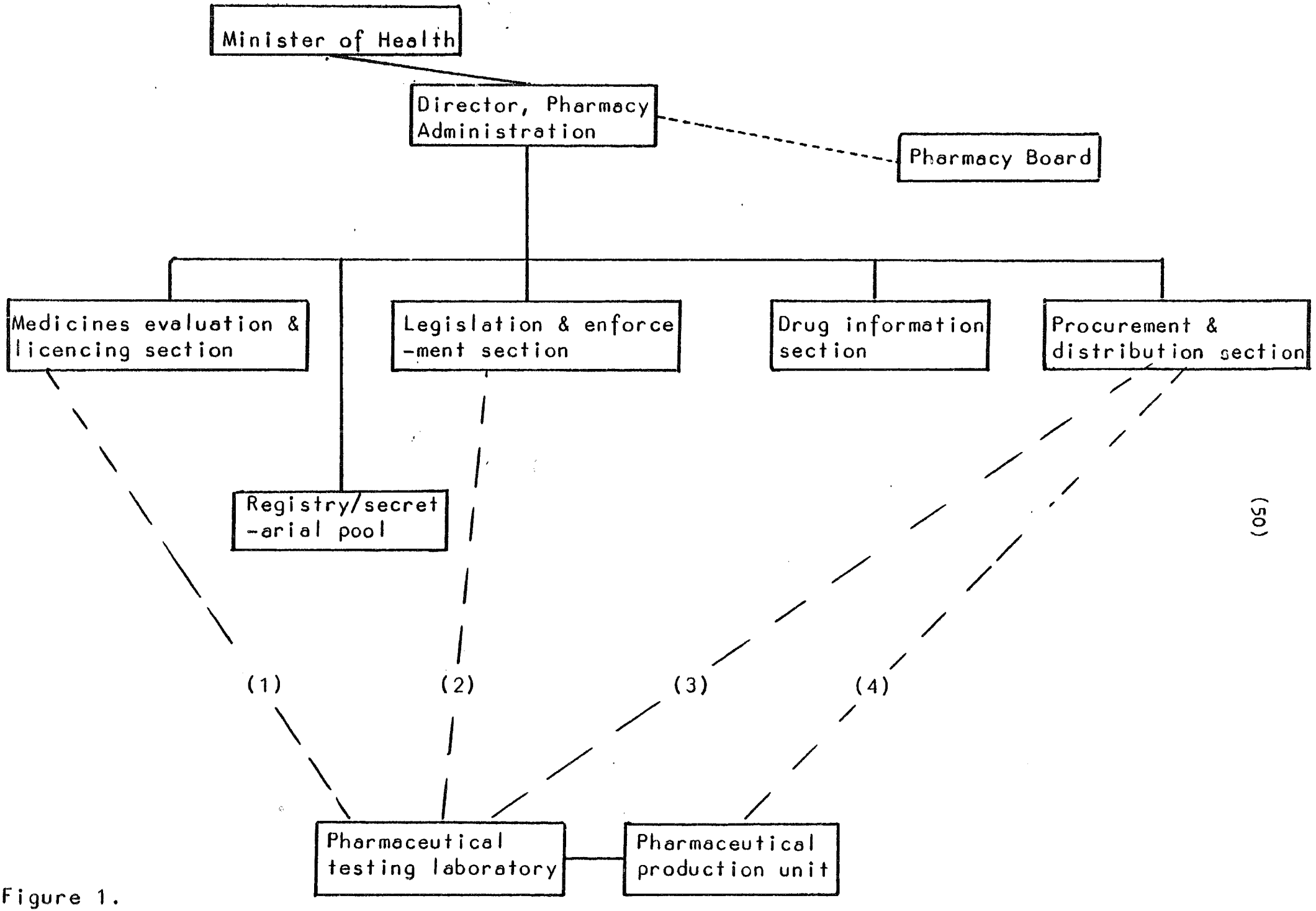

Figure 1.

Administrative structure of the Pharmacy Administration.

