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19015

Distr.
LIMITED

ID/WG.505/6(SPEC.)*
12 June 1991

ORIGINAL: ENGLISH

United Nations Industrial Development Organization

Workshop on Technological Co-operation among Developing Countries for the Development of Pharmaceutical-related Ancillary Industries

Amman, Jordan, 4-6 November 1991

DEVELOPMENT OF PHARMACEUTICAL-RELATED ANCILLARY INDUSTRIES IN DEVELOPING COUNTRIES WITH SPECIAL REFERENCE TO PACKAGING MATERIALS**

Background Paper

Prepared by

UNIDO Secretariat

* This document is a revised version of ID/WG.466/17(SPEC.) reproduced for the Third Consultation on the Pharmaceutical Industry, Madrid, Spain, 5-9 October 1987.

** This document has not been edited.

V.91-25543

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1. INTRODUCTION

A review of the present status of the development of the pharmaceutical industry in developing countries reveals that packaging materials constitute an important contribution to the cost of production of pharmaceuticals. In addition, the knowledge about and availability of appropriate packaging materials at reasonable cost assumes an important role in the development of this industry on a cost-effective basis. There is an increasing interest in creating or improving the necessary infrastructure for local production of packaging materials. The subject of development and establishment of pharmaceutical-related ancillary industries, especially packaging, covering conventionally established materials such as glass, metal, paper, cardboard etc. besides plastics in developing countries within the scope of an integrated development of the pharmaceutical industry merits consideration. The processing of local natural resources, development of industrial technology, setting-up of pilot plants, regional research and development centres for development of packaging materials and the associated printing, development and exchange of information on specifications and standards for raw materials as well as packaging materials are some of the aspects on which in-depth work would be important steps in the right direction for the development of the subsector related to packaging materials.

2. THE ROLE OF PHARMACEUTICAL-RELATED ANCILLARY INDUSTRIES IN THE CONTEXT OF INDUSTRIALIZATION

Industrialization aims at raising the standard of living of people by means of increased national productivity through domestic production of consumers and capital goods thereby bringing about an expanding circuit of incomes, markets, technology and employment. This calls for a careful assessment of resources, potentials and constraints to formulate strategies and policies to guide investments in productive facilities and support services.

The creation of a healthy industrial sector with ample potential for self-sustained growth in a country or a region calls upon the parallel development of all mutually complementary and supportive activities including ancillary industries, infrastructural support activities and services. To integrate the development of industrial sectors, mutually advantageous linkages need to be maintained. One approach for ensuring the establishment of these linkages is the so-called development of ancillary industries.

In the case of the pharmaceutical industry, ancillary industries relate to services as well as the production of components. Generally the ancillary units are the suppliers and the pharmaceutical units are the buyers. Ancillary industries would generally fall under the categories of small and medium-scale industries.

2.1 Benefits of development of ancillary industries

Ancillary industries, which are generally small-scale in nature, provide a wide and valuable support to larger industrial enterprises. The promotion and development of these industries in developing economy need to be appreciated and proper environment and appropriate policies be adopted for its growth.

One major macro-economic benefit of the ancillary enterprises is that they provide for a self-contained and highly integrated process of development within a country rendering it less susceptible to external changes. It is an important source of employment generation. The ancillary production units, particularly smaller ones, have also the advantage of greater flexibility of production enabling them to adjust easier to changing demand patterns. Furthermore, ancillarization can mobilize, generate and develop local entrepreneurship.

In some cases the technology involved is simple, could be locally developed and is suitable more to the conditions of developing countries.

Besides these national benefits, there are various micro-economic advantages of ancillarization. One such benefit of ancillary units is the interdependence of interests of buyers and suppliers and the assurance of a secure market for its products. This enables the unit to sell its products on the basis of long-term contracts and in the meantime to concentrate its management efforts on future improvement and product diversification.

By and large, it is recognized that the development of ancillary industries has proved their benefits and has become highly desirable.

2.2 Promotion of ancillary industries and some major constraints

Some of the possible constraints and obstacles impeding growth of ancillarization include the following categories of problems:

1. Operation problems related to failure to adhere to quality and delivery schedules which upset the production programme of the parent enterprise, continuity in some cases of management in the ancillary unit since some small units are a one man show, lack of research and development, infrastructural inadequacies - physical related to factory accommodation and utilities, and institutional related to market, operations, finances, etc.

