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Seminar on National Self-reliance in Blood and Blood Fractions for Developing Countries

Stockholm, Sweden, 27 September - 1 October 1982

Importance of Blood as Basic Material for Local Production of Blood Derivatives Essential for the Health Care Programmes of Developing Countries

by

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1. **INTRODUCTION**

The use of blood components in recent years has enabled the clinicians to treat patients with the specific component which they lacked and also facilitated the most economic use of blood so that a single donation can be used to treat patients suffering from a variety of conditions. The component therapy also yields excess blood plasma which can be fractionated into still more therapeutic, prophylactic, diagnostic and quality control material.

Blood and blood fractions therefore, constitute essential components in the health care programme of any country. In the absence of blood products, obstructed labour and post partum haemorrhage are likely to be fatal and people with severe haemophilia seldom live more than three years. There is a constant need for human albumin in revival, nephrology and treatment of toxic syndromes. However, most of the developing countries depend entirely on imports of these essential products. With few exceptions, blood and blood fractions are produced only in the developed countries. Primarily through the promotion by the Red Cross and WHO some awareness of the importance of Blood Banks has been created in most of the developing countries. But this has not progressed much beyond this. In the result, the developing countries are unable to meet even a fraction of the demand for blood and blood fractions. This is illustrated by the fact that the average consumption of albumin per one million inhabitants in some developing countries in North Africa is about 9 kg, compared to a corresponding figure of 203 kg in Europe and 296 kg in the U.S.A. (see Table 1). The supplies of blood and blood fractions available to the developing countries are not adequate to cope with the needs of even 40 percent of the population of cities and the situation in the rural area is much worse.
2. **HOW LONG AND TO WHAT EXTENT CAN YOU DEPEND ON IMPORTS?**

Most of the developing countries have been depending on imports of blood and blood fractions. The cost of imported material is often prohibitive and well beyond the reach of many: in some countries a bottle of imported albumin concentrate costs half the annual income of an average rural family. Further, the imports of these items would mean the depletion of scarce foreign exchange resources at the disposal of these countries. Such imports also pose problems of transport. Imported material is, therefore, no answer.

Of late, the Governments of developed countries tended to limit the production of these items to the resources available in their respective countries and restrict the importation of blood for further processing. Although these measures prevent the depletion of scarce resources of blood from developing countries, they will adversely affect the availability of blood and blood fractions on the international market and boost their prices due to limited availability.

3. **WHAT THEN IS THE SOLUTION?**

In view of above, a local supply, even a limited one produced by "technology" suitable to their environment could be of immense value to the rural poor. It is only through the availability of adequate supplies of blood components that blood-banks can meet adequate standards of medical care. Self-reliance in blood and blood derivatives, therefore, constitutes an important element in the supply of these essential drugs to meet the needs of health care programmes. This is particularly so, since the raw material is available in all the developing countries.
However, there are problems, which have to be solved before a viable production of blood fractions can materialize in the developing countries. Although the raw material exists in these countries, it is not available in the requisite quality and quantity and there is considerable resistance on the part of donors of blood. The system for collection, analysis, primary processing, distribution, etc. concern the Ministry of Health and WHO. Although Technologies are available for processing human blood as well as placentas, these technologies are rather sophisticated and require certain infrastructure and skills for adoption. This aspect concerns the Ministry of Industry and UNIDO. It is in this context that this Seminar brings together all the concerned including the representatives of the Ministries of Health and Industry from the developing countries, WHO, UNIDO, and the industry from a developed country under the auspices of the Swedish Government to formulate a plan of action in this vital field.

Blood products are among the WHO model list of essential drugs. These are also included in the 26 essential drugs selected by UNIDO out of the WHO list for the purpose of production in the developing countries (see Annex 1).
Blood transfusion services in Latin America have mainly been developed and are run by private persons, individual hospitals and communities and local Red Cross organizations. Blood is often obtained from relatives of the patients and frequently from paid donors. Due to the efforts of National Red Cross societies and Latin American Association of Voluntary Donors the number of Voluntary unpaid donors is increasing. Large national blood programmes are now being developed. Component therapy is used in some of the larger centres but fractionation of the plasma is only done in three countries. Commercial plasmapheresis is still being performed.

