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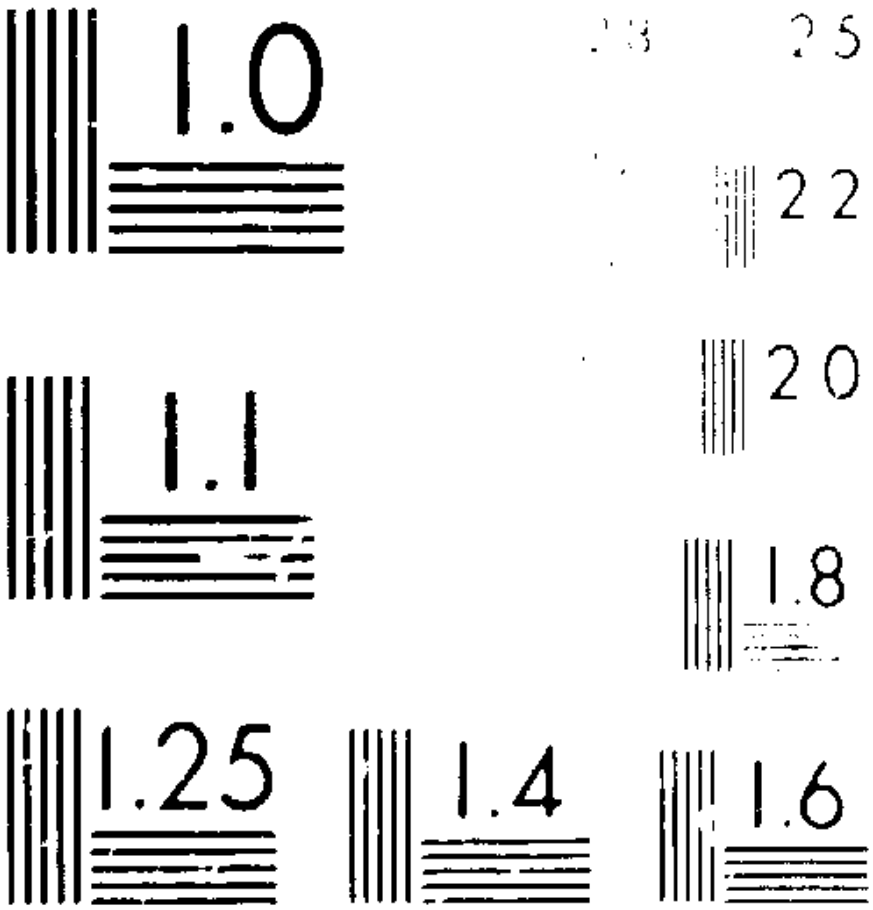
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RELEVANT TOPICS TO BE TAKEN INTO ACCOUNT IN THE PREPARATORY PHASE OF TECHNOLOGY TRANSFER ARRANGEMENTS FOR THE PRODUCTION OF PHARMACEUTICALS *)

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PREFACE

1. In accordance with the recommendation No. 3 of the First Consultation on the Pharmaceutical Industry, UNIDO has been requested to prepare a document on Relevant Issues to be taken into account for the production of pharmaceuticals.

2. This document is primarily addressed to parties negotiating contractual arrangements of technology transfer in developing countries. It is intended to provide guidance and highlight critical aspects in the preparatory phase but not to elaborate a complete set of issues to be considered throughout the project. Nevertheless, the knowledge of procedures and alternatives for the whole project period is almost indispensable.

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INTRODUCTION

3. The paper will cover the preparatory phase of arrangements for setting up of facilities for the production of bulk drugs and its intermediates as well as formulation and packaging of pharmaceutical products. It will also relate to the situation where the licensee already operates a plant for pharmaceutical forms and requires the licensor to supply only manufacturing know-how for new medicaments.

4. This document has been prepared taking into account:

a) - the recommendation No. 2 of the UNIDO First Consultation on the Pharmaceutical Industry held in Lisbon (December 1980)
b) - the UNIDO Morocco Round Table on the Pharmaceutical Industry (December 1981)
c) - the principles stated in UNIDO document PC.19
d) - the contribution to the identification and solution of economic and social problems as well as the responsiveness to health and relevant policies including import substitution etc. related to the production and use of bulk drugs (or intermediates) or essential medicaments in developing countries
e) - the likely acceptability of proposed solutions for both contracting parties
f) - the compatibility of proposed solutions with existing regulations and positions on the matter, as described for a number of issues in "Preparation of Guidelines, Background Paper", ID/WG.331/3
g) - "Items which could be incorporated in Contractual Arrangements for the transfer of technology for the manufacture of those bulk drugs/intermediates included in UNIDO's illustrative list", ID/WG.393/1
h) - "Items which could be included in Contractual Arrangements for the setting up of a plant for the production of bulk drugs (or intermediates) included in UNIDO illustrative list"; report V.83-54946
i) - "Items which could be included in Licensing Arrangements for the transfer of technology for the formulation of pharmaceutical dosage forms"; report V.83-54945
j) - the practices which are generally accepted in international licensing and trade, including fair and reasonable terms, conditions and payments
k) - comments submitted by developed and developing countries in accordance with the request made by the Second Meeting of the Ad-Hoc Panel of Experts on Contractual Arrangements in the Pharmaceutical Industry.

1) - Further aspects as may be stipulated in documents listed under REFERENCES.

5. For the sake of clarity and whenever advisable the paper will distinguish between the production of bulk drugs (or intermediates) on one side, and formulation and packaging on the other. Furthermore with regard to the latter, differentiation will be made between "generics" and "brand name products" if appropriate.

6. In its preparation, the existing Manual for the Preparation of Industrial Feasibility Studies previously compiled by the United Nations Industrial Development Organization, has been born in mind.

7. The amplification of different issues to be taken into account should indicate the scope of problems involved in a transfer of technology arrangement.

DEFINITIONS

8. For convenience the following terms are used:

- Licensor (supply party) is primarily but not only responsible for the provision of basic design, engineering and process know-how; approval of contractor's project work; performance guarantee, provided the plant has been built according to his basic know-how; assistance in training of licensee's personnel etc., or issuing only a manufacturing or product license in case the licensee operates already a formulation plant with adequate equipment. (The proper application of above functions for setting up a production or manufacturing plant will be further explained in the paper).

- Licensee. He may be called vis-à-vis the licensor: licensee, potential recipient, using party or purchaser, and vis-à-vis the contractor or consultant engineer: licensee, employer or purchaser.

- Contractor shall mean the person or persons, firm or company whose tender has been accepted by the employer and includes the contractor's personal representatives, successors and permitted assigns. In general, he plans, erects and/or equips and assists in commissioning a plant, according to the specifications of the licensee and licensor, either in solely own competence or together with other parties, including subcontractor(s).

- Partner or Party shall mean the licensee and licensor. In some instances also the contractor and consulting engineer.

- Subcontractor(s) shall mean the person, firm or company, to whom any part of the work or services or the execution of any part of the contract is delegated.

- Consultant Engineer, normally appointed by the licensee, advises and reviews all work, particularly as regards to detailed engineering, procurement of equipment, supervision of implementation and other sections of the contract if required.

- Civil Works shall mean buildings, roads, foundations, structures, sanitary, etc.

- Equipment shall mean equipment, machinery, instrumentation, spares and all items required for the production, formulation and control of the plant and products.

- Plant shall mean the aggregate consisting of building(s), equipment, services and all other facilities, required to produce a product or manufacture a medicament.

- Site shall mean the land upon which the plant is to be erected.

- Product shall mean bulk drug or intermediates.

- Formulations, Pharmaceutical forms or Medicaments are finished pharmaceutical products in dosage form such as tablets, capsules, granules, powders, liquids, ointments, suppositories, ampoules or vials, etc.

- Production is ment for chemical, enzymic and similar processes.

- Manufacturing should stand for formulation and packaging.

- Home country shall mean the domicile of the licensor.

- Host country would be the licensee's country.

- Technical information will mean all technical data, information, drawings and designs, and instructions relevant to the process.

- Know-how, in general, is understood as a set of techniques and information of unpatented nature applicable in production or commercial activities. However, there is no universally accepted definition.

- "Packaged" or "turn-key" transfer of technology should mean that the technical information and all other requirements necessary to put up a plant (supplied by the licensor), execution and control of a project lies in one hand, be it the licensor, contractor or, in exceptional cases, the licensee.

- "Unpackaged" transfer of technology should mean that the technical information and all other requirements necessary to put up a plant (supplied by the licensor), execution and control of a project lies in several hands and need general supervision either by the licensee or consulting engineer or a general contractor or even licensor.

AMPLIFICATION OF THE DIFFERENT ISSUES TO BE TAKEN INTO ACCOUNT

I. PROJECT MANAGEMENT

(1) Project sequence

9. Once one, two or more parties have announced their intention to set up facilities for bulk drug or intermediate production and/or manufacture of formulations, and have concluded some sort of "project idea", a sequence of steps may be followed and main aspects be considered on each of them during its negotiations. Thereby, under ideal conditions, the parties should already know each other.

10. A logical sequence of steps (for the negotiating phase only!) could be as follows:

(1.1) Indentification of requirements
(1.2) Examination of host country's policies
(1.3) Pre-feasibility study
(1.4) Type of contract envisaged for the transfer of technology
(1.5) Revised pre-feasibility study
(1.6) Tendering conditions for execution of project
(1.7) Governmental approval(s)

11. An alternative hypothesis would be if the potential licensee formulates first its own "project idea", identifies the technology, requirements (1.1), examines the own country's policies (1.2) and undertakes a pre-feasibility study (1.3) with the information so far available. If the outcome of the study warrants a feasible project, only then he contacts a or several licensor(s) and/or contractor(s) and proceeds with the steps (1.4) to (1.7) as outlined above.

(1.1) Identification of requirements

12. When entering into negotiations a number of facts must be known to formulate the project.

a) The major contribution for the determination of these requirements
13. expected from the licensee could be:

(1.1.1) Health requirements

14. Medical treatment belongs to the important measures to improve the health conditions in the developing countries. WHO identified several tropical diseases which are considered as endemic in these areas and need preferential attention.

These diseases are caused either by parasitic infection:

- malaria
- schistosomiasis = bilharziosis
- filariasis = elephantiasis
- trypanosomiasis: African sleeping sickness and Chagas' disease
- leishmaniasis

or by human contact:

- leprosy

Other leading causes of disease or death are:

- injuries and wounds caused by accidents or violence and poisoning
- diarrhoeal diseases
- cariovascular diseases
- respiratory diseases
- malignancies
- malnutrition

(1.1.2) Product requirement

15. To cope with the above mentioned diseases a variety of medicaments is available. The World Health Organization Expert Committee prepared a model list of essential drugs out of which UNIDO identified 26 most essential drugs for the integrated production from raw materials and intermediates (Table I).

(1.1.3) Epidemiological work

16. Available or to be carried out confirming the local need for the pharmaceutical(s) in question.

(1.1.4) The market size

17. The requirement for the country or region (expressed in product weight or in package volume per year for manufacturing) is convenient to be known already at the preliminary stage of negotiations.

(1.1.5) Availability of public and/or private facilities for marketing

18. Sales facilities for products or distribution systems for medicaments capable of purchasing and marketing should be investigated already at the preliminary stage of negotiations. Its degree of usefulness will have a major impact on the structure of the licensee's enterprise.

b) The major contribution for the identification of requirements from
19. the foreign partner(s), actually the licensor(s), could be:

(1.1.6) complete information of technology for:

20. . bulk drug production, starting with raw- and auxiliary materials or partially with natural resources, or starting with intermediates performing only part of the whole process sequence

. formulation, starting with bulk drugs and auxiliary materials

. packaging, with imported and/or locally available packaging material components

. approximate manpower requirement

. envisaged energy consumption

. infrastructure (communications, storage facilities, transport)

(1.1.7) first estimate on financial requirement based on:

21. . comparison with similar already executed projects

. or characteristic figures, such as investment per produced kg of bulk drug or manufactured finished package per year (e.g.

0,5-1,0$/pack, year for formulation and packaging in developed countries, and depending on product mix, dosage form(s), package size(s) and length of shelf life

c) Additional useful information about requirements can be found in documents of international organizations like: UNIDO, WHO, World Bank, etc.

(1.2) Examination of host country's policies

23. A number of governmental policies will affect the project and must be carefully studied with regard to its impact on the project:

- procedures and rules for license agreements to be observed by both parties
- patent law situation
- capital investment possibilities and restrictions for domestic and foreign sources
- transfer of dividends, compensations, remunerations such as lump sum payments, license- and service-fees, royalties and grant-back conditions, etc. to the licensor(s), who normally will expect these payments in his home country, thus involving foreign exchange, or wants to reinvest in the possibly local established enterprise
- government subsidies, tax exemptions, export incentives, etc. which will influence the rentability of the project
- import policy for equipment and material for the project - but also for the operational phase
- other legislative measures such as the stipulation requiring the "unpackaging" of technology transfer
- tariff or non-tariff protection of raw materials, bulk drugs, intermediates, formulated pharmaceuticals, packaging materials, which all will decisively influence the price of the finished product
- special legislation due to the membership of a community such as the Andean Pact.

24. A local lawyer experienced in the above matter may be useful to advise the negotiating parties.

(1.3) Pre-feasibility study

25. In the preliminary phase of investigations a state will be reached with sufficient data and information available to work out a pre-feasibility study. It

should allow to decide whether the already envisaged project terms are sufficient or need to be extended and/or changed, such as legal aspects, explanatory notes to process or manufacturing know-how, design criteria, production or manufacturing capacity, etc.

26. The pre-feasibility study does not mean an exact calculation of the return on investment but rather a general apprehension of all factors which may lead to the successful outcome of the anticipated venture.

27. A résumé indicating scope, content and methodology of such a study is given in Appendix I.

(1.4) Type of modalities envisaged for the transfer of technology

28. The access by developing countries to technologies required for setting up a pharmaceutical industry, can take place through a number of alternative ways. Two main categories of arrangements for that purpose between the licensor and licensee (private or governmental partner) may be conceivable. One criterion would be, whether there is any need to accept foreign capital or not. Another criteria distinguishes between a "one package" or "turn-key" deal and an "unpackaged" transfer of technology. The following paragraphs are elaborating certain possibilities.

(1.4.1) Transfer of technology not related to foreign investment

29. If the technology transfer occurs without foreign equity participation, a set of contractual modalities may be used, depending upon the distribution or degree of centralization of responsibilities involved in the execution of the project. Assuming that new productive facilities are to be established, the recipient (employer, purchaser or licensee) may either opt for a "turn-key" or "product-in-hand" type of comprehensive transaction, or for the "unpackaging" of the various components thereof, in a manner that the license of patents and/or know-how, the procurement of equipment, the engineering and the erection of the plant are provided by different sources. Of course, between the two extremes - complete centralization and decentralization of duties - a large number of intermediary alternatives exist.

(1.4.1.1) Turn-key and product-in-hand transactions

30. In **normal turn-key operations** a sole contractor or holder of the turn-key contract assumes vis-à-vis the purchaser all the responsibility for the establishment of the plant according to the licensor's specifications wherever required, and takes the purchaser's place with respect to other participants in the project.[1/] In other words, such an agreement covers the design and engineering, constructing, equipping and complete preparation of the plant for operation. The contractor is responsible for the successful demonstration of the performance guarantees set forth in the contract.

