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STRENGTHENING THE ROYAL DRUGS RESEARCH LABORATORY

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NEPAL

Technical report: Findings and recommendations*
1988-1989

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

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* This document has not been edited.

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PREFACE

The evaluation report presented to the TPR held on 1st August 1988 covered the project from its inception. It gave a background of the project and its justification, the project profile & its objectives, followed by the results achieved, the strengthening of RDRL and the R & D outputs, the perspective and made some recommendations for the phasing-out phase of the project. Much of what was reported last year still holds and this year's report should be taken in conjunction with last year's Evaluation Report 1984-88. Since last TPR there has been an "Evaluation of the Sub-Sector concerned with Plant Derived Products in Nepal", by Agro-Vision, Holland, and some useful comments and suggestions have been made concerning RDRL. There has also been a reorganisation of the Department of Forestry and Plant Research with RDRL (including Pilot Plant) as one of the four divisions (Appendix - 1); this has in turn been followed by a reorganisation of the staff structure at RDRL with a better delineation of responsibility and authority. The developments have been taken note of in the present evaluation. The uncertain relations with India have added to the problems of the supply of gas, some essential solvents and spare-parts of equipment. This has also posed a challenge for the R & D staff, how to be self-reliant under adverse conditions.

Acknowledgement: I would like to express my deep appreciation and grateful thanks to Dr. S.B. Malla, Director-General and Dr. P.M. Adhikary, Deputy Director-General for the courtesies extended, the time spent and the arrangements made during all my visits to RDRL. Scientific discussions with Drs. S.B. Rajbhandary & S.R. Adhikary have been most useful and I am thankful to them for sharing their thoughts & results so openly. I would also like to thank Mr. A.D. Shrestha & Dr. K.R. Amatya for many helpful discussions. The staff of RDRL has been most co-operative and any information I have asked for has been forthcoming promptly; my sincere thanks to them for making my visits pleasent and profitable.

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A. Background

The primary objective of this project was to increase the R & D capability of Royal Drugs Research Laboratory (RDRL) by providing equipments & instruments and enhancing the scientific and technical expertise of the staff by providing them specialised training in laboratories in more advanced countries and by inviting experts to RDRL. As a result of the inputs provided by UNIDO for the project, there has been considerable strengthening of RDRL on all these counts. This strengthening of RDRL was aimed at increasing its R & D capability to:

1. Promoting industrial production in Nepal by developing technology for products of established economic value based on plants available by spontaneous growth and or by cultivation;

2. Promoting the utilization of Ayurvedic Drugs;

3. Developing drugs to be used in modern medicine from Ayurvedic drugs or plants growing in the wild in Nepal;

4. Strengthening the quality control testing capability.

A number of immediate objectives were identified to be achieved through this R & D strengthening of RDRL, which are enumerated in the Evaluation Report. A technical review of the project from its inception (1984-88) was conducted in 1988. The progress made, as recorded in the Evaluation Report of 1988 (pp 8-11) and as also observed in the report, "Evaluation of the Sub-Sector concerned with Plant Derived Products in Nepal" by Agro-Vision, Holland, except for some reservation about the Pilot Plant, showed that these objectives have been more or less achieved.

Thus as a result of the inputs provided by UNIDO in the project the basic infrastructure and organisational framework has been created in RDRL to achieve the objectives set for the project. The project has the right perspective and the programmes are moving in the right direction. However to achieve the overall developmental objective of this project, the activities of RDRL have to be enmeshed and intertwined with those of other institutions involved in the

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utilization of the outputs. The problem to be now addressed by the project, as very appropriately presented in the revised project documents, is as follows:

Consolidation of the present level of competence of the Royal Drugs Research Laboratory in respect of its national role as a centre for the development of drugs and other natural products of economic value and dove-tail its programmes & activities with those of its sister organisations, the Herb Production and Processing Co. Ltd., as well as the Royal Drugs Ltd., which form a powerful complement of instruments for drug development and the development of natural products of economic value from the plants within Nepal.

In this complex inter-institutional framework, the Royal Drugs Research Laboratory will serve as the scientific research and technology development centre. It will develop the technologies which will be commercialized by the other two bodies and as a result it would play the key role in a continuum beginning with the renewable natural resources namely the plant material and ending with products that could be utilised by the economy within the country as for example the primary health care or could be exported to generate valuable and much needed foreign exchange.