In the Maghreb countries, the blood transfusion services are limited to providing whole blood and no plasmapheresis or fractionation is practised. The services exist either as national blood transfusion services or as independent blood transfusion services for individual hospitals but are under the control of the health authorities. The blood donors are unpaid and their recruitment is rather difficult. Often blood donors are relatives of the patients. The National Red Crescent Societies assist in the recruitment of donors.

There is a wide variation in the standard of services obtained in Asian countries. Some services have limited funds and function only intermittently.

Blood transfusion in the Pacific is now entering a stage of rapid development.
5. CONSTRAINTS TO THE DEVELOPMENT OF PRODUCTION OF BLOOD AND BLOOD FRACTIONS IN DEVELOPING COUNTRIES

The main constraints hampering the growth of blood fractionation industry in developing countries are as follows:

- Non-availability of raw material of requisite quality and quantity
- Lack of infrastructure and production facilities
- Scarcity of skilled personnel
- Non-availability of suitable technology
- Lack of National policies
- Inadequate regional cooperation

a) Raw Material

Human blood and placenta are the raw materials and technologies are available for processing these two materials respectively.

(i) Human blood: This has been the material used over the years. The technology based on human blood is available in a few developed countries and Sweden, the venue of above Seminar is one of them. This Seminar, therefore, deals with the Technology based on human blood. The collection of blood of the requisite quality and quantity is beset with a number of problems as indicated below:

- Insufficient number of donors
- Difficulty in donor accepting immunization and giving blood
- Resistance on account of superstitious belief that blood donation affects the personality and virility
- Religious beliefs
- Reticence on the part of women in some countries

......
- Sick and poor people come forward to donate as a source of income
- Difficult to obtain donors on a continuous basis

It can thus be seen that recruitment of donors does not make much headway due to ethnic, cultural and educational barriers apart from disqualification due to malnutrition, malaria or hookworm anaemia. In view of this, the promotion for donors has to be intensified. Simultaneously socio-cultural aspects have to be improved and health education spread widely.

(ii) Placenta: This material constitutes a "wastage of blood" and thus is free from the ethical problem encountered in the case of human blood collection. Placenta is available in plenty in all the countries. The technology based on placenta is available in few developed countries and France is one of them. The collection of placenta also depends on local conditions.

b) Lack of Infrastructure

This includes facilities for the preservation of raw material. Even where meagre facilities are available, they are often old for effective utilization. Lyophilization and desiccation units are practically non-existent. Inadequate infrastructure, therefore, constitutes a serious handicap to the development of this industry.

c) Paucity of Skilled Personnel

Personnel of different disciplines and skills are required to perform various functions starting from the collection of raw material. These include medical personnel, laboratory technicians, transfusion technicians, engineers, operators,
mechanics, etc. There is scarcity of skilled personnel in many of the developing countries and this restricts the development of the industry. Appropriate training both locally and abroad should be accorded priority while planning the development of this industry.

d) **Non-availability of Suitable Technology**

The developing countries generally assume that the Technology involved in the fractionation of blood is rather sophisticated and it is. As already indicated there are technologies available in few developed countries based on human blood as well as placenta. The developing countries should know what type of technology is available and what are the Terms and Conditions for the transfer of such technology. There are instances of collaboration between the developed and developing countries which facilitated technology transfer. Such transfers of technology are to the mutual benefit of the parties concerned and signify certain philosophy of human relations.

e) **Lack of National Policies**

The lack of well defined national policies often constitute a major constraint to the development of this industry in the third world. The production of blood derivatives has to be considered from the humanitarian angle conferring social benefits and not merely as a commercial proposition. Quality control measures should be enforced in the case of imported products with the same rigidity as in the case of local production.

f) **Inadequate Regional Co-operation**

Regional co-operation would help obtaining better Terms and Conditions for the procurement of Technology and adoption of the Technology suitable to their environment. Pooling of capacities to achieve economies of scale and pooling of markets
are other areas in which regional co-operation assists in the development of this industry. To achieve such co-operation, it would be necessary to define the statute, financial share of each country, mode of functioning and co-operation.