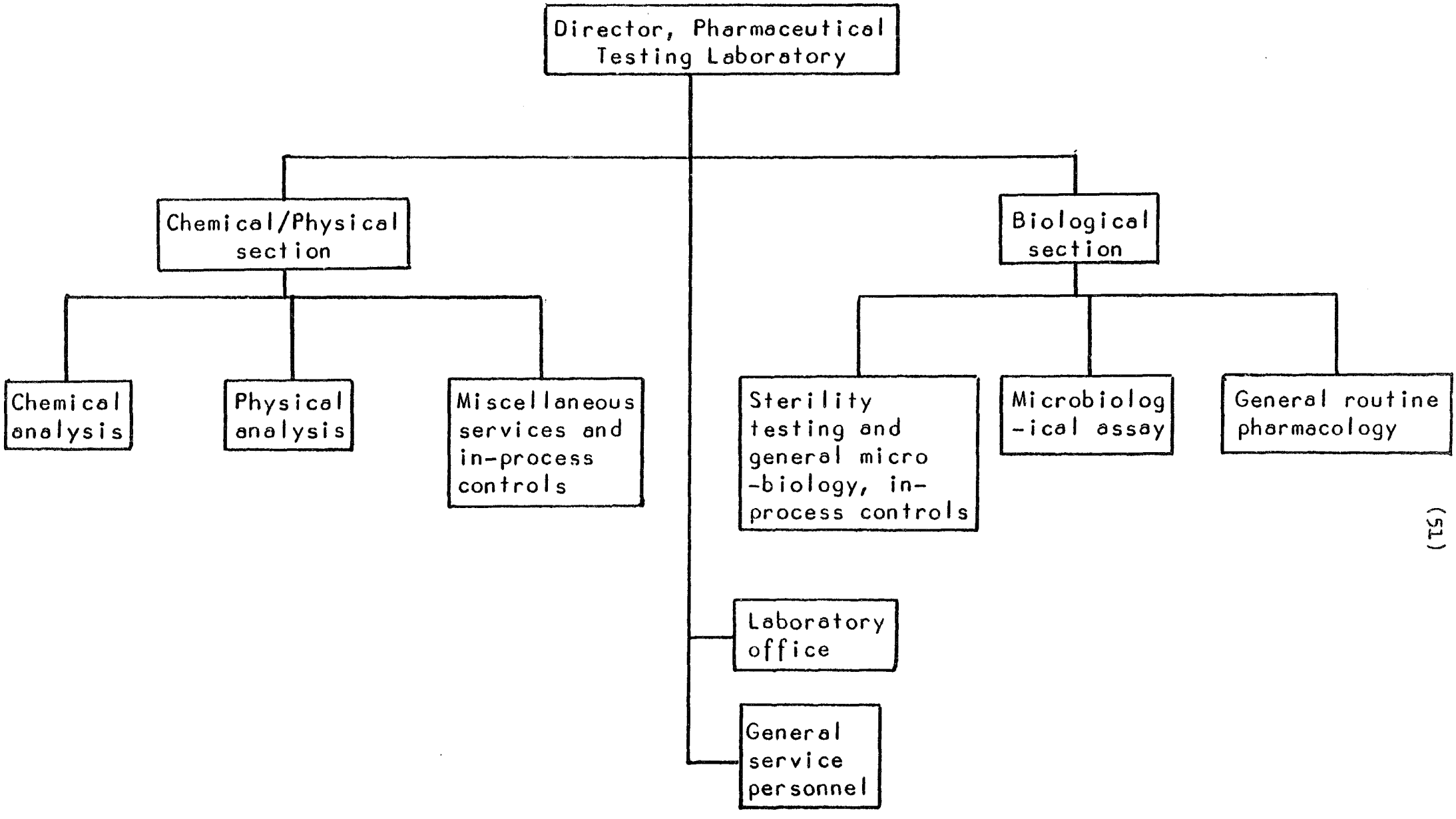

Figure 2.
Administrative structure of the Pharmaceutical Quality Control Laboratory.

Table 1.

Analysis of data on 20 selected items from the summary

Description	Quantity	Unit cost, US $	
		lowest	highest
bephenium hydroxy-naphthoate 5g sachet	1500 x 50's	4.81	59.00
chloramphenicol capsules 250mg	1000 x 1000's	11.61	285.67
chlorpromazine tablets 25mg	350 x 1000's	1.70	14.30
dextrose 5% in normal saline, 1000ml.	10000 x 1 litre	0.95	7.24
digoxin tablets 0.25mg	200 x 1000's	2.87	21.10
ferrous sulphate tablets 300mg	3000 x 1000's	1.15	6.98
furosemide tablets 40mg	1000 x 250's	1.05	60.20
griseofulvin tablets 125mg	500 x 1000's	16.20	339.40
griseofulvin tablets 500mg	500 x 500's	25.28	589.50
ibuprofen tablets 200mg	200 x 500's	17.50	107.20

of bids in response to the May 1980 tender.

median	IDA	Supplier accepted unit cost	total cost	name of supplier
14.00	13.55	4.81	7215	ICN Canada
22.15	22.15	15.20	15200	Galenika
5.70	3.60	1.70	595	Mercury Pharm.
2.17	1.08	1.56	15600	Dott Bonapace
9.80	5.03	2.87	574	Nilcon Int.
3.94	2.41	2.41	7230	IDA
3.58	2.10	2.10	2100	Ciech
31.00	25.25	24.50	2250	ICI
56.00	34.80	25.80	12900	Chemothera
24.60	-	17.84	3568	Chem. & Pharm.

table 1, continued.

Description	Quantity	Unit cost US $ lowest	highest
indometacin capsules 25mg	1000 x 1000's	5.28	217.40
methyldopa tablets 250mg	500 x 500's	11.05	82.67
metronidazole tablets 200mg	2000 x 500's	3.58	333,75
neomycin and bacitracin oint.	4000 x ?g tubes	0.46	5.00
nitroglycerin tablets 0.6mg	200 x 1000's	2.26	21.60
paracetamol tablets 500mg	3000 x 1000's	3.25	18.17
phenoxymethyl-pen. tabs. 250mg	500 x 1000's	13.95	227.50
phenylbutazone tablets 100mg	700 x 1000's	2.10	79.80
trisulphonamide tablets 500mg	1200 x 1000's	10.60	32.27
water for injections 10ml	2000 x 100's	3.62	42.42

median	IDA	Supplier accepted unit cost	Supplier accepted total cost	name of supplier
14.80	5.28	5.28	5280	IDA
27.39	35.46	11.05	5525	Nilcon Int.
6.76	4.14	7.16*	14320	Servipharm
?	-	0.46	1840	Danimex
2.70	-	2.26	452	Internat. Enz.
7.80	5.76	3.25	9750	Nilcon Int.
22.00	18.39	13.95	6975	Scandrug
6.89	6.78	2.10	1470	Nilcon Int.
15,25	13.74	10.60	12720	Joba BV
8.35	6.00	3.62	7240	Internat. Enz.

Table 2.

Bids accepted in the drugs invitation to tender of May 1980 amounted to US $889,137. The proportion of this total that was allocated to groups of individual bidders is summarized. Bidders were grouped according to the percentage of the total order that they secured.

Percentage of the total amount awarded to an individual bidder.	Number of bidders in the group.	Percentage of the total amount secured by the group.
1% and less	45	15.7%
1.1% to 2.0%	16	23.7%
2.1% to 3.0%	6	15.8%
3.1% to 4.0%	0	0.0%
4.1% to 5.0%	2	9.1%
5.1% to 6.0%	2	11.6%
6.1% to 7.0%	0	0.0%
7.1% to 8.0%	1	7.8%
greater than 8%	1	16.3%

Table 3.

Analysis of data on costs of all purchases of 20 items c

Description	Total quantity purchased	number of purchases
ampicillin capsules 250mg	3742 x 1000's	9
aspirin tablets 300mg	7900 x 1000's	9
benzyl benzoate application	2954 x 2 litre	4
bephenium hydroxy-naphthoate sachets 5g	2850 x 50's	4
chloroquine tablets 250mg	19880 x 1000's	11
chlorpromazine tablets 25mg	650 x 1000's	4
diazepam tablets 5mg	1011 x 1000's	3
digoxin tablets 0.25mg	162 x 1000's	5
ferrous sulphate tablets 300mg	13813 x 1000's	6
furusemide tablets 40mg	1544 x 250's	3

over a period of almost two years.