2. External constraints, i.e. insufficient promotional and policy incentives, problems of price fixation, over-dependence of the ancillary unit on the major partner - the problem is to ensure steady partnership with a sufficient degree of flexibility and a scope for dynamism for development. Problems related to overall policy and policy of buyer - Failure to observe delivery schedules - Many of these problems are problems of small-scale industry development in general. The establishment and operation of links between small and large companies in the development of an ancillary industries programme are confronted with particular constraints. These constraints broadly concern the identification of opportunities for such links, the motivation for their actual establishment and the operation and dynamic development of such intercompany relationships. Given the potential benefits that can be attained through development of ancillary industries for the entire industrial development process of a country, many governments have established sets of promotional policies and measures to alleviate these constraints.

2.3 Promotional policies

The first level of policies concerns the creation of a macro-economic climate within which the advantages of ancillary industries are appreciated and encouraged, be they large or small units, and a general commitment towards ancillarization as a desirable objective is established. Real headway can be made only if such a favourable environment exists. The general efforts to encourage ancillary industries development should also involve the participation and commitment of private industries and their chambers and associations. The general measures should thus ensure that production through ancillary units indeed is economically and commercially beneficial for the parties involved and that constraints hindering their development be removed. The basic thrust for promoting ancillary industries has to come from national Governments which should secure the co-operation of industries in the public and private sectors and the relevant associations, chambers of commerce and industries.

Besides the above-referred policy measures, other specific measures could be singled out as important steps for the promotion of ancillary industries. These can include:

- Industrial licensing system as a promotional means;
- Eligibility for maximum facilities and incentives provided to these important industries; one example is that facilities and incentives wherever available for small-scale industries may be given a higher ceiling for ancillaries;
- Exemption from heavier tax liabilities etc.;
- Support to investment and expenditure made in R&D facilities etc.;
- Taxation reliefs to large units for carrying out R&D, tools & jigs, dies and moulds etc. for ancillary materials.

2.4 Administrative and operational support to ancillary industries

Apart from the general policy framework and specific promotional measures, operational and administrative measures could be designed to facilitate the establishment of ancillary industries. Such measures cover action by bodies such as promotional agencies, industry associations, chambers and financing institutions as well as individual companies. The measures could include:

- Selection of suitable industry;
- Provision of industrial profiles and prefeasibility studies for the proposed ancillary units;
- Identification of local entrepreneurs and, when needed, of counterparts from other countries;
- Provision of technical know-how and training;
- Provision of long-term contracts for purchase of products and guaranteed payments;
- Legal safeguards for timely payment and rejections;
- Quicker procedure.

3. PACKAGING INDUSTRIES OF SIGNIFICANT RELEVANCE TO PHARMACEUTICAL INDUSTRY

As packaging is an economic activity, it plays an important part in the production and distribution chain of pharmaceuticals. Correct packaging is the principal way of ensuring safe delivery of a product to ultimate users in good condition at an economic cost. It is often said that packaging is an integral component of a product and this is particularly true of pharmaceuticals. While the packaging requirements of pharmaceuticals have much in common with those of other perishable consumer products, there are significant differences:

Pharmaceuticals are related to health and they are often required to have a longer shelf life. Many pharmaceuticals, if not adequately protected, may deteriorate to the point not only of losing all efficacy but of becoming toxic and a danger to health or even to life. Apart from failing to give adequate protection, wrongly chosen or inadequately tested containers may themselves, because of their incompatibility, adversely affect or contaminate drug contents. In addition, a faulty component of a pack, say seals, may allow ingress of contaminants or unwanted moisture or the egress of active principles or solvents. Permeability of the container itself also may allow the migration or sorption of active principles or the leaching of contaminants.

As the pharmaceutical package is considered an integral component of the final product, the manner in which a new product is to be packaged should be considered at an early stage of product development so that necessary work on package development can be conducted parallel with the development of the product itself. Stability tests are carried out on the proposed containers, and suitability of other alternatives are compared. For instance, if a plastic container is to be used it may be necessary to avoid the use of a bacteriostat preservative which is absorbed by the plastic material, or it may be necessary to include a humectant to hydrous unguent if the proposed container is permeable to water vapour. A metal container may necessitate the addition of a corrosion inhibitor or an appropriate agent.

The subsectors of the packaging material industry detailed hereunder are of significant importance to the pharmaceutical industry:

- Paper and board wrappers and containers;
- Glass, plastics and metal containers;
- Fibreboard packaging cases;
- Wooden containers;
- Regenerated cellulose film, plastic film, aluminium foil, flexible laminates;
- Adhesives and sealing tapes.