6. BLOOD AND BLOOD FRACTIONS

The launching of a blood programme can be approached in the following three stages:
- the procurement, storage and use of whole blood
- the use of component therapy
- the use of plasma fractionation

The financial and technical implications involved at each stage should be considered carefully. The following is an outline of the technical expertise required and other considerations:

A. The development of a blood programme

This involves the following elements:
(i) Requirements for blood bank and transfusion technology.
   The transfusion centres must be competent in the following procedures:
   - Donor motivation and selection;
   - Phlebotomy technique;
   - Blood grouping and typing;
   - Blood compatibility testing; and
   - Infusion of blood and blood products

(ii) Additional technology
   (a) In the case of local hospitals with minimum facilities
      - blood component preparation and therapy
   (b) Where staff specially trained and physicians are available
      - cytopheresis
      - frozen blood cell technology
B. Production of Components

(Please see annex 2)

(i) With glass containers and a standard refrigerator, the following components can be produced:

- whole blood "fresh" (should be used within a specified time)
- whole blood
- whole blood, plasma-reduced
- red cell concentrate (to be used in place of whole blood)
- modified red cell concentrates:
  (i) leukocytes -poor
  (ii) washed or filtered to remove leukocytes and platelets
- single donor plasma (obtained from red cell concentrates)
- plasma, recovered (obtained from outdated blood)
- Autotransfusion (for elective surgery)

(ii) with glass containers, a refrigerator and a -20°C freezer, the following component can be produced.

- plasma frozen

(iii) with a refrigerated centrifuge capable of handling 600 ml blood containers, the following components can be produced:

(a) using glass or plastic containers:
  - plasma, fresh frozen (can be used as a source of factor VIII or for other plasma fractions)
  - plasma, platelet-rich (used for patients with thrombocytopenia)

(b) using plastic equipment:
  - platelet concentrate (used for patients with thrombocytopenia)
  - cryoprecipitate (as a source of factors VIII, XIII and fibrinogen)
  - leukocyte concentrate
(iv) components produced by plasmapheresis

Plasmapheresis is the procedure whereby red cells in a blood donation are returned to the donor and the plasma is retained. Its use should be reserved for making good any deficit of plasma that there may be after launching a comprehensive blood component programme.

- platelet rich plasma
- platelet concentrate
- cryoprecipitate
- Leukocyte concentrate
- cryoprecipitate poor plasma
- source plasma frozen for further manufacturing

(v) Fractionation of plasma.

The following preparations can be obtained from cryo-precipitate-poor plasma.

- fibrinogen
- prothrombin complex concentrates with factor VII
- prothrombin complex concentrates without factor VII
- factor VII
- normal serum immunoglobulins
- specific immunoglobulins
  - antitoxins: tetanus, botulism, diphtheria, venoms and others;
  - antibacterial: pertussis, staphylococcus, pseudomonas and others;
  - antiviral: rubella, measles, zoster, variola, hepatitis, rabies;
  - anti-cell antigens: rhesus and other red blood cell antigens, white blood cell-HLA antigens
- plasma protein fraction
- albumin
- antithrombin III
- C₄ esterase inactivator
- choline esterase
- plasminogen
- plasmin

Some of the above fractions can be prepared also from placental sources such as:
- albumin
- immunoglobulin
- antirejection factor
- factor XIII

(VI) Several reagents can be produced from human plasma such as:
- grouping and typing sera for human blood cells (red cells, white cells)
- human control sera, purified and impurified
- radiolabeled diagnostics (fibrinogen, aggregated albumin, etc.)
- reagents for coagulation tests

C. CONTAINERS

A developing country launching transfusion service must choose between:
- plastic containers imported from a long distance
- glass containers prepared locally or in a neighbouring country

The preparation of glass containers with anticoagulant is an exacting operation in order to ensure proper sterilization and to avoid pyrogens. Production, should, therefore, be centralized in each country in one unit or several adjoining countries might support a common production unit.
In the case of plastic containers large scale production is essential. Most transfusion Services, therefore, buy such containers ready for use. Advances in the fabrication of plastics, their adaptation to medical uses and progressively lower costs have brought about the total adoption of disposable transfusion taking and giving sets and a rapidly growing use of plastic bags for the collection and preservation of blood and its components.