Unit cost US $			Total purchase price
lowest	highest	weighted mean	
43.00	83.00	45.78	171,322
1.00	3.50	1.95	15,383
4.25	14.56	5.13	15,161
4.81	39.82	9.70	27,637
9.50	19.95	11.52	229,071
1.70	5.53	2.28	1,484
2.50	149.60	2.73	2,763
7.50	80.00	8.00	1,296
1.45	6.25	1.93	26,598
1.86	4.38	2.09	3,223

table 3, continued.

Description	Total quantity purchased	Number of purchases
indometacin capsules 25mg	1000 x 1000's	3
insulin zinc suspension 40IU/ml	1448 x 10ml	4
isoniazid tablets 300mg	500 x 1000's	2
metronidazole tablets 200mg	4563 x 500's	5
benzylpenicillin sodium aq. inj. 1 mega unit	850 x 100's	2
phenoxymethylpenicillin tablets 250mg	5582 x 1000's	3
phenobarbitone tablets 30mg	980 x 1000's	5
phenylbutazone tablets 100mg	1710 x 1000's	5
streptomycin sulphate injection 5g	320 x 50's	2
tetracycline capsules 250mg	4050 x 1000's	6

Unit cost US $			Total purchase price
lowest	highest	weighted mean	
9.00	17.55	11.12	11,115
2,22	5.05	2.80	4,054
3.00	14.75	10.05	5,025
3.36	12.60	5.76	26,264
17.97	22.50	21.17	17,993
13.95	33.00	23.59	131,681
0.94	3.00	1.70	1,666
2.10	5.90	3.24	5,533
15.80	37.80	17.18	5,496
13.60	21.25	15.41	62,418

Table 4.

A comparison of tender prices accepted and the weighted mean price for all purchases of an item during an approximately two year period. The British wholesale price

Description	Pack size	Tender price $	Weighted mean price $	British wholesale price, $
bephenium hydroxy-naphthoate sachets 5g	50	4.81	9.70	37.15*
chlorpromazine tablets 25mg	1000	1.70	2.28	7.08
digoxin tablets 0.25mg	1000	2.87	8.00	12.91*
ferrous sulphate tablets 300mg	1000	2.41	1.93	5.93
furosemide tablets 40mg	250	2.10	2.09	11.40
indometacin capsules 25mg	1000	5.28	11.12	77.57
metronidazole tablets 200mg	500	3.58	5.76	107.33*
phenoxymethylpenicillin tablets 250mg	1000	13.95	23.59	25.50
phenylbutazone tablets 100mg	1000	2.10	3.24	7.44

Note. The British wholesale prices are taken from a December 1980 price list and refer to the generic drug except when the price is marked with an asterisk.

Table 5.

Wholesale prices of selected drugs, - a comparison between the private sectors of Liberia and Britain.

Generic name or description	Pack size	Brand name	Wholesale Price US $ Liberia	Britain
aspirin tablets 300mg	100		0.37	0.42
allopurinol tablets 100mg	100	Zyloric	17.10	25.49
ampicillin capsules 250mg	500	Pentrexyl	47.76	47.62
benzyl benzoate application	200ml	Ascabiol	2.00	2.26
chlordiazepoxide capsules 5mg	100	Librium	7.57	2.62
chloroquine phosphate tablets 250mg	100	Avloclor	1.44	1.80
chlorpropamide tablets 250mg	100	Diabinese	9.50	16.03
co-trimoxazole tablets	100	Septrin	20.70	19.61
co-trimoxazole tablets	100	Bactrim	29.83	19.61
diazepam tablets 5mg	100	-	1.10	1.49
diazepam tablets 5mg	100	Valium	13.60	3.46
digoxin tablets 0.25mg	1000	-	3.72	5.81
digoxin tablets 0.25mg	1000	Lanoxin	8.00	9.55
doxycycline capsules 100mg	50	Vibramycin	53.80	63.00
furusemide tablets 40mg	250	-	5.00	12.24
furusemide tablets 40mg	250	Lasix	38.80	30.96
methyldopa tablets 250mg	100	Aldomet	11.97	11.04

table 5, continued.

Generic name or description	Pack size	Brand name	Wholesale price US $ Liberia	Britain
norethisterone tablets 5mg	100	Primolut N	23.90	18.84
oxytetracycline eye ointment	3.5g	Terramycin	0.57	1.15
diuretic tablets	100	Moduretic	21.55	16.56
laxative capsules	30	Dorbanex	1.77	1.73
multivitamin syrup	100ml	Becosym	3.00	1.08
oral contraceptive	21	Eugynon	2.13	1.06

Table 6.

Pharmaceutical products that might be selected for manufacture in Liberia.

The figures in column 3 are based on estimates of current demand according to the National Medical Supply Depot. It is believed that the actual need will be very much higher.

Product description	Purpose or class	Estimated current annual consumption
amodiaquine tablets 200mg	antimalarial	1.25 million
benzyl benzoate application	scabies, topic -al treatment	8000 litres
chloroquine sulphate tablets 200mg	antimalarial	10 million
ferrous sulphate mixture paediatric	antianaemic	?
intravenous fluids (various)	rehydration	115,000 litres
methyldopa tablets 250mg	antihypertensive	2 million
methyl salicylate liniment	counterirritant	2,500 litres
metronidazole tablets 200mg	antiprotozoal	1.25 million
oral rehydration salts	rehydration	50,000 sachets
paracetamol syrup	analgesic and antipyretic	8,000 litres
paracetamol tablets 500mg	as above	6 million
piperazine syrup	anthelmintic	12,000 litres
piperazine tablets 500mg	anthelmintic	4 million
sulphadimidine tablets 500mg	antibacterial	1.25 million
water for injections, 10ml	general	500,000 ampoules.

total of all tablets	25.75 million
total of all non sterile liquids	33,000 litres

Table 7.

Proposed manufacturing operations in Liberia. Pre-fe
and capital investment costs.