3.1 Subsectors of the packaging industries

The subject of packaging is vast. The materials and components used for making the packs are large in number, hence no attempt to itemize the same in this paper is being made. The matter is compounded by the fact that the manner in which a product is to be used often dictates the nature of the container. The choice of component is closely interrelated with formulation. The main prerequisites for the successful development of pharmaceutical packaging are on the one hand an intimate knowledge of all aspects of the products themselves and their purposes and on the other hand an understanding

of the nature, properties and behaviour of packaging media. Standards for materials and products are of great significance and these play an enormous part in the economic development and deserve special attention.

The scope of discussion in this paper will be restricted to three major packaging materials, namely glass, plastics and metals, which are considered to be the most important from both economic and technical points of view.

3.1.1 **Glass**

The main constituents of glass are silicates (from sand), lime (from calcium carbonate), soda (from synthetic sodium carbonate) and aluminium oxide or hydroxide.

The efficiency and usefulness of glass stems mainly from its relative chemical inertness. Pharmacopoeiae such as USP prescribe the standards to which glass containers should conform.

The major types of glass used in pharmaceuticals are the following:

Soda glass	For most pharmaceutical preparations the so-called soda glass or white flint glass containers are used; they consist mainly of 72% silica, 11% lime and 14% soda.
Amber glass	Composition differs little from that of white flint glass, except that a small proportion of iron oxide is added to it. Amber glass gives protection against UV rays.
Neutral glass	borosilicate type of glass in which boric oxide largely replaces limestone or calcium oxide. Soda content is minimal.
Sulphated glass	Soda glass inner surface is treated by sulphating. Containers used for injections - meet standards laid down in European and United States pharmacopoeiae.

3.1.2 **Plastics**

The pharmaceutical industry is a fast growing consumer of selective plastics - synthetic polymers which can be divided into two groups:

- Thermoplastics which can be softened by heat and which harden again upon cooling (majority of plastics for packaging fall into this category);
- Thermosets which are soft only at one stage in their manufacture but on being heated harden permanently and cannot thereafter be modified by heat without degenerating (these have few applications except for some closures).

Polythene is one of a group of thermoplastics known as polyolefins which include polypropylene, polystyrene, polyethylenes, and polyvinyl chloride. They are the most economically and widely used in the pharmaceutical industry; the most frequently used remain polyehtylene and polyvinyl chloride.

Plastics are finding increasing applications. Although glass and metal have traditionally been used over a long period for pharmaceutical products, it cannot be assumed that they are inert or that they are ideal materials,

since all types finish up as a technical-commercial compromise. The drastic increase in the use of plastics has frequently been attributed to its convenience in manufacturing, the greater ability to produce packs and devices in functional and complicated shape involving less weight, extreme purity, dimensional accuracy, withstanding sterilization by various agents as the need may be, and last but not least, at economically acceptable prices.

The important aspect in the use of plastics is the need for a maximum degree of standardization of material, selection of the right and specific grades and the information about the additives used for the purposes stabilizers, colours, plasticizers, antimicrobial preservatives and fillers. Because of the nature of usage in the pharmaceutical industry, producers of plastic worldwide and local regulatory authorities have a big role to play in providing and demanding for complete information on plastic material and container required to ensure product and pack compatibility, safety and shelf life declared on the pack. FDA, USP, B.P., DHSS provide guidelines on national standards for plastic containers.

3.1.3 **Metals**

Although now use of metal for packaging materials is on the decline, however metal containers have been used to pack a wide range of pharmaceutical products. There are two types of metal packs: (i) rigid containers including aerosols and (ii) collapsible tubes.

The material used for rigid containers is usually based on tin plates or aluminium. Both can have their compatibility properties improved by the addition of lacquers.

Tin plates used for making packaging material consist of low carbon steel coated with a layer of tin either by a hot dipping or by an electrolytic process.

In addition, rigid aluminium containers are also commonly used. Aluminium is also used for making foils to be used as packaging material.

Collapsible tubes are manufactured from tin coated lead, tin and aluminium and have a variety of usage. The metal aluminium tube (lacquered internally if necessary) offers the same positive advantage, i.e. ease of closure, collapsibility in use, non-permeability etc. which is difficult to achieve with plastic.

Pharmaceutical aerosols mainly use metal of tin plate or aluminium origin.

British standards BS 1679 and 4230 give details for containers for the pharmaceutical industry.

3.2 General caution

Although background knowledge on the chemical and physical properties of packaging materials more specifically plastics is a prerequisite, special information which coordinates glass, plastic and packaging technology is equally important. To achieve success in packaging all activities from the chemistry of material right through to the final use of the product need to be identified and studied.