31. However, frequently turn-key operations do not appear in a pure form - as a full package - but with different degrees of unpackaging, most typically with regard to civil engineering and construction. While these exclusions reduce the scope of the contractor's obligations, there is a relatively new contractual modality which adds responsibilities to those of a typical turn-key holder. Such is the case of the product-in-hand arrangements whereunder the contractor assumes post-commissioning responsibilities even though he has no equity ownership. In effect, under such arrangements the contractor remains tied to the management of the enterprise after completion of the plant for a period, during which he will supply technical assistance and training for the proper operation of the facility. In this way, the final reception is delayed until the purchaser's personnel is capable of exploiting the plant efficiently.

32. The main advantage of turn-key and product-in-hand operations is that the responsibility for the project is centralized by the contractor. This facilitates the enforcement of performance guarantees or the attribution of responsibility in case of failure, and may contribute to the execution of the project more rapidly than under other contractual arrangements requiring the participation of various sources.

33. However, those kind of "packaged" operations imply likely higher costs, particularly in the case of product-in-hand arrangements, where the contractor's obligations extend for a longer time and the risks of failure are higher.

34. In case of a foreign contractor, the "packaged" operations may attenuate the likelihood of local participation in the execution of the project, and may reduce the potential development of construction and engineering firms, as well as of equipment suppliers, in the purchaser's country.

35. A further disadvantage of the "turn-key" approach is that it does not necessarily ensure an effective absorption of the technology since the plant is erected with a minimum participation of the purchaser, a deficiency that the product-in-hand form has attempted to overcome.

36. Another disadvantage of the "packaged" forms of technology transfer may be that they lack the checks and balances that exist when the project is assigned to various participants, particularly when the contractor also supplies the basic equipment. 2/ Here, remedy shall be provided by the proper institution of a consultant engineer.

37. For these reasons, some developing countries have established policies or legislation requiring the unpackaging of technology transfer transactions and have set out methodologies for helping the purchaser to undertake such a task. 3/ The provision of information for allowing the "unpackaging" of such transactions has also been recognised as an obligation of the technology supplier, in the draft of an International Code of Conduct on Transfer of Technology (Chapter 5.2.c.).

38. The degree of centralization or division of responsibilities among various sources is generally linked to the level of technological development existing in the purchaser's country. For territories with very low capabilities and experience in plant erection, the "packaged" transactions might be necessary in order to give the first steps towards the establishment of a pharmaceutical industry, while in cases where the "unpackaging" is possible, it is likely to entail advantages in terms of the cost of the project, the learning and absorption of the technology, and the use and development of local resources.

39. For matter of clarity it should be noted that for the above described types of contract the licensor normally remains without further obligation after the proper hand-over of the complete and comprehensive technology to the licensee and contractor(s). They will take the risk in ultimately successful operation of the plant or enterprise.

40. For additional transfer of technology such as new research and development information, post-contractual services, delegation of specialists, etc. adequate clauses in the contractual arrangements will be required.

(1.4.1.2) Separate, "unpackaged" contracts

41. After the licensor has provided the licensee and/or contractor(s) with the technical information and all other requirements necessary to set up a pharmaceutical plant, the conclusion of separate contracts for each group of executing operations imposes on the purchaser the need to coordinate the different parts of the work. It obviously requires a certain technological capability, and the assumption of higher risks by the purchaser.

42. While this approach is likely to entail advantages, inter alia, as regards to cost, the absorption of the technology (the purchaser obtains a substantial familiarity with the plant), and the development of local sources of supply, the overall responsibility for the proper functioning of the plant basically lies with the purchaser. Hence he would have to bear the consequences of defects of the plant, except if it is proven that a contracting party has failed to duly comply with its contractual obligations. The same applies to consequences of inappropriate co-ordination or delays due to organization of the work.

43. These disadvantages may be compensated or at least attenuated by means of

(i) a proper drafting of the performance and other guarantees that the suppliers should provide, including the establishment of performance bonds or first demand bank guarantees;

(ii) an adequate linkage among the obligations of various parties, e.g. by requiring that the supplier of the know-how and basic engineering approves the civil and detailed engineering, and other measures aiming at specifying the scope and extent of the responsibility of each contracting party;

(iii) the proper organization and co-ordination of the work, eventually with the assistance of a design office and/or consulting engineer which/who would act as an accredited representative of the purchaser vis-à-vis the other participants in the project.

(1.4.2) Transfer of technology related to foreign investment

45. Transfer of technology involving a supplier's share in the capital of the recipient company, may adopt the form of a wholly owned associated company or of a "joint-venture" including the participation of local enterprises or State.

46. Obviously, the requirements and consequences of each alternative vary considerably. The following paragraphs provide some indications as to the relative advantages and disadvantages referred to from the stand point of would-be recipient of the technology and host country, assuming that a new facility needs to be erected in order to undertake the industrial production or pharmaceutical manufacturing.

(1.4.2.1) Wholly owned associated company

46. The establishment of wholly owned associated companies has been often considered another means of transfer of technology. Its impact on the host country and particularly on the development of a local pharmaceutical industry, are substantially different from the cases as described in the other types of contractual arrangements.

47. This version may especially be applicable to more complex basic production where local expertise would be not yet sufficiently developed, or indigenous capital is difficult to be obtained.

48. Only indirect or limited transfer of foreign technology into the host country may occur. 7/

49. Direct transfer of technology between the parent and associated company may also create fiscal and foreign exchange problems. Some developing countries have limited or prohibited compensation and/or royalty payments.

50. Should aspects as mentioned above not be desirable by the associated company or local authorities another type of contract will have to be chosen.

(1.4.3.2) Joint-venture with different possibilities of equity participation

51. This version, applicable to all types of technology transfer - either in "packaged" or "unpackaged" form - may be linked to the establishment of a joint-venture, where the licensor has some equity participation and the licensee is also interested in long term relations.

52. The negotiations between the partners, properly conducted by experienced individuals, should result in as many benefits as possible for:

(i) the licensee:

53.
- considerable technology transfer
- import protection
- partial investment for local equipment
- consumption of local available material
- training and employment of indigenous personnel with chance of participation in responsible positions and absorption of know-how, hence raising the local, educational level
- better access to foreign markets through the know-how of the licensor

(ii) the licensor:

54.
- contributions made by the licensee as regards to knowledge of the local regulations, suppliers, better access to the host market, and general conditions for doing business. 4/

(iii) for both:

55.
- better diversification and reduction of risks
- sharing of capital
- continuity of common interest in success of the joint-venture
- question of management not necessarily dependent on mode of participation
- better informal flow of information

56. Some developing countries have limited the establishment of wholly owned associated companies and permit only foreign investment in association with local entrepreneurs or the State. Other countries strongly promote the setting up of joint-ventures by means of incentives and measures of different nature. Such a policy has been applied in connection with the pharmaceutical industry, in particular, in a number of Latin American countries, where the governments took the initiative for setting up joint-ventures for the local production of bulk drugs. 5/

57. In general, but not exclusively, small and medium enterprises seem to be more inclined to joint-ventures, whereas transnational corporations apparently rather prefer associated companies. 6/

(1.4.3) Financial investment is not or only minor involved

58. For the sake of completeness it should be mentioned that a kind of contractual arrangement for technology transfer may be convenient in the following hypothesis. An enterprise in the developing country with available free capacity - production or manufacturing - may be interested to work for a certain period of time for an expatriate firm and offers its services in form of loan agreement. To satisfy the expatriate's requirements it may be necessary to set up a technology transfer contract for acquainting the staff with the operational procedures and making use of existing equipment but with certain adaptations at minimum cost.

59. Similar situations might exist with plants in industrial estates or duty-free areas.

(1.4.4) "Packaged" versus "unpackaged" transfer of technology

60. In principle, for all types of technology transfer - except for loan production/manufacturing agreements - a "packaged" or "unpackaged" solution is possible, independent of equity participation and not necessarily causal related to the parties involved in the project.

(1.4.4.1) "Packaged" or "turn-key" transfer of technology

61. This set up is aimed to assure the complete and proper application of the know-how gained and exercised by the licensor to build facilities,

efficiently produce, sell and possibly also distribute bulk drugs, intermediates and/or formulated pharmaceutical forms in defined quality, sufficient quantity at lowest feasible cost, with the outlook of provision to receive updated information to improve any sector of activity. The cost of such an arrangement might but need not be substantially higher than for an "unpackaged" one. The execution may be more rapid than under "unpackaged" conditions. The responsibility lies in one hand. Perhaps less involvement and technology absorption of the licensee. Advantageous for enterprises with starting capabilities and experience.

(1.4.4.2) "Unpackaged" transfer of technology

62. This set up is aimed to end up with a cheaper project, more involvement of the licensee in the learning process and technology absorption and development of local resources. On the other hand, consideration should be given to eventually a longer implementation time, adaptation work at boundary positions of different (sub-)contractors, careful coordination and supervision of the whole project, likely more contractual arrangements and paper work with (sub-)contractors. This type of technology transfer may be primarily recommended to licensees with already advanced technical, marketing and managerial know-how.

63. Several ways of "unpackaging" are conceivable as outlined below.

(1.4.4.3) Civil engineering

64. Based on data and drawings supplied by the licensor an erection of the building(s) is carried out by a separate contractor, independent of the remaining technology transfer. In this case the distribution of responsibilities among the parties involved is relatively easy and should not cause any serious problems.

(1.4.4.4) Civil and mechanical engineering

65. Based on data, drawings and machine lists, including connections and performance of the equipment supplied by the licensor, work is carried out by either one or two separate contractors, independent of the remaining technology transfer. The implementation of the building(s)

and the subsequent erection and also testing of equipment needs especially for bulk drug or intermediates production, already a careful coordination among the parties involved.

(1.4.4.5) A further splitting of tasks

66. Acquiring process know-how from different sources (e.g. splitting of a process sequence or different product components for a certain bulk drug manufacture) require an overall responsibility in one hand. This person or project team or consultant must make sure that the suppliers issue not only their exact process know-how but formulate also clear conditions at the transition from one process to the other. A perfect co-ordination is of paramount importance. Certain risks are involved in this kind of technology transfer because misunderstandings between the partners and lack of co-ordination may result in considerable delay of the project and unexpected cost increases due to correction work and delayed start of production. The licensor may require a secrecy agreement vis-à-vis his co-licensor.

67. A thorough evaluation of the contract possibilities will show the advantages and disadvantages of each type relevant to a given project task. The final decision depends on criteria such as, but not limited to:

- policy of the partners;
- financial situation of the licensee or host country;
- amount of the envisaged foreign investment;
- degree of existing technology know-how in the host country.

(1.4.5) Type of project execution

68. The actual execution of a project is delegated either to one single responsible body or to a group of contractors acting independently, or to the own project team.

(1.4.5.1) Turn-key ("one package") contract

69. The contractor (or licensor) assumes full responsibility to set up a plant according to a complete package of information until civil commissioning of the site and buildings and mechanical commissioning of the whole equipment.

(1.4.5.2) The project realization is delegated to several contractors ("unpackaging")

70. A practical split-up would be:

- civil contractor for site and buildings
- specialist for well water tapping
- contractor for steam generation
- contractor for electrical work
- contractor for HVAC (heating, ventilation, air conditioning)
- contractor for compressed air
- contractor for water treatment and supply
- contractor for piping
- contractor for insulation
- engineering firm for the installation and mechanical commissioning of equipment, which is common for chemical plants and rather an exception for formulation and packaging
- further contractors for e.g. sanitary with plumbing; effluent treatment plant; installation of laboratories for in-process control, quality control (micro biological-, chemical- and physical laboratory), packaging material control; kitchen and canteen; laundry; gardening; housing facilities (if not included in the civil contract of the factory); etc.

71. As stressed earlier this type of "unpackaging" an execution of a project works only in conjunction with a strong own project team or project manager which/who is fully familiar with the whole technology transfer and can effectively co-ordinate the various efforts or, by calling a competent and reliable consultant.

72. The expected advantages of an "unpackaged" project realization will be compensated to a certain extent by the effort demanded from the project team or by the cost invelved when hiring a consultant.

(1.4.5.3) Execution by the own project team

73. This version is quite realistic if only sections of the implementation are involved, e.g. installation of the compressed air system, installation of the water deionization/destillation system, installation of formulation and packaging equipment where relative little work is involved.

74. But it must be kept in mind that the primary task of the project team or project manager is the stipulation, organization, promotion, control, follow up and conclusion of a project.

75. It belongs to one of the major tasks of the pre-feasibility study to find the most appropriate way of the project implementation.

(1.5) Revised pre-feasibility study

76. The purpose of this study should be to give an upgraded picture of the first pre-feasibility study, especially with regard to costs.

77. At this stage the licensee should have made up his mind as to what type of technology transfer contract(s) he will choose for the execution of the project. The costs and possible other consequences with regard to the execution should be known in an order of magnitude of - say ± 30% and be considered in the revised pre-feasibility study.

78. A cost idea in the same order of magnitude of ± 30% or better should be collected by now for all items related to the new enterprise, such as:

- production
- raw material prices
- products/medicaments to be sold
- overhead (administration, marketing, etc.)
- land
- energy supply or generation
- services
- etc.

79. The result of this revised pre-feasibility study should be, whether the envisaged terms of project are sufficient to warrant a "go ahead" or need further evaluation.

(1.6) Tendering conditions for execution of project

80. In theory, the licensee or licensor may be in a position to execute a project, and actually will make use of it in case of minor work involved. It is conceivable that adaptation work in an existing production or manufacturing plant will be carried out by the licensee's project team, minimizing or even eliminating, thereby, effort and expenses for outside consultation.

81. However, the normal case will be that the licensee alone or licensee and licensor (in case of joint-venture) will invite selected contractors for tender.

(1.6.1) Tendering to private contractors

82. This means in general great flexibility with regard to sometimes occurring changing conditions during the implementation phase and good exchange of information even among competing contractors. Another feature is the great mobility and interchangeability of personnel. In most cases, experience from the execution of similar projects will be available. The disadvantage of private contractors compared with

contractors in the public sector is the greater risk of discontinuation of works in a particular country and sometimes slow allotment of building/construction material.

(1.6.2) Tendering to public sectors

83. This normally means a reliable execution until the end of the project, better access to regulative information, building/construction material and a better financial background. Perhaps easier approval of equipment import license. On the other hand, less flexibility, experience and movability of personnel may have to be encountered.

(1.6.3) Conditions of payment

84. A lump sum contract means in essence that all expenses borne by the contractor/licensor are pre-estimated and calculated wherever possible, and summed up in one figure. It will be obviously higher than actual costs and prices to cover the contractor's risk of variations during execution. It could be to his profit or loss. The payment will be effectuated by negotiated periodical instalments.

85. Another modality would be the payment after the completion and measurement (if applicable) of a defined portion of the contract. It involves less risk for the contractor, additional work for the employer and the danger of losing control over the whole project expenditure often at the end of implementation.

(1.6.4) Evaluation for the execution of pharmaceutical projects

86. Which preferences should be considered depends largely on the capability and reputation of the contractor, and on the degree of co-operation to be expected and the degree of clear formulated clauses for unexpected situations.