Production or service unit	Annual capacity	Equipment costs	Buildings "w'house standard" $250/sq.m
intravenous fluids	150,000 l	$200,000	220sq.m $55,000
oral rehyd -ration salts	4,000,000 x 29.5g	$ 78,000	128sq.m $32,000
liquid prepar -ations, NS	300,000 l	$ 70,000	300sq.m $75,000
tablets	120 million	$160,000	300sq.m $75,000
warehouse, procurement, prod'n planning	-	$ 39,000	600sq.m $150,000
quality control laboratory	-	$138,000	
Grand total			

easibility study estimate of capacity

Buildings "office standard" $400/sq.m	Electrical and other services	Furnish -ings	Total Cost
40sq.m $16,000	$25,000	$2,000	$298,000
40sq.m $16,000	$8,000	$2,000	$136,000
40sq.m $16,000	$20,000	$2,000	$183,000
40sq.m $16,000	$15,000	$2,000	$268,000
200sq.m $80,000	$15,000	$10,000	$294,000
500sq.m $200,000	$15,000	$20,000	$373,000
			$1,552,000

Table 8.

Proposed staffing and possible salary structure for a Pharmacy Administration*.

Appointment or grade	Number	Annual salary $	Totals of annual salaries $
Head of department	1	15,000	15,000
Senior scientific officer	2	12,000	24,000
Scientific officer	4	10,500	42,000
Secretary to head of dept.	1	7,000	7,000
Secretarial pool	5	5,500	27,500
Unskilled	3	3,000	9,000
		Grand total	124,500

*Excluding the procurement section, - the presently existing National Medical Supply Depot.

Table 9.

Proposed phasing of development of a Quality Control and personnel requirements.

Phase	Capability	Equipment costs $
1	General chemical/physical analysis to provide a useful degree of control, including UV spec.	58,200*
2	Add microbiological assay for potency testing of antibiotics	15,315
3	Add flame analysis for control of oral rehydration salts; dissol -ution testing, fluorimetry.	10,650
4	Add facilities for control of IV fluids, i.e. sterility test and LAL "pyrogen" test.	12,935
5	Add IR spectrophotometry; start microbiological assay of vitamins	16,000
6	Add gas/liquid chromatography; basic pharmacological testing.	14,200
	Totals	127,300

*Includes the cost of one vehicle.

Laboratory showing investment in equipment

Expendable materials costs $	Personnel requirements			
	Profess -ional	Technic -ians	Secret -arial	Others
8,000	2	2	1	2
1,000	+1	+1	+1	+1
400	+1	+1		
500	+1			
400				
400	+1	+1		
10,700	6	5	2	3

Table 10.

Proposed staffing and possible salary structure for a Pharmaceutical Quality Control Laboratory .

Appointment or grade	Number	Annual salary £	Totals of annual salaries £
Head of department	1	15,000	15,000
Senior scientific officer	2	12,000	24,000
Scientific officer	3	10,500	31,500
Technicians	5	7,500	37,500
Secretarial	2	5,500	11,000
Unskilled	3	3,000	9,000
		Grand total	£128,000

Table 11.

A scheme for the allocation of costs for analysis and other quality control services by the Pharmaceutical Quality Control Laboratory.

Product group or general service.	number of batches or samples.	cost units, analysis.	cost units, other services.	total cost units.
intravenous fluids, production batches.	250	180	60	60,000
oral rehydration salts, production batches.	540	60	30	48.600
liquids not required to be sterile, production batches.	300	90	45	40,500
tablets, production batches.	600	120	60	108,000
miscellaneous samples from Pharmacy Administration.	960	200	-	192,000
procurement(buying) samples from Pharmacy Administration.	800	80	-	64,000
boiler waters from manufacturing complex, daily samples.	240	60	-	14,400
effluent from manufacturing complex, weekly samples.	50	120	-	6,000
			Grand total cost units	533,500

Table 12.

Estimation of the annual cost of operating a quality control laboratory having the functions and capacity envisaged in this report.

source of expenditure	details of expenditure	amounts £	totals £
buildings at cost £200,000	depreciation @ 8%	16,000	
	maintenance @ 1½%	3,000	35,000
	interest on tied-up capital @ 8%	16,000	
equipment and furnishings at cost £158,000	depreciation @ 15%	23,700	
	maintenance @ 3½%	5,530	
	additions @ 5%	7,900	49,770
	interest on tied-up capital @ 8%	12,640	
expendable materials	stationery	2,000	
	chemicals	5,000	7,000
services	electricity, water etc.	25,000	
	telephone, postage etc.	3,000	31,000
	use and maintenance of one vehicle	3,000	
personnel	wages and salaries, as table 10	128,000	128,000
Grand total			250,770

Table 13.

Estimation of the annual cost of carrying out the regulatory functions of a Pharmacy Administration as envisaged in this report.

source of expenditure	details of expenditure	amounts $	totals $
buildings, 300 sq.m at cost of $120,000	depreciation @ 8%	9,600	21,000
	maintenance @ 1½%	1,800	
	interest on tied-up capital @ 8%	9,600	
equipment and furnishings at cost $15,000	depreciation @ 15%	2,250	4,725
	maintenance @ 3½%	525	
	additions @ 5%	750	
	interest on tied-up capital @ 8%	1,200	
expendable materials	stationery	3,000	3,000
services	electricity and water	10,000	120,500
	telephone, postage etc.	6,000	
	use and maintenance of vehicle	3,000	
	local transportation (taxis)	500	
	laboratory testing	96,000	
	external services (inspection)	5,000	
personnel	wages and salaries, as table 8	124,500	124,500
Grand total			273,725

Annex 1.

An outline of a scheme for medicines licencing covering phase 1, Interim Product Licences and phase 2, Manufacturer's Licences.

1. Introduction. A comprehensive licencing scheme, in addition to the two classes of licence to be considered here, would include :

   full product licences,

   licences for subdivision and repacking,

   licences for clinical trials and animal tests.

   The granting of a licence to market a product is very likely to be understood to signify that the licencing authority is well satisfied with the product's usefulness and safety. The thorough eveluation that would be necessary to justify such confidence would be so time consuming as to delay the application of a licencing system for many years. For this reason, the concept of "Interim Product Licences" is introduced. These are somewhat akin to the "Licences of Right" such as were granted for established products when licencing was introduced into countries such as Australia and Britain. However, in the proposed scheme, licences would certainly not be granted as a matter of right.

   In phase 1 of the proposed scheme, applications for Interim Product Licences would be evaluated on the basis of a minimal level of data that would be required.

   In phase 2, when applications for Manufacturer's Licences* would be considered, the rejection of an application would automatically result in the withdrawal of any Interim Product Licences previously granted for products of the manufacturer concerned.

   *Licences would be required both by local and overseas manufacturers.

