



TOGETHER
for a sustainable future

OCCASION

This publication has been made available to the public on the occasion of the 50th anniversary of the United Nations Industrial Development Organisation.



TOGETHER
for a sustainable future

DISCLAIMER

This document has been produced without formal United Nations editing. The designations employed and the presentation of the material in this document do not imply the expression of any opinion whatsoever on the part of the Secretariat of the United Nations Industrial Development Organization (UNIDO) concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries, or its economic system or degree of development. Designations such as “developed”, “industrialized” and “developing” are intended for statistical convenience and do not necessarily express a judgment about the stage reached by a particular country or area in the development process. Mention of firm names or commercial products does not constitute an endorsement by UNIDO.

FAIR USE POLICY

Any part of this publication may be quoted and referenced for educational and research purposes without additional permission from UNIDO. However, those who make use of quoting and referencing this publication are requested to follow the Fair Use Policy of giving due credit to UNIDO.

CONTACT

Please contact publications@unido.org for further information concerning UNIDO publications.

For more information about UNIDO, please visit us at www.unido.org



19924

Distr.
LIMITED

ID/WG.531/1(SPEC.)
6 November 1992

ORIGINAL: ENGLISH

United Nations Industrial Development Organization

Global Preparatory Meeting for the
Regional Consultation on the Industrial
Utilization of Medicinal and Aromatic
Plants in Asia and the Pacific

Vienna, Austria, 18-20 November 1992

*in 2 parts
diagrams*

**DEVELOPMENT OF INDUSTRIAL UTILIZATION
OF MEDICINAL AND AROMATIC PLANTS
IN COUNTRIES OF ASIA AND THE PACIFIC REGION**

Background Paper

Prepared by

the UNIDO Secretariat

Table of contents

	<u>Page</u>
PART I: THE UNIDO SYSTEM OF CONSULTATIONS AND THE PHARMACEUTICAL SECTOR	1
1.1 Introduction to the System of Consultations	1
1.2 The System of Consultations and the pharmaceutical sector	1
2. Role of medicinal plants - and an overview of the plant-based industry: Prospects and constraints	2
3. Proposal for a regional consultation meeting on industrial utilization of medicinal and aromatic plants in Asia and the Pacific during 1993	5
 PART II: PROPOSED TOPIC FOR DISCUSSION AT THE REGIONAL CONSULTATION	 5
<i>An integrated approach towards the development of industrial utilization of medicinal and aromatic plants encompassing (i) policy, (ii) agro- and process technology, quality, pharmacological evaluation and regulatory requirements, (iii) research and development, (iv) human resources, entrepreneurship and marketing development, and (v) regional and international co-operation.</i>	
4. General discussion of the issue: Policies, strategies and methodologies for development	6
4.1 Development of health and industrial policies/strategies - Need for establishing a national policy and planning committee	8
4.2 Development of appropriate infrastructure and industrial requirements at the national level - Use of modern technology, agro-, process and development technologies for industrial-scale production	10
4.3 Role and need for research and development	15
4.4 Human resource development for specialized technical and management skills	17
4.5 Regional and international co-operation for the development of the subsector	17
CONCLUSIONS	19
References	21
Annex I: Medicinal Plant Resources	22
Annex II: Stages in Drug Development from Medicinal Plants	23

PART I: THE UNIDO SYSTEM OF CONSULTATIONS AND THE PHARMACEUTICAL SECTOR

1.1 Introduction to the System of Consultations

1. The System of Consultations is an instrument through which the United Nations Industrial Development Organization (UNIDO) serves as a forum for developed and developing countries in their contacts and discussions directed towards the industrialization of the latter countries. Participants in the Consultations include government officials, as well as representatives of industry, consumer groups and others. The System facilitates exchange of information and experiences as well as negotiations among interested parties.

2. Benefits deriving from this activity include the identification of obstacles to industrial development in developing countries; the monitoring of trends in world industry with a view to identifying action-oriented measures for increasing the industrial output of developing countries; and the search for new forms of international industrial co-operation in North-south and South-South relations.

1.2 The System of Consultations and the pharmaceutical sector

3. The statistics on pharmaceuticals suggest that 75 per cent of the world population living in developing countries scarcely have access to and consumed about 20-22 per cent of the world's pharmaceutical production. The 1990 studies also reveal that estimated production of pharmaceuticals in developing countries was around 21 per cent of global figures.

4. In its promotion of industrial development, UNIDO has endeavoured to allocate first priority to industrial activities that meet the fundamental needs of the people in developing countries. Pharmaceutical products are essential to ensuring both the immediate and long-term welfare of society, they have a major impact on people's health, their social well-being and economic performance. Consequently, many developing countries consider the pharmaceutical industry a strategic area for development. UNIDO recognizes the validity of this approach and has focused upon the development of the pharmaceutical industry. It has devoted considerable efforts and resources to strengthening this industry in fields of both preventive and curative medicine, including the one based on medicinal plants on which the majority of the population of developing countries rely for their primary health care needs.

5. UNIDO has so far convened three Consultation meetings in the pharmaceutical sector. The last was the Third Consultation on the Pharmaceutical Industry, held in Madrid, Spain, from 5 to 9 October 1987. This Consultation laid special emphasis on the industrial utilization of medicinal plants and there was a general recognition of the importance of herbal medicine and drugs derived from medicinal plants that play a vital role in health-care programmes of large segments of the world's population, especially in developing countries.

2. Role of medicinal plants - and an overview of the plant-based industry: Prospects and constraints

6. The importance of medicinal plants as source of therapeutic agents and contributor towards health care programmes and economies of both developing and industrialized countries is well established. The earliest medicines used were obtained from plants as plants were available in the immediate environment. Ethno-medical traditions resulted through trial and error methodology in selection of plants for treatment over long periods. In many cultures such as Chinese, Indian, Japanese, Korean, Arab, etc., the experience got systematically recorded and incorporated into a regular system of medicine and became a part of materia medica of the traditional system of medicine. A significant proportion of the population, particularly in developing countries, uses traditional medicine on account of their faith in these medicines as well as lack of easy access to modern medicine.^{2/} In addition, as a result of research and development activities, a number of plant-based medicines or intermediate products are used in modern medicine. Of ever increasing importance are pure substances or purified and standardized extracts which permit better analytical characterization and so meet the quality and safety requirements with which every modern drug, whether natural or synthetic, must comply.