(1.7) Governmental approval(s)

87. With the project information so far available one or several documents are to be prepared for submission to the authorities. The following aspects are a selection of requirements which may be incomplete and depend largely on local laws and regulations.

(1.7.1) General requirements

88. Approval and/or registration of:

- contract(s) involved in the transfer of technology, including licenses and patents
- foreign investment, remunerations, royalties, etc.
- safety measures
- air pollution handling, effluent treatment and waste disposal measures
- land and building concepts
- expatriate contractors, experts and/or services, trips to foreign countries
- evidence of bank guarantees if applicable
- local or foreign transport facilities to be used

(1.7.2) Requirements related to bulk drug and intermediates production

89. Approval and eventually registration of:

- process used
- import licenses for
  - = equipment
  - = raw material and intermediates
  - = packaging materials and utilities where applicable

(1.7.3) Requirements related to manufacture of medicaments

90. Approval and eventually registration of:

- formulations by health authorities
- import licenses for
  - = equipment
  - = bulk drugs and accessory material
  - = packaging material and utilities where applicable

91. Since the procedural steps towards agreement might take months, it could be advisable to seek an informal contact with the relevant authorities at an earlier stage. This may reveal the necessity to collect further information for approval of a particular application.

(2.) Composition and duties of project organization

91a. For the realization of a plant with technology transfer the inauguration of a project organization is recommended. It is preferably composed of a project principal, a project team and specialists as and when required.

91b. In the preliminary phase its main task will be devoted to the collection and preparation of data and information for the pre-feasibility study and the submission of the application regarding the transfer of technology agreement to the authorities. At the same time an order of magnitude of the anticipated plant and its operation may be elaborated in form of a pre-project.

(2.1) Project principal

91c. This function lies within the responsibility of both contracting parties or is in most cases delegated to a representative of their confidence.

91d To their or his duties normally belong:

- guidance and promotion of all activities which are leading to the transfer of technology and the realization of the plant;
- formulation or adaptation of licensee's company policy;
- vote in case of difference of opinion among the contracting parties or the different working groups;
- selection and securing of funds;
- nomination of the project manager and a voice in the selection of his team members: indigenous or expatriate;
- contact with the authorities;
- vote in the selection of consultant(s), contractor(s), specialists, architect(s), lawyer(s), etc.
- evaluation of technology transfer, contract alternatives and assistance in decision for final contract modalities.

(2.2) Project team

91e. Normally it consists of a:

(2.2.1) - project manager;
(2.2.2) - project engineer;
(2.2.3) - chemist and/or pharmacist;
(2.2.4) - expert or delegate of marketing section;
(2.2.5) - expert or consultant, capable to carry out a feasibility study, if this is not already included in the scope of work of the above functions;
(2.2.6) - specialists as and when required.

The main duties of the team can be circumscribed as follows:

(2.2.1) - Project manager (with managerial qualities)

91f. He is responsible for the nomination of the team members and their qualification, also for calling in experts as and when required.

91g. He will formulate the tasks of the team, guide and co-ordinate the work, initiate corrections where necessary and surveys the results achieved.

91h. He fixes dates for periodic (e.g. bi-weekly) project team meetings, reviews the agenda for the forthcoming meeting and sanctions the notes or protocol of the previous session.

91i. He prepares in co-operation with the team specialists, contractors and possibly also with the indigenous authorities a tentative time schedule for the negotiation - and implementation phase.

91j. He reports periodically to the project principal.

91k. He suggests or nominates alternative candidates as consultant(s), contractor(s), architect(s), civil engineer, quantity surveyor (where applicable) etc., and submits a proposal to the project principal.

(2.3.2) - Project engineer (with theoretical and practical experience, preferably in project execution)

91 l.He studies, assesses and implements the data and information of the technology to be transferred.

91m. Main points are:

- for bulk drug manufacture: flow sheets, process procedures, formulas, equipment lists, layout, mechanical engineering, utility requirement, environmental pollution and waste disposal proposals, safety, fire fighting, etc.
- for formulation and packaging: manufacturing procedures, equipment lists, layout, mechanical engineering, utility requirement, waste disposal proposals, safety, fire fighting, etc.
- for erection or expansion of the necessary manufacturing plant, or installation of equipment in an existing plant: design, civil engineering, floor load requirement, building material requirement where essential with regard to product influence or wear and tear etc., safety and fire protection measures, building concept e.g. plinth level, ramp height respectively for monsoon areas, or bonded rooms and zones in certain countries, or anti vibration measures, etc.

- establishment of contacts with the contractor(s), briefing and transfer of data/information, control and co-ordination of work, etc.

- in co-operation with the team and specialists evaluation and elaboration of a (pre-)feasibility study.

(2.2.3) - Chemist and/or pharmacist (with theoretical and practical experience)

91n. He or they should at the best be already familiar with, or better, have some practical know-how of the chemical processes of bulk drugs and intermediates, and the manufacturing procedures of the finished pharmaceutical products, which are normally the core of the technology transfer. Otherwise they have to study the matter or must receive a training until they will become competent partners of the team.

91o. The first task is to translate the marketing requirement, eventually together with other specialists, into a

- yearly bulk drug or intermediate production programme with batch size and requirements split up into raw materials, auxiliaries, intermediates, purified water; personnel split up into categories; energies; social; storage capacity

- yearly formulation with batch sizes and campaigns, yearly packaging with lot sizes, and requirements split up into bulk drugs, auxiliary material, packaging components, deionized and sterile water; energy; personnel split up into categories; social; storage capacity

91p. Ideally, they should be also qualified to judge

- the quality control requirements
- the use of indigenous and other competitive alternative materials
- the factor "economy of scale", at least for the sector of production and/or manufacturing
- all other factors which influence the operation of a plant

91q. To their duties should belong also the ability to assist in price calculations.

91r. Co-operation within the team and with contractor(s) to assure the proper interpretation of the process/manufacture know-how.

91s. Co-operation within the team and with specialists for the evaluation and elaboration of a (pre-)feasibility study.

(2.2.4) - Expert or delegate of marketing section (preferably with practical experience in local and transnational marketing)

91t. Here an assistant is expected capable of evaluating all available marketing information relative to the products for which the technology transfer is anticipated.

91u. Relevant parameters are:

- Health requirement
- national and international market requirements as well as possible competition and actual sales figures, in particular in the sector where the new product(s) should be launched
- the sales prospects under optimistic and pessimistic assumptions
- export possibilities
- influence of legislative, (protective) tariff, competitive, subsidised nature which influences the sales price structure and the sales volume.

91v. Interpretation of market requirements including all above listed indicators into yearly

- bulk drug and intermediate requirements
- package requirements split up into dosage forms, dosage strength, package size and presentation.

91w. Close co-operation with the chemist, pharmacist or consultant with regard to product pricing and determination of the break-even point of the business.

91x. Co-operation with the team for the evaluation and elaboration of a (pre-)feasibility study.

(2.2.5) - Person or consultant to carry out a feasibility study

91y. This task can be performed by anyone who possesses logical judgement and knowledge of estimating and calculating the factors involved in a feasibility study. In the negotiating phase a weighing of facts is as important as the first guess of return on investment.

(2.2.6) - Specialists (as and when required)

91z. In the negotiation phase the legal advisors (usually one of the licensor and one of the licensee) play an important role until the contracts are prepared, submitted to the authorities and finally approved. But later on a lot of legal problems emerge which make the advice of the lawyer(s) again necessary.

91aa. During the course of the project planning and execution, specialists like the architect, soil test firm, well water sinker, air conditioning specialist, waste treatment companies, etc. will be invited to join the project team to help solving the particular tasks or problems.

91bb. For a period of time the contractors will be a member of the project team.

91cc. The project team may be regarded as the organ for collection of data, co-ordination, supervision and to some extent organizing matters, in the transfer of technology phase until the plant and the enterprise have started successful operation with satisfactory sales of reliable bulk drugs, intermediates and/or medicaments.

II. CRITICAL ASPECTS ON FEASIBILITY STUDIES

92. A lot of aspects being considered in the feasibility study phase are very sensitive, like patents, know-how, experts, training, etc. These sensitive issues have been discussed already in its legal and operational form between experts of developing and developed countries. The final version is laid down in the documents g), h) and i) listed in the preface on page 1.

(1.) Availability and characteristics of process know-how

(1.1) Investigation of the status of process know-how

93. For the 26 essential drugs for which in the developing countries facilities for the local production of active ingredients should be established (Table I) in general, process technology of several sources are existing. Contacts with the suppliers of technology for one and the same drug and the study as well as comparison will reveal the feasibility of the process in question.

94. In view of the dynamic development facts must be evaluated in relation to the ideal concept of "most cost-effective and efficient currently available technology to be transferred, given the conditions in the recipient country".

95. A new developed technology may cost more (license fee, royalties, etc.) and the process involved could still have starting problems and bottle necks. A technology already for a long time in use will be more tested and should be certainly free of initial start-up troubles. This process may even cost less. Obsolete processes are not to be considered, but the possibility of a technology to become obsolete must be judged.

96. The availability of alternative processes or steps thereof should be realistic and must be carefully studied. It will allow to make a feasibility study more transparent, will broaden the knowledge of the licensee. It places him in a better negotiation position.

97. In technologies with a number of process steps the feasibility "buy versus make" should be carefully checked. It is quite possible that a whole process starting with basic raw materials and auxiliaries is easier than the realization of only part of it, starting with intermediates, or vice versa.

98. In the latter case the licensee's staff may easier absorb the know-how involved and gain experience. Failing to cope with a multitude of problems and achieving unsatisfactory results, when starting with the whole process at once, must be frustrating. In taking over only part of the process the chances are better that local equipment and material can be successfully introduced, tested, adjusted, modified and improved.

99. Especially for bulk drug and intermediate production the problems of environmental pollution become more and more important. In particular the adequate protection of workers against such influences need be considered (e.g. poisonous exhaust gases, contact with cancerous matter, continuous inhalation of fine dust leading to silicosis, excessive noise leading to hearing damage).

100. For formulation and packaging where manufacturing procedures are widely standardized, primarily the legal aspects of the technology transfer will need attention such as trade marks, patent laws and retransfer of dividends, fees, royalties, etc.

101. Hygenics and good manufacturing practice (GMP) have become an important factor in formulation and even packaging. They should be observed as good as possible and sometimes even at higher costs.

(1.2) Complexity of process and/or know-how

102. The complexity of processes varies widely and is particular significant for bulk drug production. In a complete manufacturing process of a corticoid up to some 40 steps are involved when beginning with basic raw materials, whereas for acetylsalicylic acid only 3-4 steps are required.

103. Similar complexity applies to know-how. An automated sequence of operations for a high-pressure-high temperature reaction in a glass lined 1000 liter pressure kettle or in a glass column needs considerable more skill of a whole team than the dissolving of sugar in a 100 liter stainless steel mixing vessel.

104. In pharmaceutical formulation the question of complexity is somewhat less important but still existent. An automated spray granulation with organic solvent in a fluidbed dryer needs substantial more safety precautions than the drying of tablet mass in a tray dryer.

105. To formulate a sterile product and fill under sterile conditions into ampoules or vials needs more experience than the preparation of tablet mass and subsequent tabletting.

106. It will depend on the capability, competence and skill of the licensee's staff and operators how much of technology transfer one can expect that they will be qualified to absorb at once. A gradual take over of technology could be achieved either by step wise introduction of processes or by addition of expatriates during the start up period or for a longer period.

107. In the case of choice most probably the more complex technology would be the more expensive one.

(1.3) Patent situation

(1.3.1) Introduction [8/]

108. A brief attempt is made to show how licenses and patents are related to a technology transfer agreement.

(1.3.2) Possible definition of technology transfer agreement

109. The legal framework for commercial transfer of technology is the TECHNOLOGY TRANSFER AGREEMENT. It considers the interests of both parties, the law and other public requirements practiced in the country where the parties are domiciliated, but last not least the creation of a climate in which technology-supplier and -recipient can achieve goals of common interest.

(1.3.3) A technology transfer agreement may consist of:

110. - LICENSE(S)

- supply of technical and other know-how by agreement
- supply of management assistance and technical services by agreement
- agreements covering other aspects such as
  - transfer of improvements and development
  - future or related rights for sub-contracting or -licensing

  - import and sale of capital goods
  - methods of compensation
  - settlement of payments
  - most-favourable conditions and terms
  - changed conditions or events, default, remedies, waiver
  - entry into force, expiration, extension, duration, term, termination
  - injury or damage to third parties, insurance
  - settlement of disputes
  - modification, amendment

- preamble, introductory aspects, recitals, whereas clauses
- difinitions of abbreviations, expressions, key words
- approval of authorities and execution
- sundries
- notes, references, appendices

111. (1.3.4) A license is the authorization to exploit a PATENT, to use a registered trademark/tradename or other subjects of "industrial property", which are protected under the respective law. The owner of the patent, trademark/tradename or industrial design (licensor, patentee) grants its exploitation or use to some other person or party (licensee) by means of a license, which is limited in time either by law or by agreement between licensor and licensee, in the case of exclusive licenses the right to preclude third persons/parties from its exploitation/use. A license is granted for e.g. a:

- PROCESS PATENT
- PRODUCT PATENT
- trademark or tradename
- and other subjects of "industrial property".

112. (1.3.4.1) In connection with the grant of a license the technology supplier expects a "price" which is termed "compensation". He needs a fair share for a number of risks, effort and expenditures. Points of argument are:

- prefinancing of research and development which is to be continued under risks
- compensation for all process and technical know-how
- compensation for assistance and services
- compensation for all the risks he takes with the grant of license, including the creation of a potential competitor in form of the technology recipient, abuse of patents, etc.

- risk of change of patent/trademark law, etc.
- other expenditures like records for quality and validity, improvement of safety, etc. and entrepreneurial risks

113. (1.3.4.2) "Remuneration" paid for the exploitation or use of the license, assistance, services, etc. by the technology recipient are "costs" to him which he likes for many reasons to keep to a minimum. Remuneration may be split up into three categories.

114. - Lump sum payment: to reimburse the technology supplier a pre-calculated amount, once or in installments for the

. industrial property license
. process and technical know-how
. assistance and services
. goodwill created in the host country, etc.

before any use is made of the license, etc.

115. - Royalties: to reimburse the technology supplier post-calculated recurring amounts in function of quantities/units produced or sold, or of other criteria relevant to the technology transfer.

116. - Fees: to be reimbursed to the technology supplier as compensation for assistance and services of any kind, related to the technology transfer of agreements such as:

. transfer of technology costs including patents etc.
. training of personnel
. delegation of expatriates and experts
. assistance and services in managerial or other respects such as acquisition of market data, etc.
. etc.

117. (1.3.5) A patent means a document, issued upon application, by a government office (or regional office acting for several countries), which describes an invention and creates a legal situation in which the patent invention can normally be exploited only with the authorization of the patent owner (licensor, patentee). The legal protection is limited in time (generally not more than up to 20 years).

(1.3.6) Aspects concerning patents
(See UNIDO documents ID/WG.393/1 and V.83-54945)

(1.3.6.1) Patent application

118. The patent law greatly varies in different countries. In connection with licenses the parties of the technology transfer must carefully study the legal form of application and grant of a patent. Some countries permit licensing already before the grant of a patent, others require a granted patent.