The advantages of plastic blood collection equipment are:
- a closed system (bacterial contamination significantly reduced)
- more components can be produced
- they are disposable (risk of cross infection reduced)
- they are lighter in weight for shipment, and
- there is less breakage during shipment.
As already indicated, any developing country wishing to embark upon a blood programme would be advised to approach it in three stages based on the availability of technical skills and infrastructure.

(i) The procurement, storage and use of whole blood. All transfusion centres must be competent in the following procedures:
- donor motivation and selection
- phlebotomy technique
- blood grouping and typing
- blood compatibility testing
- infusion of blood and blood products

(ii) The use of component therapy

The easiest components to prepare are red cell concentrates, plasma, and platelet-rich plasma. Transfer of components must be done aseptically and a refrigerated centrifuge is necessary. In case glass bottles are used, transfers should be made in a sterile area. The use of double plastic containers for this purpose is desirable. Red cell concentrates are preserved in the same way as whole blood. Platelet-rich plasma is preserved for not more than 48 hours after blood collection (between 1°C and 24°C). Plasma is preserved frozen at or below -25°C.

Platelet concentrates and cryoprecipitate require the same equipment as above, but the final products will have to be tested using very specialized techniques. Hence separation of these components should be undertaken in laboratories where these tests can be done.
(iii) The use of plasma fractions

Preparation of plasma derivatives (fibrinogen, factor VIII and IX concentrates, immunoglobulins, albumin) requires specialized equipment and accommodation and is most economic when large volumes of plasma are available. Plasma fractionation should, therefore, be carried out at a central place and should only be undertaken in developing countries with not less than 10 million people.

The above three groups represent three further phases in the development of a transfusion service after the initial phase of providing whole blood only. A plasma fractionation laboratory can prepare specific immunoglobulins provided it has access to the so-called 'specific plasma' with a high titre of the requisite immunoglobulins. This is achieved by screening donations for high antibody content, by plasmapheresis of selected donors, or by deliberate immunization of volunteers.

(iv) Quality control

Quality control starting from blood, in-process control as well as final product testing assumes great significance in the case of blood and blood products. This is also essential in assessing the suitability of methods of preparation. Very specific techniques are involved in testing components such as platelet concentrates and cryoprecipitate (in vitro tests of platelet function, assay of coagulation factor VIII). In view of this, preparation of these components should only be undertaken in laboratories where these tests can be done.

(v) Training

There is need to train the personnel involved in blood collection, fractionation and quality control. The training must
be appropriate for the stage of development of the blood programme in the country.

(vi) **Programmes within the framework of TCDC**

Technical co-operation among developing countries offers good scope for Programmes relating to blood and blood products due to several reasons:

- Preparation of platelet concentrates and cryoprecipitate requires laboratory facilities where tests using very specialized techniques can be done.
- Preparation of plasma derivatives requires specialized equipment and accommodation, and is most economic when large volumes of plasma are available. It is desirable to centralize plasma fractionation with a coverage of at least 10 million inhabitants.
- Where glass containers are proposed to be used, it is preferable to centralize production in one unit and several adjoining countries might with advantage combine to support a common production unit for such containers.
- Where plastic containers are proposed to be used, large-scale production of such containers is essential and this involves considerable investments in equipment and technology.

In view of above, it is desirable to launch programmes for the production of blood fractions at a sub-regional level within the framework of TCDC.
8. CONCLUSION

In the foregoing, an effort has been made to make the issue of production of blood fractions transparent. It is up to the Governments of developing countries to decide upon the course of action which they would like to take in order to find a lasting solution to the problem of inadequate supply of blood and blood fractions to meet the requirements of national health care programmes. It is clear from above that a large measure of self-sufficiency can be attained in this field through production on a national/sub regional level resulting in the conservation of scarce foreign exchange resources.