2. Licencing procedures. Applications for licences would be made on standard forms such as presented here as document ML2 and outlined in document ML4. The technical data given by the applicant would be assessed by the permanent staff of the Medicines Evaluation and Licencing Section of the Pharmacy Administration, (henceforth referred to here as the "Professional Secreteriat").

   In straightforward cases the Professional Secreteriat would make the recommendation for acceptance/rejection of the application in accordance with guidelines (see documents ML1 and ML4) for confirmation by the Director of the Pharmacy Administration.

Annex 1, continued.

However, it is desirable that there should be an appellate body to which either the Professional Secretariat or the applicant could refer in cases of doubt or dispute. Such a body will be designated here as the "Medicines Committee". It would include representatives of the medical and pharma-ceutical professions and, when appropriate, others such as the dental and veterinary professions.

Annex 1, continued.

Document No. ML1.

Interim Product Licences, notes and guidance for applicants and for the Professional Secretariat.

1. General information. After the 30 September 1982*, medicines may only be imported or manufactured for distribution in Liberia if they are the subject of a full or Interim Product Licence.

It is planned that all medicines currently being marketed in Liberia should be reviewed within the shortest possible time in order to eliminate without undue delay, any that appear to be undesirable on first examination. Interim Product Licences may be granted without prior approval of the manufacturer.

Application for Interim Product Licences may be made for any medicine currently being marketed in Liberia, or for any new prescription item if this appears to represent a significant advance over existing remedies. The data required by the Licencing Authority is set out in section 2 of this document. It is simple and thus can be examined expeditiously.

Grounds for disallowing a licence would include :

The essential composition is not clear from the declaration made on the label, carton and insert leaflets.

The drug is unduly hazardous for treatment of the condition for which it is intended.

It is ineffective or is outmoded and can be replaced by more effective or less hazardous drugs.

Information on the label, carton, insert leaflet or other published information includes misleading claims, fails to draw attention to significant side effects or to give appropriate warnings concerning the use of the product, or if information on dosage is inadequate or misleading.

Interim Product Licences may be withdrawn at any time if new evidence of significant hazards comes to light.

The thorough evaluation that will be necessary prior to the grant of a full Product Licence for each of the several thousand medicines believed to be marketed now will clearly be a major task. Accordingly, an order of priority will be established for the re-evaluation of products that are the subject of an Interim Product Licence. Order of priority will be decided in accordance with medical importance and potential hazards from their imprudent use. It is envisaged, for example, that antibiotics and corticosteroids would rate high priority for review.

Annex 1, continued.

It must be expected that during the review process, some products that are the subject of an Interim Product Licence will fail to survive a detailed scrutiny, or the manufacturer may not be granted a Manufacturer's Licence. Thus, the granting of an Interim Product Licence does not imply that a full Product Licence will be granted ultimately.

2. Form of application. The information that is requested in an application for an Interim Product Licence must be submit-ted in duplicate in the English language. It is simple and is basically as follows :

(a) The full name and registered address of the applicant (normally the importer or local manufacturer).

(b) The full name and registered address of the manufacturer.

(c) The brand name of the product (if applicable).

(d) The equivalent generic name (if applicable) together with reference to a pharmacopoeial monograph.

(e) The pharmaceutical form and composition of unit dose or the entire package, as appropriate, as stated on the label/package.

(f) The pack sizes currently being marketed.

(g) Duplicate samples of each label, carton, insert leaflet etc. bearing written data concerning the product and its use.

(h) The proposed legal category,
A. Prescription,
B. Non-prescription, pharmacy only,
C. Non-prescription, registered medicines stores,
D. Unrestricted.

3. Timing of application. The Licencing authority intends that all applications shall be considered, and when the decision is favourable, Interim Product Licences be granted by 30 June 1982*. Thus, there will be a three month period remaining before restriction on importing/marketing comes into force on 30 September 1982.

To facilitate work planning and processing of applications, it is requested that intending applicants notify the Licencing Authority by 31 May 1981* of the approximate number of products for which Interim Product Licences will be sought. This number is for guidance only and will not be binding.

4. Additional requirements. The Licencing Authority reserves the right to require additional information and samples.

*Dates are included to illustrate the time scale and are not intended to be fixed.

Annex 1, continued.

Document No. ML2.

Application form for an Interim Product Licence.

To be completed in duplicate in the English Language.	For use by the Licencing Authority. Application number ..... Fee paid .....

1. The full name and registered address of the applicant.

2. The full name and registered address of the manufacturer.

3. The name under which the product will be marketed.

4. The equivalent generic name (if applicable) together with reference to a pharmacopoeial monograph.

5. Pharmaceutical description,
   a. pharmaceutical form.
   b. composition of unit dose or of the entire content of the package as appropriate, as stated on the label and other component of the package.

Annex 1, continued.

6. The peck sizes that are to be covered by the licence.

---

7. Attach to both copies of this application, one sample of each label, carton, insert leaflet etc. bearing written data concerning the product and its use, for each pack size.

Use additional sheets for this purpose.

---

8. The proposed legal category. Delete those not required.

A, B, C, D.

---

9. Declaration

I/We apply for the grant of an Interim Product Licence on behalf of the company/person named in section 1, in respect of the product named in section 3 and conforming to the descript-ions given in sections 4, 5 and 6 and annexed samples of packaging materials as required by section 7 of this form. It is understood that the said Interim Product Licence will have an initial validity of not more than 3 years and shall be subject to the following conditions :

9.1 The Licencing Authority may at any time withdraw or modify the terms of the Licence if there is new evidence suggesting an undue hazard to health.

9.2 The licencing Authority may at any time require the Licence Holder to submit detailed information in an application for a full Product Licence.

9.3 No variation may be made in the composition, packaging and descriptive material except in accordance with the written agreement of the Licencing Authority in the form of a codicil to the licence.

9.4 No material information has been omitted from the application (within the knowledge of the signatory).

Date .....

Signature.....

Name, block letters.....

Capacity in which signed

.....

Annex 1, continued.

10. For use by the Licencing Authority.

Evaluated by (i) .....

(ii) . .....

(iii) .....

10.1 Decision/recommendation of the Professional Secretariat.

Licence to be granted for ..... category.

Licence not to be granted for the following reasons :

.....

.....

Licence to be restricted to the ..... categories for the following reasons :

....

.....