119. This aspect is of importance because the eventuality exists that an application of a patent after months or even years might be refused or a granted patent declared invalid. If compensations or remunerations have already been paid, ways and means must be provided for reimbursement. In this respect, the exchange of warranties is of some significance.

(1.3.6.2) Patent protection

120. In pharmaceuticals, wherever patent protection is recognized, concerns the process, including secret know-how of production (process patents) of a basic drug (a chemical entity), or the basic drug itself (product patents). When one or more patents are involved, the contract will have to contain a number of specific clauses related to the license of patents.

121. The manufacture of formulations on the basis of finished basic drugs does not entail the use of process patents, which may refer to the production of the basic drugs, but not generally to that of the formulations themselves. Therefore, depending upon the legislation in force in the licensee's country, this matter of process patents will not normally arise in regard to the manufacture of pharmaceutical formulations. For this reason, arrangements for the transfer of technology (other than those involving industrial property rights) for formulations may be limited to the supply of technical assistance for short periods, or alternatively to other type of arrangements which do not oblige the recipient to effect continuous payments or observe restrictive conditions.

122. In practice, however, arrangements for the formulation of pharmaceuticals are very often framed as licensing agreements, involving the provision of active ingredients, the communication of medical and other

scientific information needed for the registration of the products and the licensing of the relevant industrial property rights.

123. The same would apply if the protection conferred by process patents is extended to the products manufactured with that process, for instance, if the patent owner is entitled to prevent imports of such products into the country where the patent is in force.

124. A licensing agreement for formulation may, wherever product patents are involved, include the following stipulations:

i) Specification of the number, and eventually the date of granting and expiration, of the patents licensed

ii) Licensor's warranties regarding its title to the patents and the validity

iii) The action to be undertaken in case of infringement of licensed patents. That action may be jointly assumed by both parties, or left to only one of them (normally the licensor).

iv) The obligation (normally at the licensor's charge) to maintain in force the licensed patents, by paying the renewal fees, if required.

125. Where product patents exist (see Table II) the licensee will need a license to make use of and sell the patented basic drugs entering into the formulation, even though the licensee will not manufacture the basic drug itself. A survey is to be undertaken in order to examine the status of patent situation as regards essential drugs, contained in the WHO model list of essential drugs, including the UNIDO illustrative list (Table I). Process patents may have already expired, though know-how may still be secret.

(1.3.7) Infringement

126. Two different situations should be covered by the technology transfer arrangement.

127. (1.3.7.1) Infringement by the licensee of third partie's rights, when using the licensed patents.

128. (1.3.7.2) Infringement by a third party of licensed patents.

129. For the legal aspects see UNIDO document ID/WG.393/1.

(1.3.8) Territorial scope of patent protection

130. The "territoriality" of patent rights is one of the basic principles of the patent system. It means that the rights conferred by a patent only apply to the country where it has been granted.

131. In general, pharmaceutical projects are mainly intended to satisfy a demand in the prospective licensee's country. Often, however, the latter also desires to export to neighbouring countries, or to a wider territory. In this hypothesis, the evaluation of the patent implications of the project should cover the prospective licensee's country, as well as all other countries where he may be able and willing to sell the new products, provided it is also in the interest of the patentee.

132. The legal situation in such countries may vary considerably, not only - in general - as to the recognition or not of product or process protection and the rights conferred thereunder, but also - in particular - with regard to the status of registered patents for a defined product or process. Differences in this latter sense may mainly arise from:

a. different terms of patent protection (it broadly varies not more than up to 20 years);
b. the recognition or not of an import monopoly as a part of the patentee's right;
c. the existence (and eventual enforcement) of sanctions against non-use of patented inventions, involving - as it is the case in some developing countries - the forfeiture of the patent (e.g. if it is not exploited after 2 or 3 years from its granting);
d. the eventual judicial challenge or nullification of the relevant patent.

133. All these factors should be carefully considered when appraising the potential markets and restraints that the prospective licensee may encounter abroad. If necessary, he may seek for voluntary licenses, eventually as an integral part of the license granted for the production and sale in his own country.

(1.3.9) Information on patents

134. In order to make a proper evaluation of the patent implications on the project, a would-be licensee would therefore need to obtain updated and complete information as regards to:

a. the legal framework in force (in his own country or abroad), also valid for the patentee;

b. the status, validity and enforceability of relevant patents, and the identification of the patent holders.

135. The search for this information within the prospective licensee's country is relatively simple, and may generally be obtained with the help of the Patent Office. International information may be more difficult to obtain. For this purpose, the assistance of international "banks of patents" may be looked for. [10]

(1.3.10) Remarks

136. Apart from the legal patent situation for the transfer of technology in the pharmaceutical industry there are also additional impacts - based on law - to be observed.

(1.3.10.1) Enactments on pharmaceuticals

137. Possible local legal restrictions must be investigated with regard to the sale of specific pharmaceuticals.

(1.3.10.2) Price regulations

138. Similarly, for certain or all pharmaceuticals in the public health sector, prices are either fixed or upper limits are given.

139. It will be wise to acquire such knowledge of restrictions/regulations already before entering a technology transfer agreement.

140. To appraise the patent and license conditions in its full complexity a local legal advisor and in many instances also an expert on international law will be indispensable.

(2.) Material supply

141. When discussing transfer of technology the following items are termed as materials:

- raw materials and auxiliaries
- intermediates
- packaging material components
- utility material
- and - in certain cases formulated dosage forms (tablets, liquids, ointments, sterile powders or solutions etc.)

(2.1) Import possibilities

142. Provided there exist no restrictions, in theory, in every developing country raw materials, intermediates and medicaments should be available. A possible local offer can easily be made up by a multitude of tenderers from different countries, essential drugs concerned. This allows a sound comparison of prices and other terms of a purchasing contract. But dealing with pharmaceuticals, a series of additional requirements must be met, e.g. the continuous accessability and acceptable as well as uniform quality, or the adherence to tolerances for packaging material components, etc.

(2.2) Restrictions

143. Restrictions of current or anticipated future actuality may be:

- Lack of foreign exchange, one of the reasons to acquire technology to produce with as many local resources as possible and also cheaper, if possible.
- The enforcement of an import license, which is normally accompanied by tedious bureaucratic procedures.
- Import duties which, in the case of protective tariffs, could render a purchase from abroad impossible.
- The political instability of a country or region.
- The limited supply of local sources which may coerce the necessity of imports, even under adverse conditions.

144. In disadvantage of the licensee import restrictions for raw materials, auxiliaries, intermediates, bulk drugs or formulated bulk may be seen. It

could even happen that in certain instances difficulties on transfer of technology could be encountered.

145. In favour of the licensee count import restrictions on competitive material, in particular finished pharmaceutical products and competitive technology adversely affecting its own enterprise.

146. The negotiating partners must fully realize that the development and promotion of the market takes place to the largest extent independent of the technology transfer.

(2.3) Guarantee of supply

147. It lies in the public interest that the supply of products and medicaments is assured. For economic reasons the enterprise must endeavour continuous production. Both postulates can only be met if the uninterrupted flow from the source of supply is guaranteed.

148. To prevent unacceptable surprises it is commendable to investigate safety measures and alternatives.

- An internal measure is the adequate allocation of stores with primary and intermediate materials to prevent risks at least for a limited period.
- For common available materials and intermediates the purchase could and even should be split up to two sources, preferably located in two countries.
- For more scarcely available matter long term contracts may be the solution, which may be accompanied by a minimum take over obligation.
- If no other choice is left, for bulk drug production, for instance, even the change over to another technology must be taken into account, e.g. synthetically manufactured 6 amino penicillanic acid (6-APA) from Potassium Penicillin G as against by enzymic process or vice versa.

(3.) Market survey

(3.1) Domestic demand

(3.1.1) Licensee's contribution

149. Considerable investigations for the sales requirement have been carried out by international organizations such as UNIDO, UNCTAD, WHO, World Bank, etc., and may serve as a background paper. Additional studies will be available through local sources such as the health authorities, universities, hospitals, and last not least by the licensee, who collects and surveys the information. He amends it by his own market research.

(3.1.2) Licensor's contribution

150. Similarly the prospective licensor will proceed and investigate the market prospects thanks to his knowledge of the products and/or in collaboration with organizations like institutes for tropical diseases.

(3.2) Forecast

151. The conclusions drawn from the survey, expressed in local money, in weight for bulk drugs and intermediates, and in quantities per year for formulated and packed medicaments, must be based on a time grid, the span of which can be set in average between 3 to 5 years. Since the transfer of technology, beginning with negotiations until start of operation, under average conditions takes 2 to 4 years for a manufacturing plant and even longer for a bulk drug production plant, depending on the duration of negotiations, approval by authorities, planning, type of contract, implementation and unforseen variations which may happen during the course of the project, the practical forseeable sales demand of 3 to 5 years ahead is rather short. A trend study for up to 10 to 12 years must complete the more precise sales requirement as outlined above. It most probably consists of only percentage figures or indications like "rising", "stable" or "moderate falling", etc.

(3.3) Price development

152. A decisive portion of market survey consists of the appraisal of the price development.

153. The material prices in particular are a direct function of:

- world market prices
- supply and demand
- transport facilities (rail, ship, truck, air carrier, pipe line)
- distance from supplier to user
- insurance
- import duty
- sundries

154. The finished goods price is composed of:

- material prices (bulk drug, auxiliary material, packaging material)
- labour and other personnel costs
- operational costs in addition to above components
- overheads (research + development, marketing, administration, social, etc.)
- profit
- quantity sold in one lot
- size of finished package (unit dose, standard package, hospital package)
- component related to policy (competition, monopoly, government subsidy, etc.)

155. The combination and consequences of all these factors determine the price development.

(3.3.1) Evaluation of material prices

156. The fixation of material prices for self manufactured bulk drugs, intermediates and/or formulated dosage forms is the main task of the purchasing division. These prices depend on several factors which are often difficult to be judged in advance. Some factors are discussed below.

(3.3.1.1) - Raw-, auxiliary- and utility material-, intermediate- and packaging-material-prices

157. A confrontation of competitive prices from sources, possibly including the licensor, and indigenous firms will reveal the products of choice. Here, too, assurance must prevail with regard to continuous accessability, acceptable and uniform quality as well as stable prices,

at least for a certain period of time. Import duties and other merchandise restrictions, government subsidies, transfer price agreements between the licensor and associated companies must be taken into account, equally the order quantity, long term contracts, rate of inflation, varying exchange rates, the timely comparability of the submitted quotations, etc.

(3.3.1.2) - Development of government regulations

158. In every country it may happen that government policies and hence also regulations could change to the effect that material prices will be persistently influenced. It may concern: anticipated protective tariffs, change in the policy of subsidies, control of intra company price arrangements, restriction in license grants and patent law, price reglementation, centralized material purchasing, etc.

(3.3.1.3) - Labour cost

159. This cost is another decisive price component. For labour intensive operations the forecast of these costs and the impact of possible fluctuations will have to be considered.

(3.3.1.4) - Other costs

160. In principle, all other cost factors will have also to be evaluated for a reasonable quality of the feasibility study.

(3.3.2) Pricing of the finished product

161. A comparison of the calculated value of the own product, be it a bulk drug or an intermediate or a medicament, with the selling price of competitive products available on the free market will reveal the actual situation. The own price will be also influenced, whether the product ranges under a trade or generic name, by the batch size, manufacturing sequence, utilization of the plant and size of manufactured quantity (economy of scale), by the possible necessity for splitted prices - one for domestic sale and one for protected export markets where price fixing practices or other restrictions may exist.

162. The economy of scale may become controversial. Developed countries stress the importance of this point whereas documents exist denying it, at least for formulation plants.[11/]

(3.4) Export possibilities

163. It is understood that export possibilities are officially stimulated in most of the developing countries.

164. For bulk drugs and intermediates situations may occur in the world market when an outspoken demand exists. In any case, sales promotional measures will have to be considered and the coordination with international operating sales organizations studied.

165. Very often the licensor will have already covered the territory of licensee's interest with his own market strategy. Between complete freedom and the full restriction to export, a wide range of intermediary alternatives exists. (See UNIDO document ID/WG.393/1, page 46 and 47.)

166. The export price may have to be adjusted to the conditions prevailing in countries of licensee's interest and might differ from the indigenous sales price.

(3.5) Distribution facilities

167. The requirement for intermediates and bulk drugs is generally concentrated on few recipients throughout the world and needs no special distribution facilities.

168. Different with medicaments. A well functioning system of distribution is a prerequisite for successful sales of pharmaceuticals. Either the State has his own distributional organization or the private industry builds up a sales promotion force which at the same time renders medicinal information to the recipient of pharmaceuticals, normally hospitals and pharmacies, and doctors.

169. In or around populated centers, as a rule, medical treatment facilities consisting of doctors, hospitals and pharmacies do exist. To reach here also the less propertied population, subsidized private health organizations or a governmental health care must become active with medical educational campaigns, voluntary practicing doctors and social workers.

170. In the rural areas of developing countries the health care must be further developed on all levels to enable the penetration with medicaments and ultimately relieve the sick population from pain.

171. Epidemiological work will help to set priorities in the affected regions as to treatment and medicinal aid.

172. It is obvious that to the distribution facilities belong also a road or navigable river system, dry and vermin free distribution centers and control/withdrawal of not any more validity conform pharmaceuticals.

(4.) Location

173. The location for the erection of a new plant is of utmost importance. Once one has built, the chances to move are almost nil. A wrong decision has often grave financial consequences.

(4.1) Soil conditions and ground water

174. An important factor in the selection of a site is the soil condition. Where possible the choice should be made in favour of sandy or rocky ground. Often it is overlooked that certain clay soils need expensive piling, large foundations or even a reinforced concrete bottom floor shell under the whole factory building.

175. Ground water is desirable. Decisive is the water level. Water in a depth between 10 and 100 m. can be pumped via well. Surface ground water existent in filled up areas next to harbours or in marsh territory is specially inconvenient because it rises in rainy seasons up to the surface and does not drain any more.

176. In case of doubt and in absence of certified soil data even in the prenegotiating phase a soil test expertise should be ordered.

(4.2) Size and shape of site

177. Since an enterprise can be compared with a growing organism, size and shape of the land to be purchased must cope with future ventures of the licensee's business enterprise. As a guide, the location in question should allow the acquisition of, say 30,000 to 40,000 m2. In general, an approximate square shaped area of the site allows convenient expansion possibilities, when the initial development starts in one corner and a master plan devides the lot already into zones. An option for an additional land acquisition should be investigated.

(4.3) Topographical situation

178. The terrain need not be completely flat. A difference in hight of one storey e.g. can eliminate the necessity of elevators and, properly applied, will reduce building costs. The use of gravity may be applied more successfully.

(4.4) Infrastructure

179. Under infrastructure of a site a variety of different aspects is ment.

180. The energy supply would consist under ideal conditions of:

- electric power (6', 12' or 20'000 Volts)
- water (treated or untreated)
- fuel or gas or steam
- brine.

181. As a minimum, fuel or gas supply must be available. Electricity can be generated, water can be pumped from a well. Steam and brine normally will be produced to the amount of need.