7. The World Health Organization (WHO) estimates that some 1.5 billion people have no access to essential drugs. It also estimates that about 80% of the world population rely chiefly on traditional medicines for their primary health care needs and the bulk of this is plant-based. Herbal medicines have cultural acceptance and preference. They bridge the gap between the availability of and demand for medicine.^{2/} Until late in the 19th century such was the situation in developed countries as well. In industrialized countries to provide herbal products, industrial units had taken up manufacturing and pharmacists started to rely upon commercial sources of standardized phytopharmaceuticals while in developing countries this was done by small-scale industries or physicians themselves and many of these were processed in kitchens. With the passage of time, the industrial revolution reflected its impact on this industry, too.

8. The work of the early part of the 20th century brought an evolution of the pharmaceutical industry, the active ingredients isolated are essential drugs today. The know-how acquired from the development and operation of medicinal plant processing factories contributed to the general evolution of research methodology in the pharmaceutical industry. As stated earlier, until the 19th century even conventional medicine depended largely on crude drugs. During the 20th century, the progress in chemical techniques and with the growth of the pharmaceutical industry, crude drugs have been replaced gradually by pure chemical drugs. A decline in popularity of medicinal plant therapy was noticed at one time but the pendulum has again swung and resurgence of interest in study and use of medicinal plants has come about. Many traditional remedies are in therapeutic use, including plants as such, or extracts prepared in accordance with the pharmacopoeia of the country where they are used; in any case, all such products when they have pharmaceutical claims must be controlled for their constancy, safety and efficacy.

9. Annex I broadly explains the three main areas wherein medicinal plant resources are used; Annex II explains the stages in drug development from medicinal plants: production of modern drugs and traditional prescriptions in new dosage forms.^{2/4}

10. Medicinal plants are valuable in modern medicine in four basic ways: (i) they are used as source of direct therapeutic agents, (ii) they serve as a raw material base for the elaboration of more complex semi-synthetic chemical compounds, (iii) the chemical structures derived from plant substances can be used as models for new synthetic compounds, (iv) and plants can be used for the discovery of new drugs.

11. The prospects of an industry ultimately depends on the confidence of its consumers. Through concerted efforts, the introduction of a comprehensive mix of policies and measures covering elements such as regulatory system, production, quality control, research, cost and trade, etc. at national and international levels and harmonization of such steps are likely to be of great significance for the developmental process of the plant-based medicaments subsector.

12. In developing countries, industrial-scale utilization of medicinal plants can be expected to be an effective measure for alleviating shortage of medicine for health care, and give an impetus to the development of the pharmaceutical industry. The level of development of the subsector varies from country to country. There are constraints of policy, economic and technical nature which hamper the development process.

13. The constraints to the development of the subsector are both ideological as well as technical in nature. Ideological constraints relate to the acceptability of proven plant-based medicaments for health care. The other constraints relate to the lack of an adequate physical infrastructure capable of development of agricultural and industrial aspects, lack of capabilities to take advantage of modern agrotechnological techniques and practices, lack of establishment of industrial units for production on scientific and commercial scales as well as technological support in the form of research and development, quality control, pharmacological evaluation, etc. In addition to the above, prevalence in developing countries of inadequacies in technical universities, training centres and human resource development institutions. And finally there is lack of entrepreneurship and non-availability of financial resources. All these aspects warrant attention and consideration, for remedial measures.

14. Plants are a good source of essential oils. Essential oil concentrates, such as concretes, absolutes, spice oleoresins etc. are manufactured by extraction. These are products of commercial value. Standardization and quality control of product is of great importance. For better return, their production needs systematized development of agro- and processing technology and preparing of a co-ordination plan with potential buyers.

15. The development of agro-based medicament and essential oil-based industries would have an impact on the national and rural economy. The establishment of such small-scale industries in the subsector would serve as a source of employment, particularly for women.

16. Appreciating the importance of the subject, UNIDO considers that for economic and health reasons a more systematized approach is urgently needed, that could lead to benefits for all developing countries endowed with medicinal and aromatic flora. To improve economics of the subsector, there is a need to upgrade cultivation techniques and improve production technologies of pharmaceuticals derived from plants. There is a need for the development and enforcement of regulatory aspects. The subject as a whole lends itself to co-operation between developed and developing countries as well as among developing countries through which local resources and long-established traditions in developing countries could be wedlocked usefully to modern industrial production and health-administering technologies in developed countries. Moreover, the varied methodologies and approaches applied in the utilization of medicinal plants could interact with a view to their improvement.

17. The UNIDO approach has been for providing assistance to strengthen institutions and infrastructure for processing of medicinal plants and quality assurance aspects. Emphasis has also been laid on assessment of indigenous flora followed by plans and programme for systematic methods for plant propagation, cultivation and crop management to ensure adequate supplies for industrial processing. UNIDO would encourage developing countries that they should seek to produce not only raw materials but as far as possible partly to fully processed plant-derived products to the specifications and standards demanded by international bodies and industrialized countries. UNIDO encourages South-South and North-South co-operation in all developmental activities.²

18. In short, in providing assistance to build up developing countries' capacities in this field, UNIDO, in conjunction with WHO, has focused attention primarily on the following aspects:

- Selection of plant species of reputed therapeutic value and suitable for industrial processing;
- Assurance of quality and consistency in the plant raw materials;
- Validation of claims of traditional therapies using modern methodologies;
- Development of standards of quality assessment and analytical methods and pharmacological evaluation;
- Development of modern process technology bench and pilot scale as well as technology package for industrial processing;
- Development of human resources and entrepreneurship;
- Determining the role of traditional remedies in current health care programmes;
- Assistance towards development of regulatory mechanisms;
- Investigations leading to development of new drugs, particularly where current remedies are unsatisfactory or unavailable.

3. Proposal for a regional consultation meeting on industrial utilization of medicinal and aromatic plants in Asia and the Pacific during 1993

19. In the light of the ever increasing importance of the subject, UNIDO has planned to convene, in co-operation with the World Health Organization (WHO), a Regional Consultation on Industrial Utilization of Medicinal and Aromatic Plants in Asia and the Pacific during the biennium 1992-1993. The interest of the countries of the region in this field is manifested in the follow-up action undertaken since the Third Consultation on the Pharmaceutical Industry and in the increase in technical assistance. UNIDO maintains a large portfolio of projects and interest in the subject is evident in this region, particularly in China, India, Indonesia, Iran, Nepal, Pakistan, Sri Lanka, Thailand and Vietnam.