It is evident from the foregoing presentation that Blood and Blood Products are not subjects to be dealt with only by the developed countries. These have to be dealt with by the developing countries too. In this connection, however, the latter have to pay proper attention to all relevant aspects including organization, infrastructure, training, technology to be transferred, etc.

To do so it is essential to organize in a proper manner different activities starting from the collection, storage and production. For this purpose, there is need for co-operation between different ministries in the developing countries. The Blood banks and collection will obviously be the responsibility of the Ministry of Health. In a similar manner, the production will be the responsibility of the Ministry of Industry. Hence genuine co-operation and joint programme between the two wings of the Government are vital for the successful implementation of the entire programme. Whereas WHO/Red Cross could provide assistance in the area of organizing Blood banks and related activities, UNIDO could help in the establishment of small, medium and large scale units for the production of Blood
derivatives, training of personnel, transfer of technology, etc.

In order to develop such programmes it will be important that the overall planning should include all the above aspects, even in cases where production will be taken up subsequently. Co-operation, therefore, between WHO/Red Cross/UNIDO right from the start will facilitate proper development of all the parameters of programmes concerning Blood and Blood derivatives.
9. **UNIDO ACTIVITIES IN THE PHARMACEUTICAL SECTOR**

The programmes of UNIDO in the field of pharmaceuticals during the past ten years have tended to accent firstly the aspects of establishment, expansion, improvement and the creation of indigenous technological base for this industry in keeping with UNIDO's mandate: "To promote and accelerate the industrialization of the developing countries". Secondly, all UNIDO programmes have been developed mindful of the problems and the concerns from the standpoint of the developing countries. The scope of UNIDO interest is as wide as the industry itself and broadly looked at these programmes could be divided into the following four categories:

I Promotional

II Exploratory

III Technical Assistance

IV Consultative

**I Promotional Programmes**

A typical example of a promotional programme in the field of medicinal plants is the unique exploratory mission by a mobile unit organized by UNIDO in collaboration with the Joint UNIDO-Romania Centre. This programme was confined to the Least Developed countries of Asia and Africa. The unit consisted of two four-wheel-drive vehicles fitted with laboratory facilities accompanied by a team of scientists and technologists to carry out the following activities:

- gather data on the spontaneous flora
- list and authenticate important species of medicinal plants growing in the country
- demonstrate the techniques of phytochemical screening and pilot scale methods of extraction and distillation
- establishing liaison with interested scientific and technological persons and institutions

The exploratory mission has proved
successful as can be seen from the fact that UNIDO has already been able to initiate full fledged technical assistance programmes in Nepal, Rwanda and Botswana on the production of pharmaceuticals from plants and similar projects are on the anvil in Sudan and Tanzania.

II EXPLORATORY PROGRAMMES

The exploratory programmes are essential prerequisites for the initiation of long term assistance programmes. For example, the production of pharmaceuticals from plants on an industrial scale becomes a viable proposition only when the raw material for processing is available on a continuous basis in the required quantity as well as quality. Accordingly, UNIDO's programmes in this area have taken the following form:

- Economic mapping of the spontaneous flora
- General assessment of the plant resources

Similarly prior to the formulation of projects for the establishment of sub-regional centres for Research and Development on antibiotics, evaluation missions in Central and South America, visited the countries in the sub-regions.

Other assessment programmes of a general nature have preceded the technical assistance projects in Guinea, Cameroon, Rwanda, Cuba, Mozambique, etc. and several other such exploratory programmes are underway.

III Technical Assistance Programmes

Technical Assistance Programmes form the core of UNIDO's activities in the pharmaceutical industry sector and involve the transfer of technology on the production of pharmaceuticals. The important elements of such programmes are:
- assessment of the raw materials
- techno-economic studies
- transfer of technology
- training
- management
- in-process and quality control
- fielding of international experts
- supply of equipment
- provision of expert services from the planning stage right through to the point of independent production by local enterprises.