182. As service is understood:

- telephone, telex (in exceptional cases wireless communication)
- housing facilities for staff and workers inside or outside the own site or industrial estate
- school(s)
- hospital

- fire brigade
- food store(s)
- canteen facilities
- entertainment
- place of worship
- police.

183. Transport facilities mean:

- under all climatic conditions usable road, preferably with a hard top cover
- railway (with a near by station)*/
- airport
- harbour*/
- trucking facilities
- bus service.

184. As ancillary services would be desirable:

- workshop for larger mechanical repair
- electro workshop
- truck garage
- kettle forge*/
- instrument specialist.

185. The existence of a public sewer system or access to a river or ocean is not an immediate prerequisite but in the long run an absolute necessity. A temporary solution is a seepage pit or drainage culvert, provided the ground water will not be polluted. Similar is the case with the incinerator.

186. Since plants may also be located in rural areas (new development, industrial estates or free trade area) this condition is also included in the above check lists.

(4.5) Climatic conditions

187. In Monsoon regions the danger of flooding exists. This implies the raising of the factory ground level to plinth or ramp height level. The streets must be properly drained, preferably by open ditches.

188. For formulation and packaging an extreme humid air needs excessive air conditioning. Tabletting, tablet coating, capsule filling, blister packing and automated cartoning but also maintaining sterile room conditions require a humidity controlled, rather dry air. The more humid

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*/ Especially for bulk drug production.

the outside air, the more extensive and hence costlier the air conditioning.

189. Dusty air on the other hand causes damage to bearings of moving parts and to speed reduction gears, mostly used for stirrers in mixing and reaction kettles. Since chemical plants for economic reasons cannot be air conditioned dust has a direct influence on the life of equipment.

190. For formulation and packaging air dedusting is possible and practiced but increases the operational costs.

(4.6) Environmental conditions

191. The environmental influences are of long term nature and may be, e.g. waste treatment concerned, costly. Solvent recovery of exhaust ventilation air is still in the experimental stage. In some instances it is advisable to postpone the erection of waste treatment plants and also investment involved, provided the own workers and the inhabitants of the factory surrounding dwellings are adequately protected. But the planning team must fully implicate the later waste treatment facilities into the present plant concept.

(4.6.1) Other aspects: Visual aspects

192. An architect may be helpful in designing the façades and thus positively influencing the character of a location.

(4.6.2) Psychological effect

193. To the chapter of environmental conditions belong also the windows in the façades. Windows may be inadequate for ventilation, lighting of rooms and undesirable from the view point of heat transmission, which adversely affects the air conditioning. But if one was ever obliged to work for a longer period together with a larger group in a completely closed room one appreciates a low window band, to know whether the sun shines or rain is pouring from heaven. Such a measure properly introduced will contribute to the image of an enterprise. This is a positive influence of a location!

(4.6.3) Multiplicator effect

194. The proper delegation of work and duties to the adjacent community will have a multiplicator effect. It is a long term criterion for the choice of a location.

(4.6.4) Morale at work

195. The working conditions will be influenced by the worker's discipline and organization in unions. Unions properly managed can be a valuable spokesman for the workers and an appropriate partner for settling grievances. All this may have an effect on the selection of a site.

(4.6.5) Banking and payment morale

196. At this point it should be mentioned that the reliability of banks and other financial partners must also be investigated.

(4.7) Tax exemption and/or subsidies

197. Negotiations with the local authorities responsible for a site in consideration must reveal the option of financial or legal advantages granted to a prospective purchaser.

198. (4.7.1) The exemption from taxes are often granted for a limited period which should help to overcome the financial start-up burden. The exemption should last at least for 5 years.

199. Another type of exemption is a free trade area. A licensee who anticipates export trade will consider this possibility depending on the amount of sale abroad.

200. (4.7.2) Public subsidies range from a loan, leasing of land and plant facilities (industrial estate), land grant to non-refundable contributions like joint financing of buildings.

(4.8) Personnel recruitment

201. A considerable reduction of personnel problems results from an abundant availability of personnel, mostly workers, out of the site surrounding communities. Another possibility is the hiring of personnel throughout the country, which is willing to move and stay in the disputed location. Here the family problem arises. It can be solved either by housing facilities which are grouped according to the status of the people or by transport free of charge to their families over the week-end or by the allowance of a company car.

202. A special problem poses the managerial staff. It is practically impossible to predict the observance of a contract with a person in managerial or other higher charged position. Apparently one underestimates the desire of an educated person or of his family not to stay permanently outside his/their own social and cultural environment. One solution is a limited contract for 4 to 5 years and the timely training of a successor.

(5.) Engineering

203. The scope of engineering could be characterized as follows:

204. (5.1) Civil engineering takes care of all activities related to the site and buildings. Special groups deal with the different activities involved.

205. . Boundary and topographical survey with maps.

. Soil test boring with the determination of the different ground water levels normally not deeper than 100 m. In the initial stage one to three borings are sufficient. After the location of the building(s) is determined, another series of soil tests along the foundations is required to calculate and design their definitive size.

. The master- and zone-plan of a site is, as a rule, the duty of the own project team because it should reflect the long term company policy. But with proper instructions from the licensor and licensee an architect or consultant may also perform the job.

. The building project involves again the project team which prepares the terms of reference for the activities within the building, the layout of equipment, machine lists, energy supply and sewer disposal, exhaust ventilation, minimum room heights, etc.

With this information the architect forms together with the civil engineer the shell to suit the purpose. Boundary conditions are: safety, extension possibilities, main wind direction, sun radiation affecting the direction of the building façades in a different way within and outside the intertropicals.

An important point and greatly influencing the feasibility of a plant is the type and structure of a building. In countries with scarce steel supply it is unwise to insist on a steel beam construction if the local custom and skill suggests the use of reinforced concrete columns and beams.

. Site and building model, especially for bulk drug production.

206. (5.2) Mechanical engineering incorporates all the study, preparation, installation, and/or implementation of:

207.
- machines and equipment (kettles, filters, filling machines, etc.)
- energy transformation from public sources, generation and distribution (transformer, boiler plant, etc. with cable trays, piping, insulation, isometric drawings, material requirement, etc.)
- HVAC (heating, ventilation, airconditioning)
- compressed air (oil free and dry for instruments, oil free, dry and sterile for formulation, etc.)
- chilled water and brine
- low current installation
- all technical components in connection with mechanisation and automatisation
- design and implementation relative to adaptation of machines and equipment or creation of new facilities
- utilities
- preventive maintenance
- safety
- in co-operation with chemical/process engineering: R + D (research and development)
- for bulk drug and intermediates production: plant mock-up with columns and beams, openings, equipment, cable trays, (coloured) pipes and ducts, elevators, staircase(s), etc.
- for formulation and packaging: layout with energy connections and connection points to spot ventilation.

208. (5.3) Chemical and process engineering is in general the essential part in the transfer of technology for bulk drugs and intermediates. It requires a profound knowledge of the manufacturing processes involved, for proper assessment, for proposals to switch to indigenous substitute material, for decision whether a whole process should be adopted or only a limited number of steps beginning with intermediates.

209. Components of this engineering are:

- process flow sheets with main equipment, sequence, weight and characteristics of raw materials and auxiliaries to be used
- written process procedures with chemical formula schemes, complementing the flow sheets/schematic diagrams
- material balance sheets and equipment utilization
- determination of batch sizes
- sequence of production of different bulk drugs or intermediates, campaigns
- thermodynamic considerations in relation to exothermic reactions, study of crystallization, etc.
- evaluation of hazards
- R + D in co-operation with mechanical engineering
- laboratory tests and scaling up e.g. in pilot plants
- evaluation and determination of machines and equipment
- calculation of process costs

210. For the manufacture of finished pharmaceutical products, formulation procedures, packaging material standards with quality control regulations, and validity data for dosage forms are required. Also a machine and equipment list.

211. (5.4) Industrial engineering is a relative new discipline and deals with operational problems, logistics, optimization of processes, lot sizes, storage of material, etc. Production planning is an important link in the chain of operational activities.

212. The co-ordination of all engineering activities lies again within the responsibility of the project team.

(6.) Equipment and machinery

(6.1) Equipment and machine requirement

213. Once the equipment and machine list for the bulk drug/intermediate production, for formulation and packaging is established, type, complexity and degree of mechanization/automatization are known. A number of

items will have to be imported (e.g. high pressure-high temperature glass lined reaction kettles, rubber lined kettles, columns, vial cleaning-sterilizing-filling monobloc units, gas chromatograph, etc.).

(6.2) Local availability

214. But depending on the development in the licensee's country there could be very well available a number of less demanding items which still suit the production process for bulk drugs/intermediates or the manufacturing requirements of formulation and packaging.

(6.3) Suitability of local items

215. To find out the suitability for the anticipated processes/formulation/packaging the particular equipment/machinery must be investigated, tested and/or inspected in operation in established plants. It is not recommended to start with prototypes!

(6.4) Equipment to be imported

216. All equipment which cannot be acquired otherwise than from abroad must be listed. An application with the necessary data and arguments for requirement must be submitted to the authorities for an import license and clearing of foreign exchange. It is advisable to contact the authorities to find out whether the chance of approval exists.

(6.5) Guarantee of service and maintenance

217. A machine is as good as its performance. To maintain this, a regular service must be guaranteed.

218. It consists of maintenance which should gradually turn to well planned, well organized preventive maintenance.

219. To secure this, spare parts must be available with a local representative or supplier. If this is not the case, spare parts must

be bought together with the machines and stored. As a rule, spare parts for two years of operation should be adequate. For imported spares an import license, etc. must be applied for.

220. A special service consists in delegating control and maintenance of equipment to third parties or to the supplier of this equipment (service of air conditioning units, cooling compressors, computers, etc.).

(7.) Identification of local education and training

(7.1) Education and training of personnel

221. The better a country is infiltrated with educational and training centers for all levels of industrial activities the better the receptivity to transfer of technology.

222. In rural areas and provincial towns elementary and high-schools are expected. Vocational schools for industrial and business training are desirable. But an absolute necessary educational element for mechanics, skilled and unskilled workers are workshop facilities. If these are not existent, then an own center should be established and incorporated in the scope of technology transfer.

223. Education on academical level is desirable at least in one place of the licensee's country. For mutual fructification a close co-operation between teachers and students and the industry is very stimulating. It can be cultivated by invitations to the plant and by posing of problems to the university. An early contact with the university and academic circles of the country will soon reveal the capability as to how much technology may be absorbed by indigenous brain and skill.

(7.2) Scientific research

224. One of the secrets of prosperous development is adaptation, progress and innovation by scientific research, again on all levels of life. The presence of a research center is by no means a necessity for successful production of pharmaceuticals but it helps in the long run to strengthen the developing country's and hence the licensee's position. What should be existent however, is a development laboratory, capable of handling bulk drug and formulation adaptation problems.

(7.3) Investigation for necessity of a pilot plant

(7.3.1) Adaptation of process(es) and/or know-how

225. Before making final decisions about switching to indigenous alternative raw materials, tests on a small sale basis in a pilot plant could be very useful. Here, the possibility, scope and implications of an adaptation can be assessed and new manufacturing procedures worked out.

226. Similarly the know-how of the own crew may be tested and the need for temporary expatriate assistance or the delegation of own staff abroad for acquiring know-how be evaluated.

(7.3.2) Training of personnel and collection of experience

227. By the same token personnel of all grades could be trained at a pilot plant and prepared for future tasks. This way experience will be collected and start up difficulties minimized.

(7.3.3) Small scale production

228. Finall the availability of small quantities of bulk drugs, interm ıates or finished pharmaceutical products is extremely useful for clinical and marketing tests.

229. To make it very clear, a pilot plant would be helpful but is by no means a necessity. The distance and communication facility between a pilot plant and the future plant will play a role for its serviceableness.

(8.) Finance

(8.1) Capital cost involved

230. For the technology transfer, in general, a new plant will be built. But if the technology can be realized in an existing one, initially

considerable less capital will be involved. In this case, adjustments of and additions to equipment and machinery will be necessary. Alterations or extensions of buildings and services may also be necessary.

231. A feasibility study reveals the advantage and disadvantage using existent facilities. Used up machines will have to be gradually replaced, the operational costs are slightly higher due to more repairs and higher maintenance. Finally a rent will be involved by using an existing plant.

232. Additional factors for a choice in favour of a working factory are: less capital risk involved, use of ready available infrastructure and organization, know-how of operating a plant, postponement of investments, etc.

233. In case of loan production/manufacture no capital is involved at all.

(8.2) Operating costs

234. These costs are divided into two groups:

(8.2.1) - Preoperational costs

235. Raw material, intermediates, bulk drugs, auxiliaries, utility material, laundry, etc. must be ordered partially long before the start of operation. Downpayments may be required.

236. Some assistance in terms of expatriates most probably will be needed at the initial stage for organizing the staff and labour force.

237. A certain amount of personnel including expatriates will be hired for organizing the operations, training of clerks and workers, performing quality control of materials, guard, including living allowances and transport for everybody who lives outside his home.

238. Preoperational expenses like telephone, telex, heating or air conditioning, electric power; insurances for building and inventory; services in favour of speedy execution of pending applications, customs control and settlement, or completion of work.

239. The project costs are also preoperational costs.

(8.2.2) - Operational costs

240. These costs are at first calculated and used as such for the feasibility study. After the beginning of operation the theoretical value will gradually be adapted to reality.

(8.3) Local financing

241. For the financial requirements of the licensee local sources are at disposal.

(8.3.1) - Banks

242. Banks are usually willing to lend money on the basis of warranties, guarantee bonds or securities like company-, conditional- or credit-guarantee or by government declaration.

(8.3.2) - Private investors

243. They are in most cases shareholders of the licensee's enterprise. Their guarantee are the fixed assets, the reputation and potency of the licensee and the outlook of successful enterprise.

(8.3.3) - Government subsidies

244. These are limited or unlimited tax exemptions, interest free loans, other government grants like free land and/or buildings, etc.

(8.4) Foreign financing

245. Foreign financing occurs when the licensee purchases items abroad (equipment, machines, raw material, etc.) or he delegates personnel to foreign countries for training, conferences with the licensor or for purchasing. The licensor is involved if he possesses equity ownership in the enterprise of the technology transfer. The World Bank (International Bank of Reconstruction and Development) or similar institutions may be dealing with this project.

(8.4.1) Banks

246. Banks are either directly involved in the enterprise or via the industry. Both, banks and industry, may obtain a governmental risk guarantee.

247. The World Bank or similar institutions could participate in the enterprise by joint financing or by the engagement of a guarantee.

(8.4.2) Licensor

248. The licensor who in some cases may be backed by financial institutions has the choice to invest in local enterprise either by direct equity participation or by providing part or whole of the capital equipment required for the project.

249. In practice a combination of several financing modes will be applied.

(8.5) Consideration of rate of inflation

250. Countries with high inflation are faced with problems of budgeting, availability of necessary funds and control. Several methods are used to keep surveillance.

251. One such method is to prepare budgets on the basis of some relatively stable currency.

252. Depending on the origin of capital (from licensor, licensee or public agencies or international organizations like World Bank) the purchase of items and material should be made in full knowledge of financial implications and possibilities.