20. The objectives of the proposed Regional Consultation are: (a) The development and strengthening of capabilities and capacities in areas of agrotechnology, technology for processing, quality control and pharmacological evaluation, research and development, regulatory mechanisms, development of human resources, entrepreneurship and marketing, so as to assure the sustained growth of the industry; (b) Promotion of regional co-operation among developing countries and between developing and developed countries in mutually beneficial areas of the phytopharmaceutical industry with the aim of improving economic exploitation of local resources. Since national approaches for the development of this subsector would be immeasurably enhanced through regional as well as international co-operation, hence the need for emphasis at these levels. Some of the proposed activities could, in fact, become viable only if such a co-operative approach is adopted.

PART II: PROPOSED TOPIC FOR DISCUSSION AT THE REGIONAL CONSULTATION

21. The development plans that could generate industrially useful products can be expected to occupy a prominent position in the list of national priorities, thus needing development of critical national capabilities, including policy framework, infrastructural, institutional, technological aspects, human skill as well as identification of financial resources. Plant resources offer development of small-scale agro-based industries, such as phytopharmaceutical and essential oils, gums and resins, tannin industries with high impact on national and rural economy.

22. The primary patterns of pharmaceutical development from plants are the following: (a) Pharmaceuticals from plants used in traditional pharmacopoeias; (b) Plants used as raw materials for obtaining drugs already accepted in developed and developing countries' pharmacopoeias; (c) Plants as raw materials for obtaining drug intermediates and new drugs. While the pattern of usage of aromatic plants is that these serve as raw materials for (a) essential oils, and (b) aroma chemicals and fragrance substances, there is a need for systematic approach to exploit the potential of these resources.

23. UNIDO has convened two workshops on the industrial utilization of medicinal and aromatic plants and a global preparatory meeting is planned for the last quarter of 1992. The main objectives of the activities undertaken include the following:

- To identify, within the scope of the broad theme referred to above, the specific and priority issues to be submitted to the Regional Consultation;
- To identify areas needing special attention and assess constraints to developing the subsector through policy measures and enhancement of the technological base;
- To identify ways and means to promote active subregional, regional and international co-operation and propose actions, identify technical co-operation and investment projects necessary to overcome constraints to and opportunities for developing the subsector in the region;
- To assess the prerequisites for the integration of medicinal and aromatic plant-based industry products within the national health delivery system as well as the national and rural economies.

24. In the light of the foregoing and without prejudice to the conclusions and recommendations that might be reached at the forthcoming Global Preparatory Meeting to be convened by UNIDO later in 1992 on the identification of issues and topics for the Regional Consultation, the participants of the Workshop on Industrial Utilization of Medicinal and Aromatic Plants held in Milan, Italy, from 24-27 March 1992, recommended for discussion the issue of "An integrated approach towards the development of industrial-scale utilization of medicinal and aromatic plants, encompassing the following elements:

- (i) Policies - health and industrial;
- (ii) Agro- and process technology for industrial-scale production of herbal medicine, phytopharmaceuticals and aroma chemicals, quality and pharmacological evaluation and regulatory requirements;
- (iii) Role and need for research and development;
- (iv) Human resource development for specialized technical and managerial skills;
- (v) Regional and international co-operation for the development of the subsector.

4. General discussion of the issue: Policies, strategies and methodologies for development

25. In general terms, to make the best use for mankind of the ethnomedical experience accumulated over millennia, certain strategic elements in drug development have to be accentuated and

these must also address the contingency situation prevalent in the developing countries, as regards the restricted availability of pharmaceuticals.

26. The three key elements will be:

- To generate factory-produced plant-derived pharmaceuticals based on traditional formulations with attendant standardization and quality control and modern manufacturing practices;
- To formulate new products (preparations) based on traditional pharmacopoeias, in new dosage forms at economic prices to suit developing countries' requirements and priority being given to areas where therapies available to modern medicine are inadequate;
- To generate new natural products and related synthetics as new therapies in modern medicine.

27. The strategy will no doubt be of great use to the developing countries but it will also seek to benefit the industrialized world particularly where modern medicine is short of adequate therapies. The strategy should draw support from all on grounds of humanitarianism, concern for the health of the underprivileged and the need to develop industries in the poorer parts of the world. The undoubted global benefits that can accrue by the sharing of research and development in this field would be profitable to both industrialized as well as developing nations.

28. A partnership could be initiated between industrialized and developing countries as well as between developing countries themselves in order to realize the best in traditional medicines for the global benefit and to meet the present dire situation that confronts those that inhabit the less privileged parts of the world. The services of international organizations, such as UNIDO, WHO, ITC etc., could be used to catalyze the development of such partnerships, based on the work carried out by these organizations, and the experience so gained.

29. Effective exploitation of medicinal and aromatic plant resources require co-ordination between a number of sectors and consideration of some basic policy issues. It would be befitting for each country to evolve a planned approach for the development of this subsector and besides efforts at a national level, international organizations, such as WHO, UNIDO, FAO, ITC, etc., may be of assistance in implementing the plans.

30. While referring to policies and strategies, the medicinal plant-based industry and governments need to work in harmony and good working relationship. An industrial policy which supports domestic production and stimulates export needs to be developed. The manufacturers of plant-based products, like the manufacturers of other pharmaceutical products, need to be supervised by health ministries and should be guided by a national health policy. A regulatory system needs to be put into force. Considerations need to be given to development of standard formularies. Good manufacturing practices (GMP), quality assurance, harmonization of

policies relating to testing and pharmacological evaluation of medicaments, safety and efficiency are some of the major aspects to be checked. In addition, pricing regulation schemes and a policy with regard to research and development need to be developed. Above all, the ethics of the industry should at no cost be ignored. Policies with respect to the establishment of both a physical and a human infrastructure as well as investment should be developed.