The projects in Guinea, Cape Verde, Tanzania, Zanzibar, Cameroon, Nepal, Rwanda, Ghana, India and Zambia are some of the examples where UNIDO is engaged in strengthening the resources and technological capability of the local enterprises. The activities of UNIDO cover practically all the facets of the pharmaceutical industry, ranging from the simple packaging of pharmaceuticals in dosage forms to the sophisticated production of intravenous fluids, injectable and active ingredients. The project in Cape Verde consists of a unit for the production of simple pharmaceutical formulations and a quality control laboratory while the unit in Zambia concerns the production of intravenous fluids. With the technical assistance provided by UNIDO, the pharmaceutical division of GIHOC increased its production several times and became one of the most profitable units of GIHOC.

Production of bulk drugs

For the purpose of integrated production of bulk drugs from intermediate chemicals and raw materials, 26 essential drugs have been identified by UNIDO out of the model list of essential drugs drawn up by WHO Expert committee and these have been approved by WHO. The selection of these drugs is also in conformity with the criteria laid down by the UNIDO panel of Industrial Experts
for the production of drugs in developing countries. Further, these drugs cover therapeutic groups of utmost importance to the developing countries based on the most common diseases prevalent and are needed by these countries in large quantities. Blood and blood fractions are among these 26 drugs.

**Multipurpose plant**

The scale of production needed in a developing country will depend primarily on the size of the domestic market; hence many developing countries require the production of a range of products in limited quantities only.

To meet this need, UNIDO is promoting the multipurpose plant, which permits a variety of drugs to be produced in small quantities from the same manufacturing unit. Multipurpose plants are particularly suitable to the needs of countries in which the sophisticated technology necessary for large-scale production of drugs from raw materials and intermediates is either not available or unsuitable in local conditions, and where insufficient investment funds exist for large-scale plants.

### IV. CONSULTATIVE PROGRAMMES

The main events of recent UNIDO programmes in this category include:


b) Technical consultation on the production of drugs in a Multipurpose plant
   Visegrad, Hungary, 1982
c) In-plant Group Training Programme on the Production of Pharmaceuticals from Medicinal plants, Francophone African Countries, Bucharest, Romania, 1982

d) Workshop on the essential oil Industry, Lucknow, India, 1981

e) First consultation on the Pharmaceutical Industry, Lisbon, Portugal, 1980

f) In-plant Group Training Programme in the Field of Medicinal Plants: Anglophone Countries, Bucharest, Romania, 1980.

g) Ad-hoc Expert Group Meeting on Biomedical Equipment, Vienna, Austria, 1980

h) Ad-hoc Expert Group Meeting on the Production of Veterinary Drugs in Developing Countries: Vienna, Austria, 1980


j) Regional Seminar on the Industrial Application of Microbiology in the Pharmaceutical Industry Havana, Cuba, 1979

k) Technical consultation on Production of Drugs from Medicinal Plants in Developing Countries, Lucknow, India, 1978
One of the crucial needs in developing countries for the purpose of launching projects in the pharmaceutical sector would be the building-up of an indigenous scientific and technological competence of multidisciplinary nature within this area. The successful interaction of the different skills and activities creates the requisite base for the satisfactory growth and development of the industry. The rationale for UNIDO’s consultative programmes is the building-up of the indigenous competence. Thus UNIDO’s efforts will serve as a nucleus for the global effort in assisting the developing world build a pharmaceutical industry based on indigenous raw materials and skills and with maximum benefit to a greater part of the world.
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4- The availability, Terms and conditions for the Transfer of Technology for the Manufacture of Essential Drugs, UNIDO, 1980

5- First Consultation on the Pharmaceutical Industry, UNIDO, 1980


7- The Selection of Essential Drugs, WHO, Geneva, 1979


13- Co-operation Internationale et derives Sanguins, Fondation Marcel Merieux 1982
### Table 1