(8.6) Analysis of loans and aids

253. Short, middle and long term loans may be possible to obtain. The terms are accommodated to the circumstances of the client. Short term loans, e.g. for purchasing of operational matters, middle-term loans perhaps for machines and equipment of formulation and packaging facilities and long-term loans for bulk drug and intermediate production plants. Decisive are the pay back conditions and possibilities.

254. International aid may be grouped into two categories:

255. . Bilateral aid, be it a loan or grant, is wound up between two countries or organizations. The advantage is simplicity and the possibility of survey. As disadvantage may count a certain influence on internal affairs of the receiving country or enterprise. In case of earmarked capital often the purchase in the donor country is tied in.

. Multilateral aid is neutral in many respects, supported by several countries but may be cumbersome and slow.

256. It will be left to the contracting parties if and which aid they choose as financial resource.

(8.7) Return on investment (equity and long-term loans)

257. The calculatory part of the feasibility study is based on Return on Investment (ROI) and can be characterized as follows:

- Internal Rate of Return (IRR)
- Pay back time
- Capital value.

258. The task lies not so much in the calculation of the feasibility study but in the assessment and evaluation of basic data for the input. Considering the investment, operational costs together with the anti-

cipated overhead and taking fluctuating world market prices of raw materials and finished goods into account, one is in a position to receive a numerical economic appraisal for a bulk drug and intermediates production or for a formulation and packaging venture.

(9.) Risks

259. From the view point of the licensor certain risks may be considered in connection with the transfer of technology.

260. . Change in government policy with regard to patent life and grant, limitation of dividend and remuneration transfer, abusive use of transferred technology after the expiration of contract with the licensee.

. Inferior or changing product quality because of inadequate management, operation and quality control, or change to in quality varying or not properly adapted, substitute material.

. Difficulty with packaging material, in particular for pharmaceutical packaging (quality of thermoplastic foils, tolerances of tubes, bottles, etc.).

. Political aspects.

261. From the view point of the licensee risks do also exist.

262. . Insufficient information from the licensor with regard to know-how. It is a fact that not all experience can be put in writing. The attempt should be made to transmit it by other means such as technical assistance.

. A final product may be too expensive in the beginning. But by stepwise back-integration up to the whole process, expensive intermediates from abroad will be replaced through indigenous components, hopefully reducing costs.

. Sales prices are based on today's actual technology in use. Would a more economic one be adopted by industry, major price reductions would be inevitable.

. Insufficient gain of experience by own staff or labour troubles.

. Political aspects.

III. USE AND DEVELOPMENT OF LOCAL RESOURCES

(1.) Availability of local materials as import substitution

263. (1.1) Survey of locally available suitable materials for:

264. - raw materials
- auxiliary materials
- intermediates
- packaging material
- utility material

265. The search for substitutions will be facilitated by contacting government authorities like the Commerce Department and Ministry of Mines, or public agencies like Chamber of Commerce, or private sources like Society of Architects and Engineers, banks, or the industry itself.

266. In the case of raw materials petrochemicals may be replaced by natural gas or coal, or even produced by liquefaction of coal.

267. Edible oils and fats, may be substituted by castor (India). Synthetic Witepsol can be changed to vegetabie cocoa butter, provided that a slight variation of melting point, of some components and difference in colour is not affecting the efficacy and strength of the medicament.

268. An intermediate could be replaced perhaps by another one if more back integrated steps in a process are foreseen.

269. In tropical regions imported ACLAR or TRISTAR foil together with aluminium foil must be used if hygroscopic products like all coated tablets and capsules but also some tablets are sold in blister packs. Should indigenous glass bottles be available on the market these are a true alternativ provided screw caps and inserts (liners) are water vapour proof.

270. (1.2) For above listed categories the following criteria are relevant:

(1.2.1) Price situation

271. The price will be dependent on quantity purchased, continuity of take over, competition - local and from abroad.

272. It will lie within the judgement of the licensee to accept even higher prices, provided foreign exchange is saved.

(1.2.2) Suitability

273. A substitute is acceptable if a continuous ability to supply is guaranteed, the quality conforms to defined standards, there is chance of homogenity and it is applicable without major change of the production or formulation process. In case of major manufacturing changes exhaustive tests must precede a final decision.

(1.2.3) Adaptation of process/formulation

274. For the adaptation of chemical processes pilot plant tests or even research and development work will be necessary.

275. If bulk drugs, sugar or starch are not available in the required form, cleanliness or concentration, a mechanical treatment by comminuting, sieving and milling in a ball mill is the solution. If the bulk density of an active ingredient changes within a relatively wide range, but still within quality specifications, and the pre-selected capsule size should be kept, only the use of a special hard gelatine capsule filling machine can cope with this problem.

276. If a high speed cartoning machine cannot consume indigenous cartons of inferior quality and large varying tolerances, an effective measure is switching to hand cartoning; in developing countries often cheaper and foreign exchange and investment saving.

277. If a heat resistant, long life "heavy duty" greasing material is locally not sold, in many instances an inferior, indigenous substitute is adequate with the provision that a more frequent changing is observed.

(2.) Availability of alternative technologies

278. Alternative technologies for one and the same bulk drug or intermediate may exist.

279. - Extraction of medicinal plants often were the forerunner of chemical synthesis. This previous technology, improved, could be a true alternative in countries where the respective medicinal plant is domicilated.

- Synthetically produced 6-amino penicillanic acid (6-APA) from Potassium Penicillin-G as against by an enzymic process is another example of an alternative process step.

280. For formulation similar examples exist:

281. - glass sterilization by steam/hot air/electric or gamma-radiation
- mixing by revolving stirrer/oscillating vibrator/ultrasonic waves
- tablet mass manufacture by wet granulation/compacting
- drying by air/vacuum/infra-red radiation
- limited replacement of freeze drying by spray granulation.

(3.) Training of personnel

282. Personnel of the various categories must first be hired either through personal contact or by advertisment in news papers, trade magazines, on wall boards, through work promotion agencies, official and public sources like schools, universities, government offices, banks and even by follow-up with the already established industry.

283. Besides personal data and character, the status on particular knowledge and/or skill of a prospective person is of interest. The higher the position the more capabilities are expected. If those need improvement a certain training must be programmed according to the position the aspirant will hold in the future enterprise.

284. In principle the training should take place in the licensee's (technology recipient's) country. A trip abroad is often more justified after a gain of experience on the job.

285. Foreign training - in the beginning - will be restricted to few executives and persons, like general manager, head of production and finance (if necessary), the person in charge of quality control and the plant engineer. To support the local trainers and transmit systematic know-how a temporary presence of an expatriate for as long as the start of production might prove helpful. He should be eligible to convey knowledge but should have also ability of appreciative perception. His accommodation, medical care, salary, living expenses and the reimbursement of the licensor/technology supplier should be arranged in the agreement.

(3.1) Managers

286. They need all qualifications required to administer their sector. They should be also familiar with the jobs of their personnel. Besides this a manager's personality is characterized by character and persistency under stress. Parts of his capabilities are learnable others must be developed by carrying out day-to-day tasks and problems under varying conditions. The ability to plan (not making plans), to forecast developments in plant operations and the enterprise as a whole, is almost a gift. An executive need not necessarily be trained in the own enterprise, except the production manager who must fully absorb the technology and process know-how, preferably in the relevant licensor's plant.

(3.2) Foremen and other supervisory staff

287. They must have some managerial qualifications and a good portion of skill and a sense for improvising. They need intensive training in their particular duties to be well prepared for their forthcoming functions. Their training will take place in colleges, workshops, national productivity and other training centers. Part of this time should be spent in supervisory position.

(3.3) Chemists, pharmacists and operators

288. They need not a special training in advance but should bring certain qualifications. Their training will be on the job under the versed guidance of their supervisors.

(3.4) Maintenance staff including instrument and computer specialists

289. They should - under ideal conditions - not need a training any more. When joining the company one expects already specialists - experienced and wise individuals, left on their own in case of emergency, and reliable in servicing machines, equipment and computers. If training is required for those jobs, then well in advance until they can show convincing evidence of expertise. A wrong manipulation on a critical item may stop the whole plant. In the workshop some expert mechanics can train others. The better the maintenance the smoother and more economical the plant operation.

(3.5) Plant engineer

290. He must show already several years of practical experience in industrial plant operation, be it as plant engineer or head of a maintenance/workshop group, not necessarily in a chemical or pharmaceutical plant. His educational grade may be mechanical engineer or technician. For highly sophisticated processes with inclusion of automatization a study abroad might be helpful for the absorption of the technology.

291. Depending on the duration of his already performed service and the degree of process specialisation he will stay in the licensor's plant where the technology to be transferred is carried out. Probably he will stay in this plant for a while together with the production manager (who might be in smaller enterprises also the plant manager). His training is left to some extent to his own judgement. He must absorb as much of the technical and process know-how as he feels sure to service and maintain his plant in the developing country under the there prevailing technical-environmental conditions.

(3.6) Training periods

292. These should be kept flexible. One picks up fast, another slow. Executives should be capable to fill their post immediately. Depending on the previous occupation their training can be confined to the acquisition of the specific knowledge and problems of the department/section he will hold. This normally takes weeks or months.

293. Supervisory staff will take weeks to months, up to half a year or more.

294. Operators need weeks, if at all.

295. The core of the maintenance staff should have already completed their training before recruited. Junior mechanics will learn on the job.

(3.7) Employment of expatriates

296. Besides an expatriate for training and technology transfer other experts from abroad may be necessary in the end phase of equipment assembly and mechanical commissioning, (automated processes, air conditioning, freeze drying, etc.). Properly timed with the recruitment of personnel,they too,may have a share in training. Work permits for them must be obtained in advance.

(3.8) Build-up of cadre

297. Later, when the plant is in operation by selection, rotation of personnel and fresh-up courses a sound cadre of prospective aspirants for more demanding jobs can be built up. This cadre must radiate pride and motivation in favour of the company which is catching.

298. Personnel training and development in profession and trade is one of the big challanges of the developing countries and should be equally shared by schools, universities, workshops, government legislature, industry and temporary expatriate expertise.

IV. SELECTION OF TECHNOLOGY

(1.) Search and assessment of available technology

299. Given that the type and marketing prospects of the pharmaceutical(s) to be produced are established */, the would-be technology recipient may approach a potential technology supplier by "pre-qualification" of known candidates or through several channels:

300. - personal contact to industry
- selective advertising in pertinent foreign news papers and chemical-, pharmaceutical-, trade-magazines, in which a column for offering and requesting of technology transfer exists.
- official and semi-official agencies like universities, development laboratories, chamber of commerce, trade section of embassies, export division of the trade department, trade department of big commercial banks.
- private contact to consultants, contractors, financial institutions, etc.
- international organizations like the United Nations Industrial Development Organization (UNIDO), WHO, World Bank, etc.

(1.1) Production of bulk drugs and intermediates

301. For basic production the main aspects of the technology transfer agreement are:

302. - complex and know-how intensive chemical process steps;
- the patent situation, license(s);
- compensations (lump sum payments), dividends (if at all), fees, royalties;
- engineering, technical assistance; management services.

A further variation is the possibility of buy-back arrangements under which the licensor offers to buy back some part of the licensee's bulk or intermediates output.

303. The choice of the technology will be rather limited. But if it exists, it should be - from the view point of the technology searching party - explored. Characteristic points of importance may evolve, such us:

304. - local familiarity of technology transferor
- more cost-effective and efficient currently available technology, given the local circumstances
- quantity of materials used
- more suitable for the adaptation to indigenous substitute material or incorporation into an existing plant

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*/ See Table I

- economies of scale, especially for bulk drugs and intermediates
- possibility of export restrictions.
- easier process know-how, less complex process steps
- easier split up into steps and later back integration to the whole process
- less foreign exchange involved, less remunerations e.g. patent rights
- less legal implications for technology transferee
- potency of technology supplier and chance for additional amplification of business with him.

(1.2) Manufacturing

305. For formulation and packaging the technology transfer agreement will mainly deal with pharmaceutical manufacturing prescriptions and packaging standards, good manufacturing practices (GMP); patent situation, trade marks and names; licenses; remunerations in all aspects; marketing procedures and exporting conditions; engineering, including sterility keeping in manufacturing, preventive maintenance; training of personnel, in particular analytical and microbiological quality control and back-checking in the laboratories of the technology supplier; rights of related enterprises; management services. (See also the pertinent UNIDO documents.)

306. The choice of technology will be considerable larger than for basic production. Yet, for instance the experience with sterile production, proper disintegration of solid dosage forms, water vapour proof blister packs, validity recording must not be underestimated.

(1.3) General

In addition, relevant aspects for proper assessment would be:

307. - local familiarity or indigenous trade of technology transferor
- potency of technology supplier, suitable for other business
- degree of mechanization, automatization and work intensity in formulation and packaging
- financial advantages like favourable capital goods transfer in form of machines and material
- interest of technology supplier to export from technology recipient's country into certain markets
- favourable patent and trade name conditions
- historical connections to a technology supplier's country (language, experience with settling formalities, etc.)
- commercial treaties between the countries of technology transfer
- (legal) limitations to the technology supplier.

(2.) Suitability and critical analysis

308. There are many aspects to a technology transfer agreement which are intangible and cannot be quantified by figures. Others are, however, e.g.

(2.1) Cost of technology

309. One key aspect is taking into account whether the licensee's country is labour intensive or materials and machines are available. Other factors may be grouped according to the period of expenditure.

310. The timely limited expenditures up to the implementation of the technology transfer (normally completion of the plant) effectuated in one payment or installments, which comprise

311. - the search for the proper technology
- administrative and legal fees to acquire and settle the contract or agreement
- training of personnel by local institutions, expatriates or by delegation abroad
- project costs as a whole (project team, planning, implementation including purchase of machines and equipment, experts to check, mechanical commissioning and run-in systems, machines and equipment, etc.)
- payments to technology supplier, consultant(s) or contractor(s) in a lump sum or other modality
- single charges
- administrative fee(s) for official acceptance of the plant and work permission.

312. Expenditures due after the start-up date of the plant or enterprise throughout the whole validity of the arrangement or parts thereof, e.g. termination of contractual patent rights, use of trade marks and names, licenses, etc. comprise

313. - dividends, if foreign equity participation is involved

- royalties as a function of business turn-over, fees as a function of non turn-over dependent criteria (patents, trade marks and names, licenses, etc.)

- service charges in connection with maintenance assistance, research and development, information about new technology knowledge, marketing and management services, etc.

(2.2) Cost of raw material and its availability

314. Raw materials, intermediates, etc. required for the production of further developed intermediates or bulk drugs, or bulk drugs in itself, may be purchased from different sources under varying conditions, provided the quality corresponds to defined standards.

315. If sufficient material is offered by timely comparable quotations and conditions a choice of one or better two potential suppliers can be made on which the selection of a technology may be based. The criteria are:

316. - cost comparison including import duty, other costs
- assurance of long term firm bids
- assurance of continous delivery
- possibility to overlook exchange rate developments
- homogenity and uniform quality standards of material

(2.3) Cost of energy

317. Energy sometimes plays a major role in the selection of a technology considering that one production or manufacturing system alone may consume as much as up to 100 kW, e.g. cleaning, drying, sterilizing and filling of ampoules or vials under sterile room conditions. In addition and independent of the technology selection measures should be taken to make a plant free of one energy source and its costs.