31. Strategic decisions required by organizations concern the products to be produced and the market to be served and should be based on studies. Other decisions would concern the process, technologies, environmental protection, type of research and development. Particular attention and more support is needed for remedies for tropical diseases which are most common in developing countries, such as childhood diseases, diarrhoea and tuberculosis, and production of marketable products, as well as type of distribution system for products. Marketing strategies are of significant importance. It is established that marketing activities benefit greatly from economies of scale. This calls for integration, merger, acquisition, intercompany coalitions, etc. as is common practice in the pharmaceutical industry. Patent system and export orientation also need attention. The prospects for the plant-based medicaments subsector of the pharmaceutical industry undoubtedly depends on the confidence of its consumers. The policy makers and strategists ought to take into account the minutest details in order to make the industry a success and to enable it to meet the growing needs.^{12/}

Systematic approach to exploit the potential of plant resources

32. The need for systematic approach to exploit the potential of the plant resources is being realized in many countries. The presence of agrotechnological and botanical expertise as well as the availability of some expertise in phytochemistry, pharmacology, and pharmaceuticals is deemed as a necessary prerequisite. Aspects covering botany, ethnopharmacology, ethnomedicine, chemistry, pharmacological activity, toxicity, agrotechnology, post-harvest technology, process technology, packaging of dosage forms of prescription and OTC products, and marketing etc. need to be surveyed and studied for better appreciation of the issues. In order to achieve success, steps would need to be taken in developing and reinforcing agro- and technological bases, information systems, research, human resources and co-operation amongst and between countries in all areas of activities. Besides the factors already enumerated, the need for the assessment of plant-based products is emphasized.

4.1 Development of health and industrial policies/strategies - Need for establishing a national policy and planning committee

33. Providing adequate health care presents a significant and complex challenge. The objective of a national drug policy is to render accessible to the whole population the most effective and safe pharmaceutical products of established quality at reasonable cost. The aim of developing national drug policies is to improve the efficiency of the pharmaceutical supply system through co-operation among those responsible for health, industrial production

and trade, etc. The industrial aspects of drug policy are concerned with establishment of local production facilities and policy measures for its promotion, covering development of infrastructure, enhancing access to technology, domestic production, quality control, pricing, research and development, human resources, regulatory mechanisms and investment, etc.

34. Determining the place of plant-based medicaments in the national health care programme and evolving a methodology for an integrated use of such medicine with modern medicine is worthy of continued investigation and, after due consideration, worth its while for implementation.

35. A socially desired and officially endorsed demand for phyto-pharmaceuticals and usage of traditional/herbal medicine could be of great assistance in integrating the use of these drugs with the modern medicine in order to meet national health needs. To implement this strategy, the National Health Policy would need to include a policy on phytopharmaceuticals covering continuous supply of source medicinal plants, domestic production, quality control, distribution, R&D for new drugs, and other related aspects such as legislation, registration and human resource development. The World Health Organization (WHO) can be a guiding body in this field of activity.

36. The manufacturers of plant-based medicaments, like the manufacturers of other pharmaceutical products, need to be guided by a national health policy. The cause could be better served through the establishment of a national policy and planning committee to deal with all aspects related to the development of the pharmaceutical sector, including medicaments based on medicinal plants.

Need for establishing a national policy and planning committee:

37. The first step in achieving the goal should be that the national governments should set up a national policy and planning committee to evolve and formulate national policies and plans for dealing with all aspects of the pharmaceutical sector, including utilization of medicinal plants. The committee should co-ordinate the functioning of different institutions and agencies and monitor progress towards the implementation of the policies in question. The committee should formulate a short- and long-term plan for this sector after due assessment of needs, priorities and resources. It could set up subcommittees dealing with specific aspects of the sector, for instance, a sub-committee dealing with the phytopharmaceutical industry and another dealing with traditional medicine as well as development of new drugs. These two sub-committees should draw up policy guidelines on issues such as:

- Promoting the use of traditional medicine along with modern medicine in the national health care programme;
- Drawing up a system of registration of traditional medicine, a traditional drug pharmacopoeia and formulary, as well as the delivery aspect of such medicine into the primary health care programme;

- Cultivation, collection of plants, establishment of germ plasm bank, etc.;
- Centralizing/modernizing production facilities on an industrial scale for traditional medicine;
- Establishing a phytopharmaceutical industry in line with an enunciated comprehensive industrial policy which supports domestic production and stimulates exports.

38. In the subsector under reference, the adoption of a comprehensive approach in bringing together the main disciplines and interests concerned, i.e. health, agriculture, industry, trade, academia, under a high level co-ordinating subcommittee can be of significant assistance. Such a body would assess needs and priorities, formulate a national policy, help to mobilize resources and ensure orderly development of work and research in the field and interrelated matters stipulated by health and industry departments for the development of drug industry.

4.2 Development of appropriate infrastructure and industrial requirements at the national level - Use of modern technology, agro-, process and development technologies for industrial-scale production

39. In developing countries, one of the main obstacles for the development of the subsector is lack of adequate physical and institutional infrastructure which directly affects the output, efficiency of production units, the degree of local and regional co-operation in research and development, marketing and other supportive activities. Thus besides fulfilment of basic requirements, the efforts need to be directed to the development of other potential areas listed hereunder, to fulfil continuous availability of materials and services.

(a) Agrotechnology:

40. The application of modern standardized techniques for the cultivation and propagation of medicinal plants needs consideration in order to meet continuous availability of quality material. The potential areas needing attention cover: Preservation, propagation, cropwise cultivation, including improved seeds, standardized cultivation techniques, steps to domesticate wild and endangered species, elimination of pests and diseases, control on heavy metals and pesticides, genetic improvement, exchange of germ plasm, post-harvest treatment and storage, etc.

41. Micropropagation techniques based on tissue culture and modern methods of genetic improvement of plant species also need consideration, besides the macropropagation method.

(b) Process and development technologies:

42. The development of technologies for processing of plant materials for production of extracts, active principles, therapeutic agents as well as essential oils etc., and capabilities for production of traditional medicine and aroma chemicals on an industrial scale needs to be considered.

43. Although many developing countries export plant raw materials and import finished drugs at very high prices, production of drugs in their own countries has not commenced. The constraints to this are the non-availability of (i) technology, which in many instances is protected, and (ii) capital investment. Even if these countries could produce some of the drugs, the economy of scale of production would not be feasible unless prior marketing arrangements were established. Regional co-operation in this regard may be a favourable factor.

44. As mentioned earlier, the UNIDO System of Consultations promotes liaison between governments, industry from North and South, in particular areas of industry. Technology aspects are considered at the sectoral level. The UNIDO programme in technology transfer includes all aspects related to the selection, acquisition, adaptation, operation and maintenance of appropriate technology. The approach for any project will depend upon the specific circumstances. However, aspects which are considered in any technology transfer activity may include:

- Enhancement of awareness of technological developments;
- Training in all relevant aspects including direct technological know-how mechanisms for the acquisition of technology;
- Selection of the most appropriate technology taking into account technological, economic, energy, environmental and social aspects;
- Development of engineering capability to allow local production of hardware where possible;
- Development of institutional capability to support appropriate technology transfer and clearer production technologies.