4. FEATURES OF PRODUCTION - ANCILLARY INDUSTRIES

The features of production related to ancillary industries can be highlighted as under:

Good manufacturing practice, good laboratory practice and general regulatory aspects have increasing implications for pharmaceutical industry related packs, packaging materials and the processes by which they are obtained, stored and produced. In other words, the packaging materials for pharmaceuticals must meet certain standards related to their physical and chemical properties, storage conditions and also need clean, relatively hygienic facilities for their production coupled with good quality control.

4.1 Integration or non-integration in production processes

The situation for the production of ancillary materials includes either of the two positions:

(a) Integration in the production process of pharmaceutical plants;
(b) Segregation, i.e. non-integration and outside delivery arrangements.

The latter is a more common practice because of multiple factors such as nature of products, large variety of materials, size of run etc.

To illustrate the integration situation one may refer to a large pharmaceutical formulation unit which may deem it convenient to install a tubular glass vial making plant adjacent to its antibiotics/injectables filling facilities and thus use the inline facilities with least handling of these vials for antibiotics/injectables filling operations. Examples of manufacture of material of plastic origin in pharmaceutical factories are not uncommon.

In segregated facilities for instance bottles for filling pharmaceutical syrups or powders are manufactured under clean conditions and packed e.g. inverted in shrink wrapped trays. Such handling may not necessitate water washing of bottles before filling, only air cleaning may suffice. The establishment of segregated facilities is a common practice because of the nature of manufacturing involved and the versatile nature of usage of the items.

4.2 Interrelation between packaging material producers and pharmaceutical producers

Complete exchange of information, frequent inspection and coordination between those concerned with the product and those concerned with packaging is an important aspect. Neither of the two can be successful in isolation. To lay down the specifications and adherence to the same make things easier. For manufacturers of ancillary products at times it is necessary to purchase some raw materials such as plastics etc. under certificate of warranty to ensure the quality of the finished components.

4.3 Features of packaging materials

Pharmaceuticals entail both primary and secondary packaging materials. The primary packaging material is in direct contact with the product such as glass vial, plastic squeeze bottles, metal collapsible tubes with appropriate lacquers etc. and their closures. The secondary package material includes carton, cellophane wrapper and fibrite etc.

4.4 Ownership

Due to the diverse nature of production and management needs, the ownership of pharmaceutical units is not the same as that of ancillary units. However, in certain instances of large multinationals common ownership is not excluded.

5. PACKAGING MATERIAL MANUFACTURE IN DEVELOPING COUNTRIES

5.1 Market research to packaging material manufacture

One of the requirements for the appropriate planning of packaging manufacture consists of a market research at the national as well as the regional level covering the sectors of the product which may be expected to utilize the package under consideration.

Forecasts of package consumption at short and medium term must be elaborated. The ceiling for the packaging costs, including the costs of the materials and process must be ascertained.

On the basis of these parameters a packaging designer with appropriate technological background and/or support will be able to elaborate a tentative prototype with adequate specifications. Prototype testing will be followed by engineering study of alternative possibilities of manufacturing process.

5.2 Inventory of resources of raw materials for packaging

Most of the developing countries have some raw or semi-manufactured materials which could be used for manufacture of some types of package. An inventory of national resources in raw or semi-converted materials suitable for use for the manufacture of packaging materials which are effectively demanded in the country or region would be a positive step for the development of ancillary industries.

5.3 Common rules on the selection of the packaging manufacture process

The establishment of any packaging material or package manufacturing plant must be oriented towards the production of an article or articles according to the specifications required by the package user industries and the market concerned at a level of price also compatible with the same market.

Analysis regarding appropriateness of the available raw or semi-converted materials and selection of appropriate technology would also need to be made.

5.4 Analysis of production parameters

Availability of raw materials, water, energy, equipment, manpower, etc. may be considered as main production parameters. A contractual agreement with reliable suppliers of technology and equipment is one of the common practices in the context of development of ancillary industries. On the one hand, it is advantageous to adopt a quite recent and updated technology, but on the other hand, a too modern technology may not suit the prevailing conditions related to the envisaged package manufacture in the developing country. Technology selection thus should closely be scrutinized both from the economic point of view and suitability to local market conditions.

To operate sophisticated equipment for certain materials, well trained operators would be required. Attention would have to be paid to spare parts, availability and maintenance of the equipment.

Technical and general management would call for competitiveness.