Refer to Medicines Committee Yes/No

10.2 Recommendation of Medicines Committee :

.....

.....

Annex 1, continued.

Document No. ML3.

Interim Product Licence Number ..... Legal Category ..... (1)

Authority is hereby given to (2)

.....

.....

to import/manufacture and distribute in the Republic of Liberia in accordance with the terms of a Category .... Licence, (3) the product described in the attached application form dated .....19.., and known as (4)

.....

This licence gives approval for the import/manufacture and distribution of the product only as described in the attached application form. No change may be made in the composition of the product, nor in the content of the written data concerning its uses, dosage, indication, contraindications or special precautions on the label, carton, insert leaflet or in any advertisement except in accordance with written approval of the Licencing Authority, in a codicil to this licence.

An Interim Product Licence is granted without an in-depth study of detailed product information. The Licencing Authority reserves the right to require more detailed information at any time with a view to carrying out a thorough evaluation. As a result of that thorough evaluation, a full Product Licence might be awarded or the Interim Product Licence might be revoked.

This Licence is valid until .....19.. unless revoked at an earlier date in accordance with the recommendations of the Medicines Committee. The licensee may request an extension of validity if a full licence has not been awarded three months before the expiry of this Interim Licence.

Signed ..... on behalf of the Licencing Authority

Name, block letters .....

Date .....19..

Note : The application form is required to be submitted in duplicate. One copy will be returned to the applicant attached to the licence. That copy will bear a signature of a responsible official of the Licencing Authority certifying that it is the application that has been approved.

Annex 1, continued.

Notes referring to Document No. ML3.

(1) Insert the Legal Category, A, B, C or D.

(2) Insert the name and registered address of the Licensee.

(3) Insert the Legal Category, A, B, C or D.

(4) Insert the name under which the product will be marketed.

On approval of an application, in addition to issuing a licence, both copies of the application form should be stamped on every page (including attached pages) and signed/initialled by a responsible official of the licencing authority to indicate that this is the actual application that has been approved. A suggested form of rubber stamp is shown below.

INTERIM PRODUCT
LICENCE GRANTED

.....19..

Signed

.....

For the Medicines
Licencing Authority.

Annex 1, continued.

Document No. ML4.

Manufacturer's Licences, notes and guidance for applicants and for the Professional Secretariat.

1. Individual products may be granted a full Product Licence, i.e. a full (not interim) licence for import, manufacture, sale, distribution and use in Liberia only if the producer holds a Manufacturer's Licence issued by the Licencing Authority of the Republic of Liberia.

2. Applications for a Manufacturer's Licence may be submitted by the actual manufacturer or by his agent. In either case, a declaration as to the truth of statements written in the application must be made by a responsible official of the Manufacturer.

3. Manufacturer's Licences will define the classes of manufactur-ing operations for which approval has been granted, and will normally be valid for a period of five years. The Licencing Authority shall, however, retain the right to suspend, modify the terms of, or cancel a licence if there is reason to believe that such an action is necessary in the interests of public health and safety.

4. Applications for a Manufacturer's Licence are required to be supported by certain evidence as to the company's structure and activities. The following suggested format is acceptable (see also note 1) :

   (a) The full name and registered address of the company.

   (b) The registered capital of the company.

   (c) The nature of the company's activities (see note 2).

   (d) The address(es) of the manufacturing plant(s) at which medicines proposed for licencing in Liberia would be produced and packaged.

   (e) Company personnel, - the total numbers of professional and non-professional staff employed, the numbers engaged in production, quality control, research, administration, sales and marketing, also the numbers engaged at the individual manufacturing plant(s) named in (d) above, in production and quality control (see note 3).

   (f) The pharmaceutical forms and number of products of each form currently manufactured (see note 4). The Licence will specify that approval is for certain defined pharmaceutical forms only.

Annex 1, continued.

(g) The pharmaceutical forms and number of products of each form that will be proposed initially for licencing in Liberia (see note 4).

(h) Legalized evidence that the company is authorized to manufacture and sell in its home country pharma -ceuticals including those listed in (f) above.

5. The Licencing Authority may additionally require that the applicant agree to its manufacturing plant being visited by the Authority's inspectors, or by specially appointed representatives for the purpose of evaluating material facilities and production and quality control operations.

6. A licence fee will be charged in accordance with a scale as defined in document number ML..* The fee will be payable on submission of the application.

Note 1. The Licensing Authority reserves the right to insist on the format outlined. However, recognizing that many manufact -urers will already have prepared statements as required for licencing in other countries, these might be acceptable in Liberia provided that all essential information is presented.

Note 2. The purpose of this question is to assist in establishing that the applicant (manufacturer) is a genuine pharmaceut -ical manufacturer having expertise appropriate to the category of product that it is proposed to offer to Liberia.

Indicate whether the company is concerned wholly or part -ially with pharmaceutical products. If "partially", then indicate the proportion of pharmaceutical activity in terms of total staff involved and/or percent of the total value of the company's output. Indicate the nature of the comp: -any's pharmaceutical activities, e.g. Chemical synthesis, fermentation, extraction from natural products, pharma -ceutical processing for the production of dosage forms as indicated by the applicant, packing. Has the company marketed any products of original research ? If so, name one or more, giving dates and references. The absence of research activities is not necessarily a bar to acceptance.

Note 3 For the total and for each separate activity, show separately the numbers of professional and non-professional staff currently employed. In the context of this question, the term "research" does not include market research.

Note 4. Names and brief descriptions of products may be given if the applicant so wishes.

* Not included here.

Annex 1, continued.

Document No. ML5.

Manufacturer's Licence Number .....

Recognition is hereby granted to (1)

.....

.....

as being a company whose products can be considered for marketing in the Republic of Liberia subject to the following conditions :

1. Recognition applies only to the classes of product listed in Annex 1 of this licence.
2. Recognition applied only to products manufactured and packaged at the plant(s) specified in Annex 2 of this licence.
3. Only products for which an Interim or full Product Licence has been obtained can be marketed.
4. The licence will normally be valid until .....19.. However, the Licencing Authority shall retain the right to suspend, modify the terms of, or cancel it, if there is reason to believe that such action is necessary in the interest of public health and safety.

Signed ....., on behalf of the Licencing Authority.

Name, block letters .....

Date .....19..

Note (1) Insert the name and registered address of the manufacturer.

Annex 2.