45. Lack of finance can inhibit transfer of technology to developing countries. Beside other global and regional finance-dealing agencies, the Industrial Investment Programme of UNIDO helps in dealing with financial constraints, through its promotion of commercially oriented joint ventures between national investors in developing countries and foreign partners. The main activities of UNIDO's programme include the organization of national and regional investment promotion fora and investment promotion services.

46. There is a need to develop processing technology to enable developing countries not only to export plant raw materials but extracts, pure compounds or intermediates as well. Transfer of technology in the subsector implies enhancement of the level of national expertise in several disciplines that constitute the multidisciplinary exercise of the plant-derived pharmaceutical industry. This includes agronomy, chemistry, instrumental analysis, pharmacology, process technology and product formulation. In most developing countries some nucleus exists in the form of a multidisciplinary institution or centre in which the building-up of a process could begin.

47. It may be explained here that pilot plant technology is needed for development of process technology and for determining a variety of technoeconomic parameters needed for a relevant feasibility study prior to commercial batch scale processing. Along with the development of facilities for production of extracts and active principles, basic drugs, phytopharmaceutical formulations etc. the necessity of standardization of production as well as enforcing good manufacturing practices for all these operations would have significant importance. Good manufacturing practices (GMP) are the guidelines for application of the principles of quality assurance related to the manufacture, processing and packaging operations for medicaments to ensure their safety, efficacy and stability. WHO has developed GMP recommendations for pharmaceuticals as guidance for the industry.

48. In the context of process technology, to facilitate matters the local fabrication and use of versatile polyfunctional pilot scale process unit would be a step forward. To assist interested parties, UNIDO has developed a versatile polyvalent pilot scale distillation and extraction unit to process medicinal and aromatic plants. A practical modular engineering design complete with itemized scale construction drawings with representations of exploded sections and bills of quantities of the materials of construction involved for fabrication of such a unit is available.

49. Traditional medicines have not developed with advances of technology. The age-old methods are still used in their production. This is due to two main reasons, viz. the lack of research and development activities and the unwillingness of traditional practitioners to change due to their dogmatic approach. Besides, there have not been any initiatives by governments or modern practitioners to officially use the services of the traditional practitioners.

50. With the practices of the healer himself dispensing the medicine becoming less and less, patients had to seek the help of the herbal drug store or collectors for the plant materials prescribed. This had led to inconsistencies in plant materials and extraction methods used, bringing about quality and dosage problems. Hence there is an urgent need to standardize these medicines so that those who rely on them could get a better quality drug. These could even be formulated into modern dosage forms to ensure consistent dosage stability and easy transport and storage. UNIDO has pioneered activities in this area.

51. Traditional processing methods could be stimulated, even improved and rendered simpler by use of scientific techniques and standardization in production could be achieved. Manufacturing procedures should be established and described. The use of modern process technology for production of standardized traditional therapies on an industrial scale merits serious consideration for meeting the needs of primary health care.

52. Production of traditional medicines in factories will ensure greater availability of the products with reproducible quality. Consideration thus needs to be given to simplifying and modernizing methods of production, development of appropriate quality control

standards, setting-up centralized factories for production, developing new formulations and dosage forms, and determining pharmacokinetic bioavailability and bioequivalence parameters wherever feasible.

53. The commercial production calls for development of engineering capabilities. Thus designing, fabrication and installation of equipment is another area which should be attended.

54. There is a need for conducting market surveys covering all aspects with a view to adoption of proper marketing strategies pertaining to especially availability, quality, price etc.

55. Aromatic plants have been the source of flavours and aromas of food and pharmaceutical preparations. Many developing countries export the raw plant material or the crude oil or oleoresin extracted from the plants for use in perfumery, cosmetic and food industries. In spite of the advances in synthetic chemistry leading to synthetic aroma chemicals and fragrance substances, natural blends of fragrances substances still remain competitive. Some naturals are even more valued as their sensory properties cannot be imitated or matched. There is also a growing need for these in aroma therapy for those who prefer "natural" to artificial/synthetic materials.

56. Two factors have retarded the development of the essential oil industry in developing countries: (i) lack of technology and analytical methodology to produce oils conforming to international standards and market requirements, and (ii) inaccessibility and lack of contacts to the protected international markets. Local use of these oils is restricted due to the lack of know-how for downstream processing of the oils to produce aroma chemicals and fragrance substances. Development of the industrial utilization of aromatic plants will be economically very important and useful to the developing countries both in terms of export earnings and import substitution of fragrance substances.

(c) Establishment of standards and methods of quality, safety and efficacy assessment 2

57. Production on industrial scale and pilot plant technology must be supplemented and supported by modern analytical instrumentation for quality assessment. It has to be borne in mind that rigorous quality control requirements precede acceptance of raw materials, plant extracts, isolates, and pure phytochemicals, as well as finished products, in international trade. Thus, systematic record inventories should be maintained and modern instrumental analytical methods should be used for quality assessment and standardization of plant-derived products and for quality control of industrial scale-manufactured pharmaceuticals.

58. Safety and efficacy assessment should cover all relevant aspects. Side-effects should be documented according to pharmacovigilance principles and these should be part of the literature.

(d) Product development and stability studies

59. Attempts should be made to develop the traditional medicinal preparations into products of high quality, efficacy and stability. The stability studies have to be conducted to determine proper expiration dates to suit the climatic and storage conditions in the countries.

60. A programme would remain incomplete unless and until there can be developed standardized products which are suitable for indigenous health care programmes and products with quality assurance acceptable in international trade which could generate foreign exchange. There should be a defined formula including excipient, procedure for manufacture, and specification for each product. The physical and chemical stability of the product in the final marketing pack thus should be tested under defined storage conditions and shelf-life should be established.

(e) Conducting pharmacological screening, toxicity tests, preclinical and clinical studies

61. Pharmacological and clinical studies are the leading discipline of the programme. It has to be noted that finished formulated preparations will find little prospects of being accepted locally or in the industrialized countries as they would face formidable regulatory barriers with demanding requirements of clinical, preclinical and analytical data. Thus conducting of pharmacological, toxicity and clinical studies and tests etc. would need to be introduced as a matter of routine. The competent authority for assistance in this area is, for instance, WHO.