318. Factors to be considered are:

319. - steam-/hot-/warm-water plants operated by e.g. indigenous coal instead with imported gas or oil
- public electric power supply against own generation
- installation of an emergency power generation despite public supply because of danger of frequent interruptions - for selected dangerous or critical processes or for the whole plant
- reliability of energy supply, reserves of resources and installation of fuel tanks to guarantee a certain autarchy
- installation of multi purpose burners for the use of alternative fuels
- in rare cases the possibility of connection to two independent cross country power-cables and/or -lines fed by different public power substations.

(2.4) Cost of equipment

320. Equipment in the broadest sense is the basic instrument for the execution of biological, chemical, enzymic or all other processes yielding bulk drugs, intermediates or firnished pharmaceutical formulations. A technology purchaser should be fully aware of the possible risks he is exposed under circumstances, if he intends to change from technology supplier's specified equipment, and systems to foreign or indigenous alternatives, e.g. failure in offered constructions and performance; use of replacement material, adversely affecting the products or formulations; inadequate strength of construction parts; inadequate temperature limits; no or inadequate safety measures; level of noise; etc. Yet, he should carefully investigate the local market and make use of indegenous equipment wherever admissible.

321. On the other hand it could be very advantageous and instructive and should be tried out under all circumstances, to investigate alternative equipment with the following assessments:

322. - cheaper alternatives from local or foreign sources
- more favourable terms of payment
- easier handling, less know-how intensive, degree of automatization
- better service
- philosophy of developing the indigenous industry
- necessity to use indigenous equipment due to government restrictions
- use of same equipment which is already installed in local comparable or competitive industries.

323. If one deviates from the technology supplier's list of equipment to enhance the use of local resources, it is essential for both parties to make a common decision on alternatives and assure success by proper tests at the equipment supplier's plant or workshop, or in a factory already in operation.

(2.5) Cost of operation

324. The cost of operation for a given technology depends on several factors which influence effectively the selection of a technology transfer:

325. - volume of process-/formulation-steps
- yield of process(es) or formulation
- packaging efficiency
- industrial capacity utilization
- condition of equipment to be used
- to some extent the physical quality of process material to be used

- number of operators and administrative staff involved
- energy costs
- degree of mechanization or automatization
- consideration of immediate waste treatment or partial postponement to a later date
- consideration of overhead distribution
- consideration of additional charges and profit
- policy on goods in stock
- taxation and subsidies
- degree of quality control in cooperation with the technology supplier or solely on own premises
- to some degree working moral

(2.6) Environmental consequences

326. Increasing pollution of air, water and ground and resulting legal measures by governments and guide-lines by international organizations demand industry to include this subject into their scope of technology. Waste treatment means additional cost and hence is an influencing factor of technology selection. The following treatment possibilities exist:

327. - recuperation of gaseous or liquid solvents can be achieved by different methods

- other liquid waste should be grouped into different effluent systems right at the point of origin for proper treatment

- solid waste components suitable for recycling e.g. paper or material to be used in the building industry, etc., should be properly separated

- solid waste components unsuitable for recycling must either be burnt or, if air pollution occurs, be properly packed and transported to a suitable deposit.

328. Certain treatment procedures are rather costly and in some cases still in development. If legally acceptable and desirable for the enterprise one should incorporate into the first technology transfer only those waste treatment facilities which are simple and appropriate in cost. All other prospective environmental measures must be properly planned, (pipe) connections, place for treatment and disposal provided and the costs involved assessed. When the start-up of the plant is over and production/formulation has reached a degree of maturity, then the time has come to start with a second phase of technology transfer.

(3.) Examples

329. Two examples should highlight some aspects of costs involved in a technology transfer (see Appendix II.).

(3.1) Break-even analysis

330. This evaluation should be performed when negotiating a bulk drug production, beginning from raw materials or intermediates.

(3.2) Build versus rent

331. This investigation would be applicable, for instance, when negotiating the set-up of a simple bulk drug/intermediate production or manufacturing facilities for medicaments.

V. APPENDICES

APPENDIX I

Pre-Feasibility Study[12/]

The project idea paraphrased verbally or normally in writing a document, must be elaborated in a more detailed study. However, formulation of a techno-economic feasibility study that enables a definite decision to be made on the project is a costly and time-consuming task. Therefore, before assigning funds for such a study, a preliminary assessment of the project idea must be made in a pre-feasibility study, the principal objectives of which are to determine whether:

(a) The investment opportunity is so promising that an investment decision can be taken on the basis of the information elaborated at the pre-feasibility stage;

(b) The project concept justifies a detailed analysis by a feasibility study;

(c) Any aspects of the project are critical to its feasibility and necessitate in-depth investigation through functional or support studies such as market surveys, laboratory tests, pilot plant tests;

(d) The information is adequate to decide that the project idea is not either a viable proposition or attractive enough for a particular investor or investor group.

A pre-feasibility study should be viewed as an intermediate stage between a project opportunity study and a detailed feasibility study, the difference being primarily the detail of the information obtained. Accordingly, it is necessary even at the pre-feasibility stage to examine, perhaps broadly, the economic alternatives of:

(a) Market and plant capacity: demand and market study, sales and marketing, production programme, and plant capacity;

(b) Material inputs;

(c) Location and site;

(d) Project engineering: technologies and equipment, and civil engineering works;

(e) Overheads: factory, administrative and sales;

(f) Manpower: labour and staff;

(g) Project implementation;

(h) Financial analysis: investment costs, project financing, production costs, and commercial profitability.

The structure of a pre-feasibility study should be the same as that of a detailed feasibility study.

When a detailed project opportunity study is conducted in respect of an investment possibility, the pre-feasibility stage of the project is often dispensable. The pre-feasibility stage is also occasionally by-passed when a sector or resource opportunity study contains sufficient project data to either proceed to the feasibility stage or determine its discontinuance. A pre-feasibility study is, however, conducted if the economics of the project are doubtful unless a certain aspect of the study has been investigated in depth by a detailed market study, or some other functional study, to determine the viability. Short-cuts may be used to determine minor components of investment outlay and production costs but not to determine major cost components. The latter must be estimated for the project as a part of the pre-feasibility study, but it is not necessary to depend solely on firm quotations.

As a guide may serve the following outline of a pre-feasibility study.

1. Executive summary - a synoptic review of all the essential findings of each chapter.

2. Project background and history:

   (a) Project sponsor(s);
   (b) Project history;
   (c) Cost of studies and/or investigations already performed.

3. Market and plant capacity:

   (a) Demand and market

      (i) The estimated existing size and capacities of the industry (specifying market leaders), its past growth, the estimated future growth (specifying major programmes of development), the local dispersal of industry, its major problems and prospects, general quality of goods;
      (ii) Past imports and their future trends, volume and prices;
      (iii) The role of the industry in the national economy and the national policies, priorities and targets related or assigned to the industry;
      (iv) The approximate present size of demand, its past growth, major determinants and indicators;

   (b) Sales forecast and marketing

      (i) Anticipated competition for the project from existing and potential local and foreign producers and supplies;
      (ii) Localization of market(s);
      (iii) Sales programme;
      (iv) Estimated annual sales revenues from products and by-products (local/foreign);
      (v) Estimated annual costs of sales promotion and marketing;

(c) Production programme (approximate)

(i) Products;
(ii) By-products;
(iii) Wastes (estimated annual cost of waste-disposal);

(d) Determination of plant capacity

(i) Quantitative relationship between sales, plant capacity and material inputs.

4. Material inputs (approximate input requirements, their present and potential supply positions, and a rough estimate of annual costs of local and foreign material inputs):

(a) Raw materials;
(b) Processed industrial materials;
(c) Components;
(d) Auxiliary materials;
(e) Factory supplies;
(f) Utilities, especially power.

5. Location and site (preselection, including, if appropriate, an estimate of the cost of land).

6. Project engineering:

(a) Preliminary determination of scope of project;
(b) Technology(ies) and equipment

(i) Technologies and processes that can be adopted, given in relation to capacity size;
(ii) Rough estimate of costs of local and foreign technology;
(iii) Rough layout of proposed equipment (major components):

a. Production equipment;
b. Auxiliary equipment;
c. Service equipment;
d. Spare parts, wear and tear parts, tools;

(iv) Rough estimate of investment cost of equipment (local/foreign), classified as above;

(c) Civil engineering works

(i) Rough layout of civil engineering works, arrangement of buildings, short description of construction materials to be used:

a. Site preparation and development;
b. Buildings and special civil works;
c. Outdoor works;

(ii) Rough estimate of investment cost of civil engineering works (local/foreign), classified as above.

7. Plant organization and overhead costs:

   (a) Rough organization layout

      (i) Production;
      (ii) Sales;
      (iii) Administration;
      (iv) Management;

   (b) Estimated overhead costs

      (i) Factory;
      (ii) Administrative;
      (iii) Financial.

8. Manpower:

   (a) Estimated manpower requirements, broken down into labour and staff, and into major categories of skills (local/foreign);

   (b) Estimated annual manpower costs, classified as above, including overheads on wages and salaries.

9. Implementation scheduling:

   (a) Proposed rough implementation time schedule;

   (b) Estimated implementation costs given the implementation programme.

10. Financial and economic evaluation:

   (a) Total investment costs

      (i) Rough estimate of working capital requirements;
      (ii) Estimated fixed assets;
      (iii) Total investment costs, obtained by summing the estimated investment cost items;

   (b) Project financing

      (i) Proposed capital structure and proposed financing (local/foreign);
      (ii) Interest;

   (c) Production cost (summary of estimated production costs, classified by fixed and variable costs);

   (d) Financial evaluation based on above estimated values

      (i) Pay-off period;
      (ii) Simple rate of return;
      (iii) Break-even point;
      (iv) Internal rate of return;

(e) National economic evaluation

(i) Preliminary tests:

a. Project exchange rate;
b. Effective protection;

(ii) Approximate cost-benefit analysis using estimated weights and shadow-prices (foreign exchange, labour, capital);

(iii) Economic industrial diversification;

(iv) Estimate of employment-creation effect;

(v) Estimate of foreign exchange savings.

Note: Additional information - in particular with regard to support or functional studies - may be taken from the "Manual for the Preparation of Industrial Feasibility Studies", prepared by UNIDO, itself.

APPENDIX II

Example A

BREAK-EVEN ANALYSIS FOR A PROJECT

Example B

BUILD VERSUS RENT FOR THE IMPLEMENTATION OF A TECHNOLOGY TRANSFER

25.4.83/Mz

EXAMPLE A

Break-even analysis for a project - page 1/2

Bulk drug production as outlined in UNIDO document ID/WG.331/4-26.9.80

The figures are hypothetical.

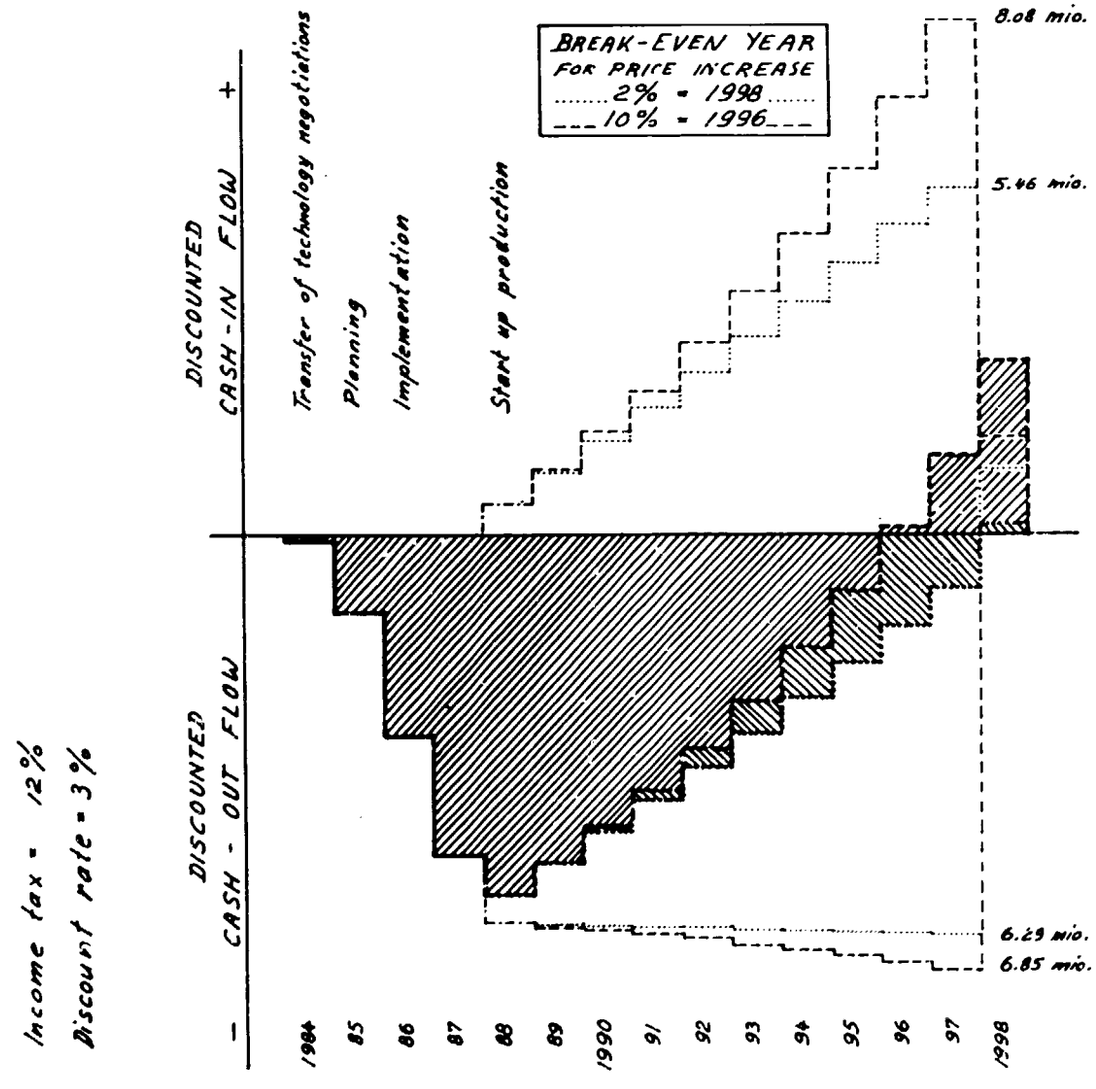
Plant capacity = 1200 metr.tons/year : 1988 = 900 metr.tons, +3%/year, 1998 = 1200 metr.tons

Price increase = alternatively: 2%/year - 10%/year

Price structure:	US$/metr.ton	%
raw material	1210 1)	56
utilities	100 1)	4.7
wages	130 2)	6
maintenance	110 2)	5.1
overhead	45 2)	2.1
depreciation	465 2)	21.5
profit	100 2)	4.6
SALES PRICE	2160	100

	1000 US$
Technology transfer agreement	50
Project planning and control	100
Building (depreciation = 20 years)	1000
Equipment (" 10 ")	4000
Infra structure (" 20 ")	300

Stock: raw mat. = 2, fin. goods = 1 month;
Deptors: 1 month



1) dependent on volume
2) fixed costs

26.4.83/Mz

EXAMPLE A ..