6. INTERNATIONAL CO-OPERATION FOR THE DEVELOPMENT OF ANCILLARY INDUSTRIES

Packaging material industries are in principle service industries and fall in the category of small-scale and medium-size industries. Developing countries need to give priority to the promotion of these industries in their strategies and policies for industrialization. Technical advisory and extension services for small and medium industries should have a major thrust on development of ancillary industries. Such services may include (a) preparation of technoeconomic feasibility studies which could help entrepreneurs to secure long-term and short-term capital from financial institutions, (b) advice to entrepreneurs on choice of technology, selection and procurement of equipment, (c) assistance in provision of information on raw materials and their quality, (d) assistance in improvement of management capabilities, specially in areas related to marketing, financial accounting, factory legislations and personnel relations, etc. Such consultancy services are also expected to assist in resolving operational problems and help in improving efficiency and productivity.

The first step in a co-operation exercise is the identification of main actors in this industry, followed by identification of their overriding interest and then determining how to bring them together on a mutual benefit basis. Packaging industries of significant interest to the pharmaceutical industry have been identified in chapter 3. The components used by the pharmaceutical industry cover a great variety which include items such as glass bottles, vials, ampoules and plastic plugs, caps, containers, collapsible tubes, cardboard carton, labels, wrappers, fibrites, etc.

There is a need to study possible forms of international co-operation between developed and developing countries and between developing countries themselves to enhance the development of pharmaceutical-related ancillary industries in developing countries through greater contribution by international, regional, bilateral, technical and financial institutions.

6.1 Sister industries

In the context of development of ancillary industries besides the stimulation of the well established and commonly practiced modes of co-operation for development involving North-South and South-South co-operation, it would be quite appropriate to highlight the recent innovative international approach of "sister industries", the concept of which involves co-operation between a developed and developing partners. It may be of interest to mention that the "sister industry" concept entails the following stages of co-operation:

- Investigation of requirements in the ancillary industry in question in developing countries in terms of new investment and modernization, upgrading of production and managerial development, etc.;

- Identification in a developed country of potential partners (senior sisters) for providing the required resources and know-how;

- Preparation of joint project proposals with specifications and costing;

- Provision through a financing agreement of plant and equipment, expertise and services as well as training in the developed country to the "junior sister company" after scrutiny by a consultancy company. The assets financed and provided through foreign entities do not entail direct foreign participation in the sister industries, but an indirect one through a national (public) holding organization in the developing country.

6.2 Exchange of experience

Experience of various countries varies and there is a continuous need to exchange experiences, information and know-how to mutually enrich the functioning of this exercise. UNIDO, jointly with developed and developing countries' Governments and/or industry, can organize national workshops in individual developing countries to arrange for policy makers and entrepreneurs from two or more countries to exchange information and experience and views on issues connected with promotion of ancillary industries. Such exchanges would assist development and promotion of indigenous entrepreneurs. Exchange of experience at policy as well as industry level is a valuable tool. The areas for such co-operation can cover investment policy and arrangements as well as plant design and constructions, machinery and equipment, operational problems, technology adaptation, repair and maintenance, specifications, quality assurance, development of competent management, export promotion etc.

UNIDO could coordinate and further expand its activities to survey developments and disseminate information on relevant promotional schemes.

6.3 Multilateralization of ancillary industries

UNIDO, through a broader information base, may help in facilitating the matching of developing countries with other countries. Jointly with the recipient developing country entities, bilateral co-operation agencies and interested industrialists of the developing countries, UNIDO could elaborate detailed schemes and their variations for twinning arrangements in the fields of production sharing, marketing process and product development, organizational matters, etc.

Promoting direct contact and collaboration between small-scale industry associations and co-operations in different countries can possibly contribute to an enlargement of the international twinning process but always keeping the industry as main actor.

6.4 Regional and subregional co-operation

The resources available in many developing countries are not sufficient. Moreover, many developing countries are too small to achieve the economy of scale that is critical to the operation of industry. Co-operative action could be an answer and could include joint purchases, distribution and production of ancillary materials and research and development work on packaging materials. Co-operation could be extended in areas such as training of manpower, quality control, store management, trade and acquisition of technology, development of industrial processes, etc.

6.5 Establishment of packaging technology institutes

National scientific and technological structures and capabilities need to be strengthened. There are enormous advantages in establishing national institutes/centres for development of packaging materials which would undertake R&D in packaging, set out and promote standards and specifications and other regulatory measures, develop and assist in transfer of technologies, train local manpower and arrange contacts with the appropriate regional and international organizations. Co-operation with developed countries to promote this aim would indeed be advantageous.

UNIDO can be of assistance in the establishment of packaging technology institutes in the developing countries which would aim at giving specialized services in disciplines such as information, training, quality control, design, engineering, standardization and techno-economic studies, applied research etc. The institutes can assist in developing local specialized advisory services and expertise.