(f) Regulatory requirements

62. The significance of fulfilling regulatory requirements is of paramount importance. The regulatory requirements for admission of products into local therapeutic usage is largely a matter for the ministries of health. Analytical profiles, toxicological parameters will have to be determined prior to acceptance as these would help in both creditability and acceptability. The registration and regulatory authorities should evolve guidelines on herbal assessment and safety, taking into consideration the work done by WHO and other international bodies.

63. It may, however, be mentioned that registration of herbal preparations for use in modern medicine or official health care systems has been difficult due to the regulatory requirements of efficacy, toxicity and quality control. But some developing countries have established different criteria for registration of traditional medicine taking into account quality and safety aspects. Recent developments in Europe have eased the requirements for registration for sale of these preparations through herbal and food stores. The major requirements being quality control from raw material to finished products and standardization of medicines to get reproducible dosages. Development work has to be done to achieve these as it is more complex to deal with extracts than pure compounds.

(g) Identification of training requirements

64. There would be a need for educated manpower capable of absorbing specialized technical and management skills. The support of academic, vocational and training institutions could play an important role in providing manpower with adequate technical and management background in specialized skills and experience. The curricula of the concerned departments in the institutes, universities etc. should be designed to develop manpower needed for the phytopharmaceutical industry. International support in building up the requisite expertise would need to be sought.

4.3 Role and need for research and development

65. The programme of drug development demands multidisciplinary capabilities. The list of plant-derived drugs indicates clearly that as a result of the scientific follow-up of well-known plants used in traditional medicine, a fair percentage of useful drugs have entered modern therapy. The same is true of the recent Chinese experience. To quote from a WHO publication: "There is therefore much in favour of establishing programmes for producing standardized and safe galenical traditional preparations for potential use in primary health care, with the eventual aim of discovering their active principles. . . Even if the active principles have not yet been identified in some of the plants used in traditional medicine, historical evidence of the value of such plants could result in useful preparations provided they are safe. Evaluation of safety therefore should be a prime consideration even at the expense of establishing efficacy of the preparation."^{1/}

66. Thus very briefly the salient R&D requirements would include:

- Ensurement of quality and consistency in plant raw materials;
- Validating claims of traditional therapies using modern methodology;
- Development of standards of quality assessment and ensurement for starting materials and finished products;
- Development of modern process technology for production of medicinal products, its assimilation and improvement to make the product competitive;
- Development of new formulations and dosage forms suited to climatic conditions;
- Determining the role of traditional system-based remedies in current health care delivery systems;
- Investigations leading to the development of new drugs, particularly where current remedies are unavailable or unsatisfactory and search for new plant sources;
- Bioequivalence, bioavailability and pharmacokinetic studies on the dosage forms developed;
- Development and introduction of cost-cutting methodologies, including in-vitro (test tube) screening through better techniques as reliable alternative to animals.

67. Research and development objectives and goals must therefore be determined with the above considerations in view.

4.4.1 R&D is an essential ingredient with whose backing national industry can grow properly. A research base is the insurance against future backwardness and underdevelopment. It is therefore necessary to take policy measures, formulate a plan of action and develop an institutional framework so as to establish the R&D facilities on sound footings.

4.4.2 The pace of technological change is so quick that no industry can hope to keep in house all the scientists they would need to do basic and strategic research. Industry thus needs co-operation with technological institutions and academia to keep it up-to-date at a time of rapid technological change. The importance of strong links between industry, academia and technological institutions is stressed.

To facilitate development of new drugs, consideration could be given to assembling a research team of independently minded scientists and academics all with a different type of training and attitude towards commercially oriented research.

4.4.3 In the field of phytopharmaceuticals the disciplines which need special attention for research activities include: agronomical, post-harvest, process technology (pilot and laboratory scale), development of phyto-formulations, quality and stability, biological activity studies, toxicity studies, chemical testing and marketing of products.

4.4.4 Traditional drugs offer much scope for improvement. Research on these drugs need to be aimed at (i) development of new drugs, and (ii) enhancement of their acceptability and usefulness through application of modern production and quality control techniques.

4.4.5 In the context of R&D, the development, storage and mechanism for exchange of information and data is of importance. Availability of accurate and updated information is a key to success and enhances co-operation between countries and regions. A common plan for the information network can be drawn and duplication of research and development activities in the region can be avoided.

4.4.6 R&D institutions play a significant role. There should be established objectives for such institutions. Schemes of regional and international co-operation should strengthen R&D activities and institutions. There should be a mechanism for accruing benefits from centralized R&D activities.

4.4.7 Consideration should be given to commercialization of research and development results. Common problems and factors affecting the commercialization process should be studied and plans and guidelines should be worked out for smooth operations. Mechanisms for commercialization should be established.

4.4 Human resource development for specialized technical and management skills

68. The importance of availability of trained personnel for establishing and operating industrial units is recognized. Well educated and well trained manpower capable of absorbing special technical and management skills is an asset. There should be an appropriate infrastructure for training of manpower. Academic vocational and technical training institutions could play an important role in providing adequate technical and management background on which to base required skills and experience. The approach to human resource development has to be comprehensive and multifaceted so as to cover both the physical and the institutional infrastructure required for industrial development. The curricula of universities should be designed to equip manpower with the necessary background for absorbing and developing the needed skills.

69. Each country should draw up its needs for training covering the higher management level as well as the technician level. The training components could cover exchange of experience in operation of industry, process technology, quality control, maintenance of equipment and machinery etc., as well as marketing of products and business management.

70. It may be mentioned that in UNIDO's training programme the imparting of training invariably falls in 3 categories:

- Training organized in co-operation with the Government of a specific country;
- Training in the form of workshops, seminars, group programmes, in collaboration with government or industry. These cover specific fields, are more intensive and comprise theoretical and practical aspects;
- Training as an element of technical assistance projects.

71. Possibilities of co-operation between developed and developing countries and among developing countries themselves for imparting training in all principal areas related to infrastructural and specific technical and management fields should be explored and encouraged.

4.5 Regional and international co-operation for the development of the subsector

72. The development of the subsector in a country requires simultaneous action on many fronts. Such action has to originate from efforts at the national level. The resources available in many of the developing countries, however, are not sufficient for the purpose. Moreover, many developing countries have limited natural resources or they are too small to achieve the economy of scale that is critical to the operation of certain parts of the supply, production or efficient procurement system.

73. Development of new drugs using leads from traditional medicine is a very expensive process unaffordable to many developing countries. This activity has to be done in collaboration with industrialized countries or companies with proper safeguards to

protect the rights of the institute or country supplying the information or extracts or the activities may be carried out through regional co-operation by a group of countries.