Pre-feasibility study estimates of costs of equipment for pharmaceutical manufacture, Costs are in US $.

1. Oral rehydration salts.

item	unit cost	number	total cost
weighing machine, 150Kg	3960	1	3960
Fitzmill	10000	1	10000
blender (powder mixer)	14900	1	14900
Al alloy drums	140	16	2240
sachet filling machine	33000	1	33000
de-humidifier	13400	1	13400
Paliton truck	500	1	500
Total			78000

2. Liquid preparations not required to be sterile.

item	unit cost	number	total cost
jacketed SS mixer & filt.	7600	1	7600
transfer pump 500l/hour	1500	1	1500
SS vessels on castors	1600	5	8000
Silverson mixer	1900	1	1900
bottle washer, 400/hour	11000	1	11000
Gravfil filling machine	2325	2	4650
heating pan, electrical	1900	1	1900
glassware & material moving equipment	11000		11000
demineraliser	9550	1	9550
platform scales, 150kg	4450	1	4450
moving belt for packing	5100	1	5100
Mettler balance 5Kg/1g	3350	1	2250
Total			70000

Annex 2, continued.

3. Tablets.

item	unit cost	number	total cost
Manesty mixer "300"	16600	2	33200
fluid bed dryer, 100Kg	25000	1	25000
Rotorgran	4500	2	9000
Fitzmill	10000	1	10000
drum mixer	1300	2	2600
compression machine "27"	33200	1	33200
" " "35"	41200	1	41200
Al alloy drums	140	15	2100
weighing machine, 200Kg	3700	1	3700
Total			78000

4. Warehouse and procurement.

item	unit cost	number	total cost
Paliton trucks	500	4	2000
weighing machine, 500Kg	7000	1	7000
" " , 200Kg	4000	1	4000
collapsible iron pallets	75	160	12000
Lansing Bagnall trucks	6000	2	12000
calculating machine	1000	2	2000
Total			39000

Annex 3.

The proposed intravenous fluids plant.

The International Dispensary Association of Amsterdam (IDA Foundation) is a foundation for the non-profit procurement of medical supplies. Its activities now extend to the provision of assistance to develop-ing countries in the establishment of pharmaceutical manufacturing facilities. A basic plan for intravenous fluid plants has been developed and currently the first of these is being assembled in Vientiane, Laos. The following brief description of the project is presented as it is felt that IDA's experience in this field may be of interest to the Government of Liberia.

The plant is being set up as a "turn-key project", i.e. supplied inclusive of :

(i) A complete building, plus offices, toilets and showers.

(ii) All equipment, inclusive of complete facilities for water treatment.

(iii) Bottles, raw materials, filter materials etc., sufficient for one year's production.

(iv) Laboratory clothing, detergents and disinfectants.

(v) Crates for transport and storage of bottles.

Completion of the infra-structure, - laying of foundations and provision of water and electricity supplies was achieved by the Laotians in January 1981 and assembly of the plant was due to begin in February. Training and production trials were expected to commence in March or April 1981.

The plant is designed to have a capacity of about 700 litres/day which, allowing for weekends and other plant shut-downs, is expected to correspond to about 150,000 litres/year. However, capacity could be increased at relatively little extra cost by the installation of a larger production vessel and autoclave etc.

Costs for the material facilities of the plant in Laos are summarized :

Buildings including services	$100,000
Manufacturing machinery	$200,000
Additional engineering, testing, packing, insurance, tools and installation	$200,000
Raw materials, bottles, labels, giving sets, laboratory clothing, household equipment etc.	$200,000
Office materials and equipment, laboratory equipment	$ 50,000
Total	$750,000

Annex 3, continued.

There would be a slight saving in Liberia on these figures, as provision for the cost of laboratory testing facilities has already been made in the overall project.

Additionally, there would be costs for a feasibility study, project guidance and expertise (which would be provided by IDA). In the case of the Laotian project, the cost of these services amounted to $300,000 but could be rather different (upwards or downwards) for Liberia.

Annex 4.

A programme for transfer of technology and for training of staff for the Pharmacy Administration and the Pharmaceutical Quality Control Laboratory.

1. Introduction. It is assumed for the purpose of planning this programme that profeesional personnel recruited for these quality surveillance and administrative functions will be of bachelor degree status but will not have had any post graduate education or relevent post graduate experience. In the event that personnel with better qualifications or experience can be recruited, then the implementation of the programme may be reduced accordingly.

2. Further education and training for Pharmacy Administration personnel. Practical experience in an established overseas authority would be generally useful in all branches of the Pharmacy Administration that are concerned with regulatory matters. Each person who is granted such training opport-unities should spend at least a part of that time in one or more of the smaller countries. For example, in the Republic of Ireland, which is a small but advenced country, and/or in the Kingdom of Jordan which is a developing country that has made good progress in recent years in regulatory matters.

   Apart from such "on the job training", short courses have been offered in recent years in the subjects of inspection and of medicines evaluation and licencing by the governments of the Federal Republic of West Germany, The Netherlands and Sweden. These, it is understood, are of a minimum of three weeks duration. If still being offered, they would provide excellent formal introductions to these specializations.

   It is proposed that a fellowship of 6 months duration be made available to the Director Designate of the Pharmacy Administration to enable him/her to attend the formal courses in inspection and in medicines evaluation and licencing, and to see the workings of at least two overseas regulatory authorities. The appointees to the positions of Heads of Sections of Legislation and Enforcement, and of Medicines Evaluation and Licencing may be awarded fellowships of 4 months each to allow them to attend the appropriate short course as well as to spend some time in overseas regulatory offices.

   The person appointed as Head of the Drug Information Section may spend two months seeing the relevent operations of overseas authorities and perhaps visit the appropriate section of the World Health Organization in Geneva.

   The three other scientific officers of the Pharmacy Administration should have the opportunity to attend the appropriate short formal courses as well as spend a little

Annex 4, continued.

time in an overseas regulatory authority. Fellowships of two months are proposed for this purpose.

3. Further education and training for the Laboratory. The capability required for the senior positions of responsibility in a quality control laboratory far exceeds what can be reasonably expected of a person not having had the opportunity to obtain a post graduate qualification or acquire relevent experience. Further training that is especially appropriate to these responsibilities is afforded by the Master's Degree courses in Pharmaceutical Analysis such as are offered by several British Universities. The course offered by the University of Strathclyde, Scotland, for example, provides a very comprehensive training in chemical and physical aspects of pharmaceutical testing. Normally, foreign students are required to study for two years to acquire this qualification.