Break-even analysis for a project - page 2/2

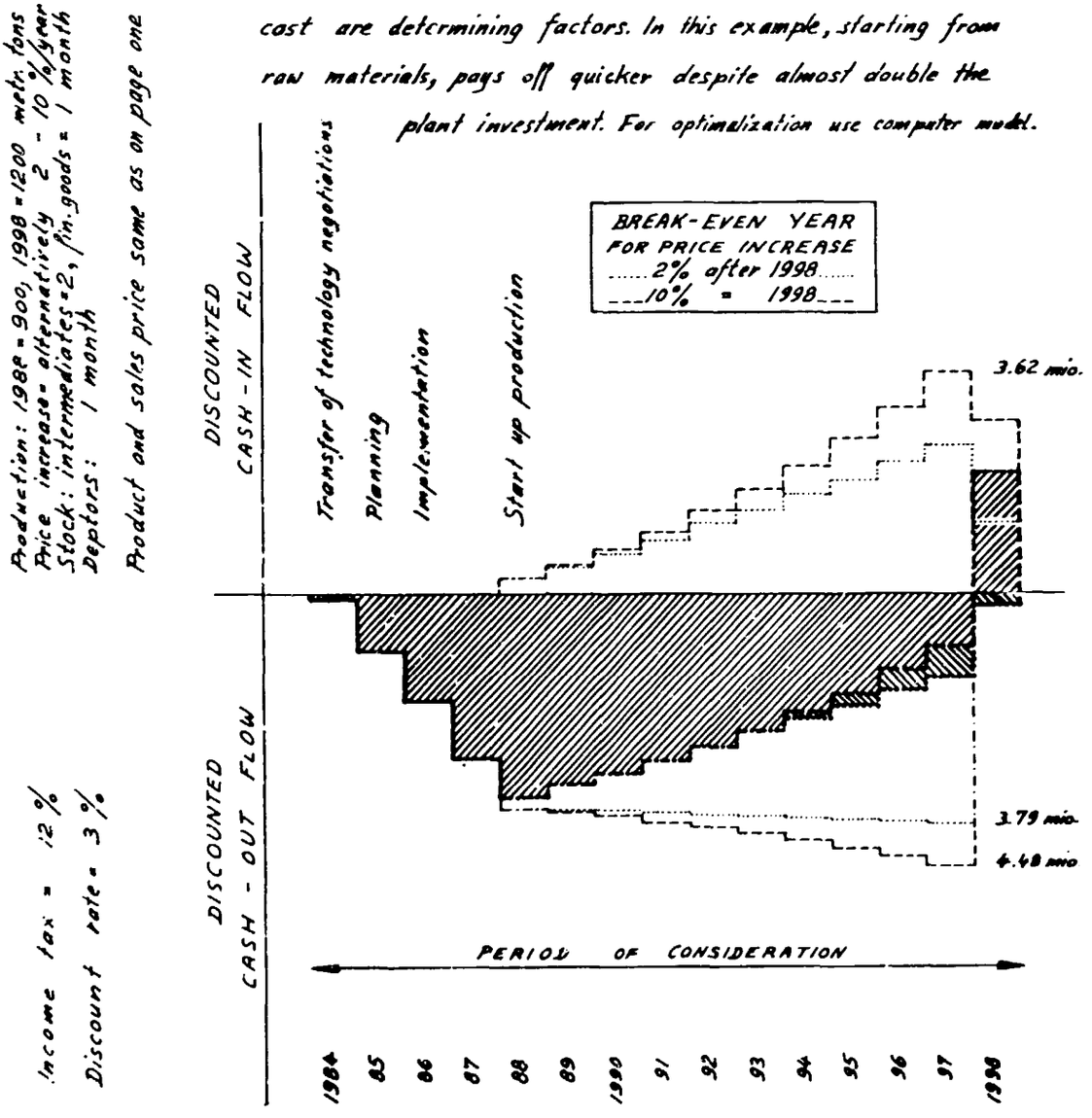
ALTERNATIVE : bulk drug production starting from intermediates.
The figures are hypothetical but related to example on page one.

Price structure:

	US $/metr.ton	%
intermediate	1670 1)	77.3
utilities	55 1)	2.5
wages	70 2)	3.3
maintenance	70 2)	3.2
overhead	45 2)	2.1
depreciation	220 2)	10.2
profit	30 2)	1.40
SALES PRICE	2160	100

		1000 US $
Technology transfer agreement		50
Project planning and control		80
Building	(depreciation = 20 years)	800
Equipment	(" = 10 ")	1650
Infrastructure	(" = 20 ")	300

The results show that raw material and intermediate cost versus plant cost are determining factors. In this example, starting from raw materials, pays off quicker despite almost double the plant investment. For optimalization use computer model.



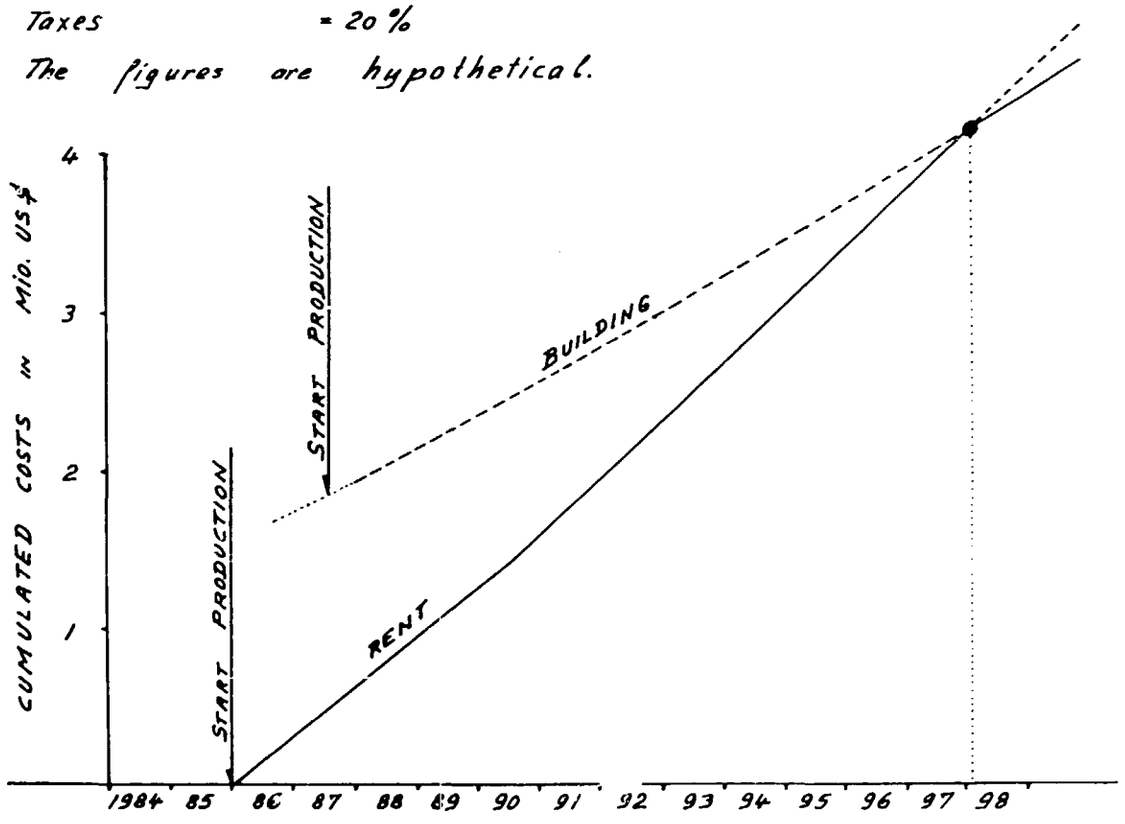
1) dependent on volume
2) fixed costs

EXAMPLE B

Build versus rent for implementation of a technology transfer

The licensee has the choice of building a plant at..... US $ 2.000.000
or to rent an existing building with infrastructure
for the first 5 years at....250.000 and further 5 years at....300.000 US$/year.
The equipment is assumed to be in both cases equal.
Maintenance of the own building costs..... 100.000 US$/year
Maintenance of rented building is first...50.000....then.....60.000 US$/year

Use of building = 40 years
Depreciation = 5 %
Taxes = 20 %
The figures are hypothetical.



The pay back time is 10 years.
IRR = 8% which is considered to be small.
After the 13th year the own building becomes more economical.
Renting an industrial building allows to start production one to two years earlier.

TABLE I

ILLUSTRATIVE LIST OF 26 ESSENTIAL DRUGS
FOR WHICH FACILITIES FOR THE LOCAL MANUFACTURE OF ACTIVE INGREDIENTS
SHOULD BE ESTABLISHED IN DEVELOPING COUNTRIES

These drugs werde identified by UNIDO out of the model list of essential drugs drawn up by the World Health Organisation Expert Committee and approved by WHO 1/

ANALGETICS

1. Acetylsalicylic acid 2/
2. Paracetamol

ANTI-INFECTIVE DRUGS

Anthelmintic drugs

3. Mebendazole
4. Piperazine

Antibacterial drugs

5. Ampicillin 2/
6. Penicillin-benzyl
7. Erythromycin
8. Streptomycin
9. Sulphadimidine 2/
10. Tetracycline 2/

Antifilarial drugs

11. Diethylcarbamazine 2/

Antileprotic drugs

12. Dapsone 2/

Antimalarial drugs

13. Chloroquine phosphate 2/
14. Primaquine

Antituberculosis drugs

15. Ethambutol 2/
16. Isoniazid 2/

CARDIOVASCULAR DRUGS

Antihypertensive drugs

17. Propranolol
18. Hydralazine
19. Reserpine

DIURETICS

20. Furosemide

ANTI-DIABETICS

21. Insulin

ORAL CONTRACEPTIVES

22. Ethinylestradiol/Norgestrel (Levo)

IMMUNOLOGICALS

23. Blood and Blood fractions

VITAMINS

24. Retinol
25. Cyanolobalamine
26. Ascorbic acid

1/ The Selection of Essential Drugs, WHO Technical Report Series 641, 1979.

2/ Essential drugs which UNIDO classified as priority items for establishing facilities for the local production.

TABLE II

Countries which do not recognize product patents for pharmaceuticals. (See also 9/).

Argentina	Iran
Benin	Iraq
Bolivia	Kuwait
Brazil */	Lebanon
Cameroon	Libya
Chad	Morocco
Chile	Mexico */
Colombia	Nigeria
Congo	Paraguay
Ivory Coast	Peru
Korea	Central African Rpublic
Ecuador */	Senegal
Egypt	Syria
Gabon	Thailand
Ghana	Togo
Guyana	Tunisia
Honduras	Upper Volta
India	Uruguay
Indonesia	Venezuela
	Yugoslavia

*/ In these countries process patents are not granted either

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(1) See ECE, Guide on drawing up contracts for large industrial works, ECE/TRADE 117, New York 1973, p.15.

(2) See CTC, "Features and issues in turn-key contracts in developing countries", ST/CTC/28, p.19.

(3) See e.g., Junta del Acuerdo de Cartagena, Método de desagregación tecnológica, J/GT/110, March 1982.

(4) See UNIDO, Manual on the establishment of industrial joint-venture agreements in developing countries, New York, 1971.

(5) For the case of Brazil, see Carlos M. Correa, "Limitaciones al desarrollo y control de mercado en la industria farmacéutica del Brasil", Revista del Derecho Industrial, T. II, 1980, p.604; for Mexico, see "acuerdo que establece el programa de fomento a la industria farmacéutica". Secretaría de Patrimonio y Fomento Industrial, 21 April 1983, article 1.5.

(6) See UNCTAD, Formas de organización de la transferencia de technología a países en desarrollo por empresas pequeñas y medianas: estudio monográfico de empresas mixtas por acciones y de acuerdos sobre technología en América Latina, TD/B/C.6/77, May 1982.

(7) A research conducted by the Development Centre Studies of OECD, regarding the behaviour of subsidiaries of transnational corporations in 12 countries of different degrees of development, has shown, inter alia, that: i) the host country does not benefit from mobility of the subsidiary's technically skilled personnel, since its rotation is very low; ii) subsidiaries do not undertake practically any R + D; iii) the relationship of subsidiaries with the local technical and scientific system is very weak. See OECD. Transfer of technology by multinational enterprises. Paris, 1977, part one.

(8) The terms used in this chapter refer mainly to the "Licensing Guide for developing countries" prepared by the World Intellectual Property Organization (WIPO), Geneva 1977.

(9) See in particular, ID/WG.331/2 and ID/WG.385/2/Rev.1.

(10) One of such banks has been established in Brazil. Another one is operated in Austria by INPADOC.

(11) Documents regarding economy of scale

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- J. Frenkel, "Technología e competícao na indústria farmaceutica brasileira", Finep, 1978, page 103.

(12) Manual for the Preparation of Industrial Feasibility Studies, UN-ID/206

UNIDO

- Background paper for discussion on the relevant issues to be taken into account when negotiating Transfer of Technology Agreements: PC.19-7/10/,81
- Preparation of Guidelines - Summary and main Conclusions: ID/WG.331/1-23/9/'80
- Relevant issues to be taken into account when negotiating Transfer of Technology Agreements: ID/WG.331/2-23/9/'80 and ID/WG.331/2LAdd.1-6/10/'80
- Preparation of Guidelines - Background Paper: ID/WG.331/3-23/9/'80
- The Pricing and Availability of Intermediates and Bulk Drugs: ID/WG.331/4-26/9/'80
- The Availability, Terms and Conditions for the Transfer of Technology for the Manufacture of Essential Drugs: ID/WG.331/5 -2/10/'80
- Global Study of the Pharmaceutical Industry: ID/WG.331/6-22/10/'80 and ID/WG.331/6/Add.1-21/11/'80
- First Consultation on the Pharmaceutical Industry, Lisbon, Portugal: ID/259 (ID/WG.331/10/Rev.1) - 1-5/12/'80
- Arrangements for the Transfer of Technology for the Manufacture of Bulk Drugs and Intermediates: ID/WG.385/1-3/11/'82
- Arrangements for the Transfer of Technology for the Formulation of Pharmaceutical Forms. Contractual conditions and Background notes: ID/WG.385/2-12/11/'82
- Contractual Arrangements for the setting up of a plant for the production of Bulk Drugs or Intermediates: ID/WG.385/3-9/12/'82
- Manual on the establishment of Industrial Joint-Venture Agreements in developing countries: UN-ID/68-1971
- Contract Planning and Organization: UN-ID/117-1974
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- "Items which should be incorporated in contractual arrangements for the transfer of technology for the manufacture of those bulk drugs/intermediates included in UNIDO's illustrative list", ID/WG.393/1

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- "Items which could be incorporated in contractual arrangements for the transfer of technology for the manufacture of those bulk drugs/intermediates included in UNIDO's illustrative list", ID/WG.393/1

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- Draft Elements to be included in the Terms of Reference for a UNIDO Study on the relevant issues to be taken into account when negotiating Transfer of Technology Agreements for the Production of Pharmaceuticals: 14/3/'83

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