74. Co-operation is to be based upon clearly defined objectives of mutual benefit to the parties. Co-operation will involve different forms of administrative and legal arrangements to determine the role, obligations and responsibilities of the parties to obtain the desired objectives. Co-operation extended at subregional, regional and international levels, for instance enterprise-to-enterprise co-operation or co-operation between enterprises and R&D centres in different countries, have proved to be most useful in improving operational and production economics of pharmaceutical/phyto-pharmaceutical producing organizations. The co-operative action could cover broadly many areas from joint purchases, distribution and production to research and development efforts in basic and applied areas as well as to specific disease patterns and particular conditions of developing countries.

75. With the assistance of international organizations, such as WHO, UNIDO, FAO, ITC, more specific co-operative efforts for the development of the subsector in agronomical, process technology, regulatory, quality and trade aspects, etc. can be directed to cover:

- (a) Establishment of R&D centres and enhancing their co-operation with academic and technological institutes with a view to facilitating the absorption and improvement of imported technologies to suit local conditions, as well as conducting joint research programmes on plants used specifically for ailments that are prevalent in a given region or for ailments for which no adequate remedy exists;
- (b) Identification and development of known therapeutically active plant-derived substances as a means to augment national essential drug requirements;
- (c) Development of a programme for improvement of traditional medicine; strategies for facilitating rationalization of production on an industrial scale to meet the primary health care needs; development of a joint quality protocol; development of technology and joint production of phytopharmaceutical preparations, safety standards, standardization of bioassay procedures and implementation of regulatory requirements;
- (d) Plans for a joint production of plant-based pharmaceutical grade auxiliary materials, such as gums, glucose, starch, cellulose etc.; development and usage of essential oils and fragrance substances;
- (e) Collation and exchange of information, establishment of regional data bases on plants as well as monitoring of development of herbal medicine;

- (f) Co-operation in development of guidelines for secrecy agreements, licensing procedures, patents and intellectual property rights etc. for plant-based medicine to encourage interaction between research institutions and industry;
- (g) Plans for co-operation in investment and operational costs etc. related to enforcement of steps for protection and conservation of medicinal plant resources as well as environmental need to be considered and necessary guidelines need to be developed;
- (h) Co-operation in purchase of equipment/machinery and technologies;
- (i) Organizing workshops for training as well as exchange of ideas and experiences at technical and management levels;
- (j) Development of entrepreneurship and management and marketing initiatives, including market intelligence and information, and strategies to facilitate rationalization of exports and trade etc.^{2/}

76. From time to time subregional schemes of co-operation surface amongst regional groupings, i.e. ASEAN (Association of South-East Asian Nations), Andean Group, CEAO (Communauté économique de l'Afrique de l'Ouest), Commonwealth Regional Secretariat for East and Central Africa, Copptec, etc. It has been observed that amongst the industrial sectors for development, the pharmaceutical sector figures out in the schemes.^{3/} The subsector related to medicinal and aromatic plants can also be included prominently under pharmaceuticals and a methodology should be developed for bringing the work carried out by such groups nearer so as to maximize on the benefits to be accrued from such co-operative schemes.

CONCLUSIONS:

77. In conclusion, while strategy and policy formulations for an integrated development are by their very nature country specific, there are common concerns and preoccupations in the developing countries which need to be addressed to promote the integrated sustained development of plant-based industry. From the considerations discussed in the foregoing sections, some areas of thrusts commended for attention, besides health-care policies and forms of regulations, include:

- (a) Development and adoption of strategies, policies and methodologies for an integrated approach towards the development of phytochemical, phytopharmaceutical and herbal preparation industries;
- (b) Establishment of mechanisms for co-operation for preservation and propagation of medicinal and aromatic plants;
- (c) Initiatives leading to the development of indigenous skills and technology for processing of plant materials;

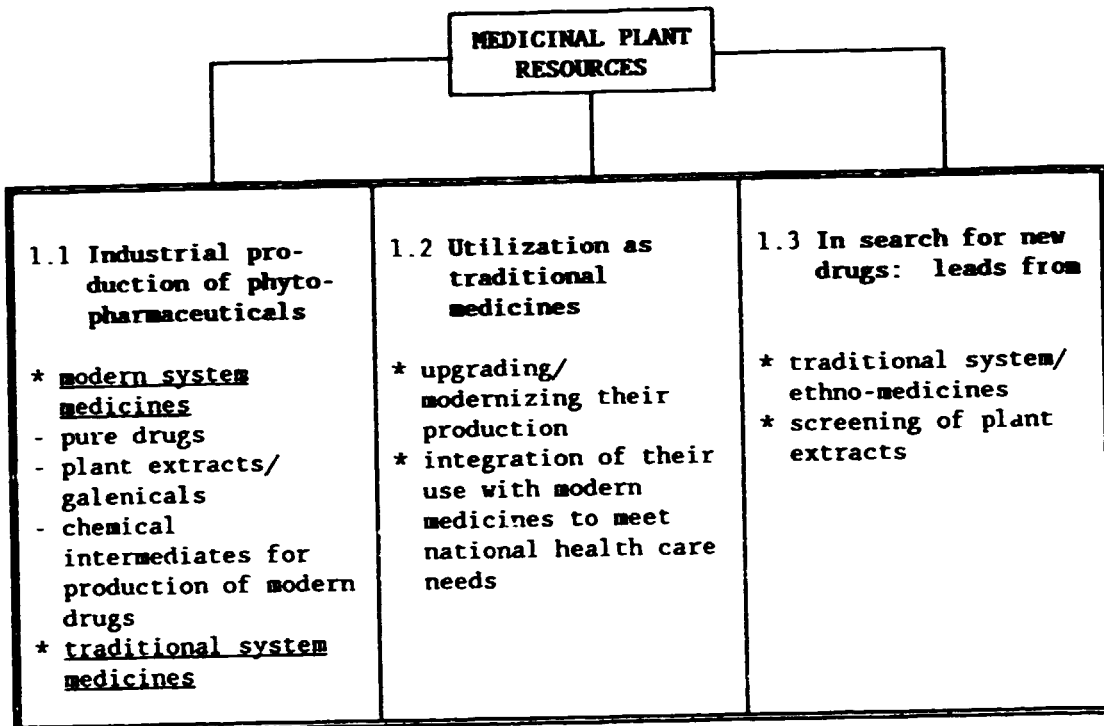
- (d) Initiatives for international co-operation for the development of methodologies for the assessment of therapeutic value of medicinal plants, their processing as raw materials and as pharmaceutical and herbal preparations, the regulatory needs for introducing plant-derived pharmaceuticals and herbal preparations from traditional pharmacopoeias into health-care delivery systems;
- (e) Establishment at subregional, regional and international levels of information networks and inter-institutional links for the development of the phytopharmaceutical and essential oil industries;
- (f) Co-operation in the establishment of research and development capabilities in developing countries, harmonization of the research programme and enhancement of their co-operation with academic and technological institutes with the objective of facilitating the absorption and improvement of imported technologies to suit local conditions, and development of joint R&D activities and introduction of cost-reducing methodologies at regional and international levels;
- (g) Co-operation in the development of human resources capable of absorbing specialized technical and management skills;
- (h) Co-operation in development of entrepreneurship, trade, pricing policy, etc. as well as co-operation and mechanisms in relation to the financing of selected research and development activities and joint venture projects.