It is suggested that one of the first steps to be taken in establishing the laboratory should be to appoint one graduate to its staff for early enrolment on such a course. In this way, the appointee should be ready to take up his duties about the time that the physical facilities are set up. At a later stage, two more appointees may be given the opportunity to enrol for such a course.

It is envisaged that all biological aspects of the laboratory's work will be undertaken within a single section. It seems appropriate, therefore, that two members of that section should have the opportunity to gain experience in all the microbiological and pharmacological aspects of the laboratory's work. This experience should include :

The control of sterile products and their production, through control of the environment and sterility testing of the finished product.

Microbiological assay for the estimation of potency of antibiotics and of vitamins. This would entail the identification and maintenance of cultures, the theory of biological standardization with particular reference to microbiological assays, factors influencing measured response and therefore an awareness of sources of error, principles of experimental design and evaluation of assays, practical techniques.

Routine pharmacological testing as applied to pharmaceutical products. This would include the pharmacopoeial tests for abnormal toxicity, hypotensive substances, pyrogens (rabbit test) and Limulus amoebocyte lysate (LAL) test. It would be useful also to acquire a broader general experience of biological testing even though the intention is that

Annex 4, continued.

only a very limited range of tests be carried out in the Liberian laboratory. The course should place appropriate emphasis on the statistical interpretation of observations.

The training may be through attachment to institutions that regularly carry out such work, for example, the National Institute for Biological Standardization and Control, Hampstead, London, England. Alternatively, perhaps some School of Pharmacy would offer short courses in this field. The School of Pharmacy, University of Bath, England, for example, adopts a very flexible approach in catering for specialized requirements.

4. Transfer of technology and administrative know-how. For the success of the proposed Pharmacy Administration and Laboratory, a strong organizational and administrative structure is essential. This would probably best be attained by the appointment of expatriate advisers in the early stages of the establishment of these two bodies. The extent and duration of such advisory appointments should naturally be dependent on the qualifications and experience of the national staff appointees and so proposals made here must be very flexible.

In the case of the laboratory, which would be providing a service to private industry, it would seem reasonable for representatives of that industry to have some voice in decisions on leadership of the laboratory, so as to assure themselves that they were being provided with a competently run service.

It is suggested that as an absolute minimum, a consultant should assist in the initial planning of the laboratory administration for a period of three months and that an adviser be recruited to guide progress on a longer term basis. An initial appointment of two years is recommended.

For the Pharmacy Administration, a consultancy of two months duration to assist in initial general planning is suggested. Additionally, for medicines evaluation and licencing, consultancies of two months duration are proposed for the implementation of each of the three phases of the programme (see section 7.2).

5. Summary of recommendations for transfer of technology and staff training.

(a) Fellowships for overseas training, Pharmacy Administration.

Attendence of formal courses and practical experience

Annex 4, continued.

of workings of overseas regulatory bodies,
1 x 6 months
2 x 4 months
3 x 2 months

Experience of operations of overseas drug information services
1 x 2 months

(b) Fellowships for overseas training, the Laboratory.

University courses leading to MSc in pharmaceutical analysis 3 x 24 months

Attachment to institutions for practical training in biological aspects of control and/or short university courses,
2 x 6 months

(c) Consultancy, Pharmacy Administration.

Initial general planning
1 x 2 months

Medicines evaluation and licencing at beginning of each of phases 1, 2 and 3.
3 x 2 months

(d) Consultancy/long term advisers, Laboratory.

Initial general planning of administration
1 x 3 months

Long term guidance
1 x 24 months initially.

6. Estimated costs of fellowships and consultancy.

Fellowships :	
travel at $2000 per return journey, 12 x $2000	$ 24,000
subsistence at $1400 per month, 106 x $1400	$148,400
tuition, M.Sc. courses at $7000, 3 x $7000 } miscellaneous totalling $7000 }	$ 28,000
Total	$200,400
Consultancy :	
travel at $2000 per return journey, 7 x $2000	$ 14,000
salary and allowances at $180 per day (short term) 320 x $180	$ 57,600
salary and allowances at $150 per day (long term) 720 x $150	$108,000
Total	$179,600
Grand total $380,000	

Annex 5.

Phasing of expenditure on laboratory equipment, - an expansion of the data in column 3 of table 9.

Equipment for chemical/physical testing laboratory, phasing of purchasing. Figures represent cost in US $.

Item or group	Phase 1	2	3	4	5	6
glassware	6800		530			
hardware, general	4450			235		
centrifuge	1050					
water baths	3390			915		
muffle furnace	1820					
ovens	4240					
refrigerators	940					
balances	5250		1750			
tablet disint.apps.	940					
tablet dissol.apps.			1350			
K.F. titration	1410					
electromet. titr.			600			
microscope	720					
UV spectrophotometer	9400					
flame analyser			2100			
fluorimeter			4320			
IR spectrophotometer					16000	
GLC apparatus						9200
pH meters	1180					
chrometog.,general	1990					
polarimeter	2980					
refractometer	1640					
Totals	48200	-	10650	1150	16000	9200

Grand total 85200

Annex 5, continued.

Phasing of purchasing. Equipment for microbiological assay, phase 2 only, sterility and LAL test, phase 4 only, general basic pharmacology, phase 6 only. Costs in the main body of the table are in US dollars.

Item or group	Phase 1	2	3	4	5	6
glassware		800		780		
hardware, general		280		260		
incubators		1260		2520		
refrigerator		560		560		
ovens		2140				
autoclaves		1255				
water baths		2840		1785		
analytical balance		1750				
centrifuge		1060				
microscope		720				
media dispenser		700				
pH meter		590				
blender		180				
calculator		470				
zone reader		710				
laminar flow cabinet				2540		
millipore equipment				2090		
LAL test				1250		
general pharmacology						5000
Totals		15315		11785		5000
Totals brought forward from previous page	48200	-	10650	1150	16000	9200
Phase totals	48200	15315	10650	12935	16000	14200

Note : Phase totals correspond with the figures in column 3 of table 9, except that here the phase 1 total does not include the cost of a vehicle, $10000.