#### Consumption of Albumin

<table>
<thead>
<tr>
<th>Country</th>
<th>Population (in millions)</th>
<th>Albumin Consumption</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Total Quantity (in kgs)</td>
</tr>
<tr>
<td><strong>Europe</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>France</td>
<td>5.3</td>
<td>4,712</td>
</tr>
<tr>
<td>Federal Rep. of Germany</td>
<td>61.3</td>
<td>34,000</td>
</tr>
<tr>
<td>Spain</td>
<td>37.1</td>
<td>6,000</td>
</tr>
<tr>
<td>Italy</td>
<td>56.7</td>
<td>6,500</td>
</tr>
<tr>
<td>Belgium</td>
<td>9.6</td>
<td>2,220</td>
</tr>
<tr>
<td>Switzerland</td>
<td>6.3</td>
<td>3,060</td>
</tr>
<tr>
<td>Holland</td>
<td>13.9</td>
<td>1,314</td>
</tr>
<tr>
<td>Norway</td>
<td>4.0</td>
<td>293</td>
</tr>
<tr>
<td>Sweden</td>
<td>8.2</td>
<td>962</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>55.8</td>
<td>2,500</td>
</tr>
<tr>
<td>Austria</td>
<td>7.5</td>
<td>2,200</td>
</tr>
<tr>
<td>Finland</td>
<td>4.7</td>
<td>1,000</td>
</tr>
<tr>
<td><strong>Europe Average</strong></td>
<td><strong>318.6</strong></td>
<td><strong>64,761</strong></td>
</tr>
<tr>
<td>U.S.A.</td>
<td>219.8</td>
<td>65,000</td>
</tr>
<tr>
<td>Japan</td>
<td>114.9</td>
<td>12,600</td>
</tr>
<tr>
<td>Tunisia</td>
<td>6.0</td>
<td>70</td>
</tr>
<tr>
<td>Algeria</td>
<td>16.8</td>
<td>100</td>
</tr>
<tr>
<td>Morocco</td>
<td>17.3</td>
<td>30</td>
</tr>
<tr>
<td>Libya</td>
<td>2.5</td>
<td>150</td>
</tr>
<tr>
<td>Egypt</td>
<td>38.0</td>
<td>150</td>
</tr>
<tr>
<td><strong>North African Countries Average</strong></td>
<td><strong>578</strong></td>
<td><strong>500</strong></td>
</tr>
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</table>
ILLUSTRATIVE LIST OF 26 ESSENTIAL DRUGS FOR WHICH FACILITIES FOR THE LOCAL MANUFACTURE OF ACTIVE INGREDIENTS SHOULD BE ESTABLISHED IN DEVELOPING COUNTRIES

ANALGESICS

1. Acetylsalicylic Acid
2. Paracetamol

ANTI-INFECTIVE DRUGS

Antihelmintic drugs

3. Mebendazole
4. Piperazine

Antibacterial drugs

5. Ampicillin
6. Benzyl Penicillin
7. Erythromycin
8. Sulphadimidine
9. Tetracycline

Antifilarial drugs

10. Diethylcarbamazine

Antileprosy drugs

11. Dapsone

Antimalarial drugs

12. Chloroquine
13. Primaquine

Antituberculosis drugs

14. Ethambutol
15. Isoniazid
16. Streptomycin

CARDIOVASCULAR DRUGS

Antihypertensive drugs

17. Hydralazine
18. Propranolol
19. Reserine

DIURETICS

20. Furosemide

ANTI-DIABETICs

21. Insulin

ORAL CONTRACEPTIVES

22. Ethinylestradiol + levo-norgestrel
IMMUNOLOGICALS

23. Blood and blood fractions

VITAMINS

24. Ascorbic acid
25. Hydroxocobalamin
26. Retinol
Treatment of Plasma used for Fractionation

Fresh Frozen Plasma

Long Cycle

- Supernatant
  - Fibrinogen

Cryoprecipitate

- Dried Cryoprecipitate
  - Antithrombin III
- Concentrate of Factor VIII

Plasma for Fractionation

Plasma of 2nd. and 3rd. categories

Short Cycle

- Fibronectin

Treatment with Ethanol
Ultrafiltration
Lyophilization/Chromatography
Albumins and Gamma Globulins