References:

1. Medicinal Plants in Therapy - Bulletin of the World Health Organization, 63(6)
2. Report of UNIDO's Third Consultation on the Pharmaceutical Industry, Madrid (Spain), 5-9 October 1987, UNIDO ID/356

Paper on WHO's Guidelines for Assessment of Herbal Medicine, O. Akerele, March 1992
3. The Renaissance of Medicinal Plants, UNIDO IO/CHEM
4. Factors Affecting the Industrial Utilization of Medicinal Plants for the Production of Plant-based Medicines, UNIDO/IPCT/CONSULT
5. The Industrial Utilization of Medicinal Plants within Developing Countries, ID/WG.466/14(SPEC.)
6. Design Options for a Polyvalent Pilot Plant for the Distillation of Medicinal and Aromatic Plants, IPCT.143 (SPEC.)
7. Report of the Consultation to Review the Draft Guidelines for the Assessment of Herbal Medicine, WHO/TRM/91.3
8. Factors Having a Bearing on Industrial Drug Policies, ID/WG.466/6(SPEC.)
9. Better Utilization of Medicinal Plants. The Phytopharmaceutical Supply System in China, PPD.47
10. The World's Pharmaceutical Industries: An international perspective on innovation, competition and policy. R. Ballance, J. Pogany, H. Forstner

ANNEX I

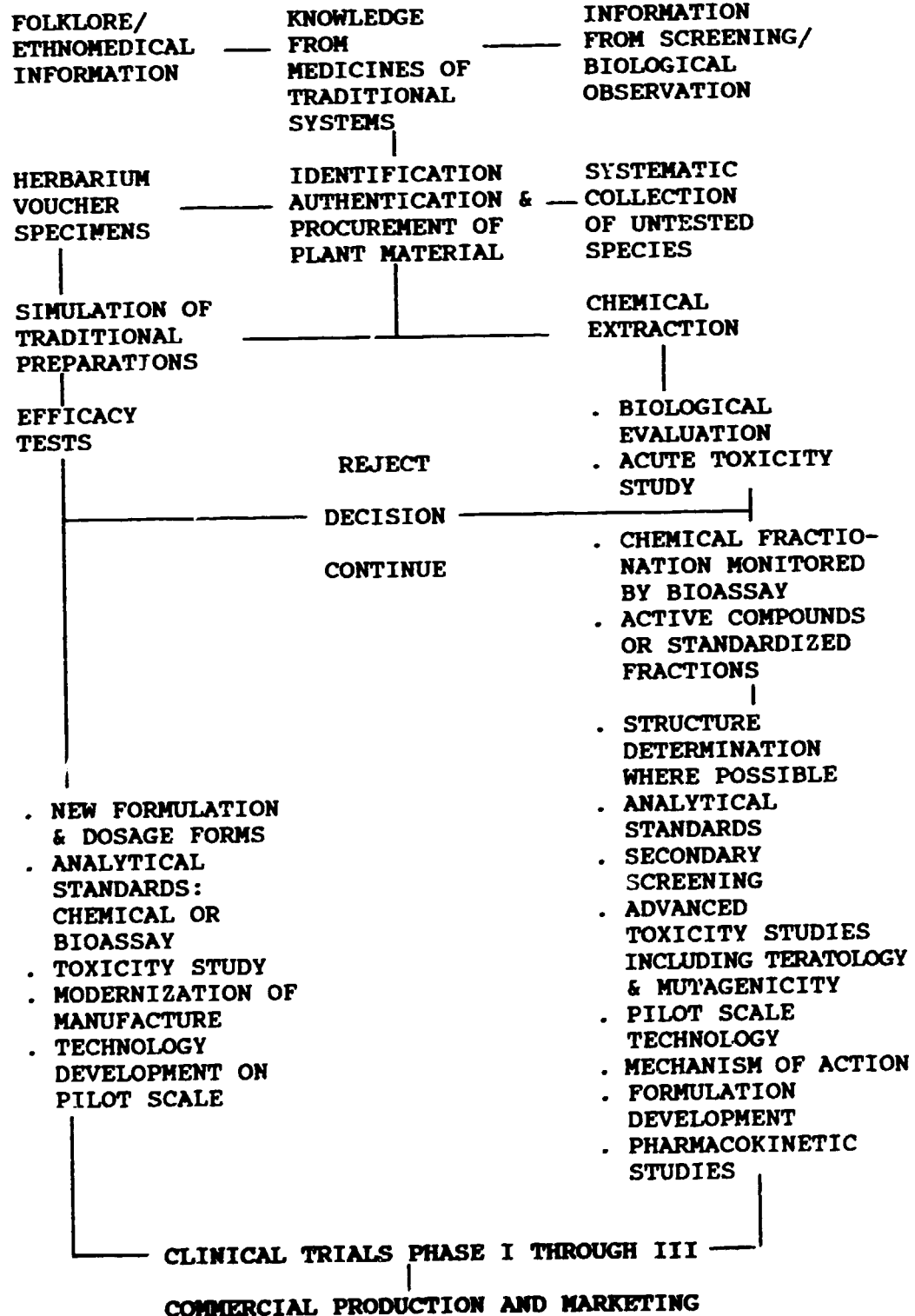


Medicinal plants: Industrial production and health care

ANNEX II

AS TRADITIONAL DRUGS

AS MODERN DRUGS



Stages in drug development from medicinal plants