Expected End of Project Situation: The present situation is that the country now possesses an adequately equipped outfit that has the necessary equipment and some measure of expertise for scientific research, both chemical, botanical and pharmacological for the development of technology in processing and for the evaluation of necessary process parameters for commercialization. By the end of the project, it would be in a position, together with its two sister organisations, to conduct the development of economic products, pharmaceuticals, essential oils etc; derived from plants and to bring them from the scientific state to that of commercialization.

Target Beneficiaries: Accordingly the primary target beneficiaries will of course be the two institutions that would utilize the technology developed by RDRL namely the HPPCL and the Royal Drugs Ltd; and of course any other

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organisations like the Ayurvedic factories particularly the Singh Durbar Vaidya Khana (SDVK), the latter organisation is the main producer of Ayurvedic drugs for the health care system in the country. The ultimate beneficiary will of course be the Nepalese population particularly in regard to the basic needs programme which as the H.M.G. has outlined include health care delivery and food.

There is a continuing role of the UNIDO, H.M.G.'s and of RDRL to achieve the developmental objectives of this project. As this would be my last report, rather than to review individual R & D products, which was done in depth last year, it seemed more appropriate to give some suggestions which are likely to help in fulfilling these objectives better.

B. Recommendations

1. UNDP-UNIDO: As a result of the inputs provided by UNIDO the basic expertise and organisation structure of RDRL has been greatly upgraded, and the phasing out grant of 1988-89 has helped to consolidate these gains to some extent. However, the need for more inputs from UNIDO-UNDP both advisory and financial on a continuing basis is necessary to make best use of the investment already made, particularly for the following specific aspects;

(a) Small Supplies Grant: Very often R & D projects are held up for the lack of a spare-parts or repair of an equipment or a special reagent, and a small foreign fund could be of great help in such situations. If UNIDO could provide a small grant of about $. 10,000.00 a year for such urgent small supplies it would greatly help the projects running effectively.

(b) Adviser/s: Scientifically Nepal is virtually isolated from the current of world science. Periodic inputs of outside expertise and review of the work would greatly help in maintaining the work at a higher level of performance and output. This could be achieved in various ways. One option which UNIDO has used in this project, and many other National & International agencies have used successfully, is to have a consultant/monitor, who spends 7-10 days, 2-3 times in a year in the Laboratory, helps in actual formulation of the

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R & D projects, monitors the progress and is continuously available for advise on various aspects of the running project. As the appointment is for a period of 3 years certain continuity is maintained in the formulation of the proposal & projects and their execution. And as the stay each time is reasonably long there is enough time to understand the national setting and there is greater possibility of interacting with the working scientist. Another option is the International Advisory Committee as suggested by the Evaluation Committee. This provides a wider expertise, but as the Committee visits for only a few days it normally does not have much time to know well enough the national setting and requirements, and the members do not have the time to interact with the working scientists. Of the two I feel the former is more useful, and would be more cost-effective. What is important is to provide some external expert inputs for some more years.

(c) Grant for attending International Conference: Another well accepted method for the scientists keeping in touch with current scientific development is to attend International Scientific Conferences/Meetings. It would be useful if UNIDO could provide two grants in a year for RDRL scientists to attend a recognised International Scientific Meeting; preferably for those scientists who have an accepted scientific paper for presentation. A budget of about $. 5000.00 would be adequate for this.

The project is just taking off, the management structure is just taking shape and it will take some more years for these changes to congeal. It takes time to build scientific traditions and research-culture in an institution; particularly in an isolated developing countries, and now when the movement of this project is in the right direction, UNIDO must help to consolidate the gains, and the steps suggested above would go a long way to do so.

2. H.M.G.: Now that UNIDO's support is coming to an end, H.M.G's support must increase so that RDRL can maintain its R & D activity in all the dimensions and expand in some directions to serve its objectives better. Investment in R & D, particularly that leading to import substitution, better and greater utilization of natural resources to produce industrial and health care products

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is the best investment for economic betterment and self-reliance. And now when Nepal is passing through a difficult phase, support to R & D should be increased and not reduced, as more R & D is the key to industrial growth. Some specific points are given below:

(a) Library: The need to increase the budget for the Library was pointed out in the Evaluation Report of 1988 (pp 112-113) and is reiterated again. Library in any institution is its nerve centre and must get some core primary periodicals except two secondary journals, Chemical Abstracts and Current Contents. The Library has not been able to purchase any Annual Reviews, Monographs or books for almost 5 years. The long term effects of this non-availability of current scientific journals on the scientific staff when they do not know what is currently happening in Science in the world, would be catastrophic. Some primary journals must be obtained by the Library; a list of journals and some books which must be subscribed to begin with is given below:

List of Journals

1. Analyst
2. Analytical Chemistry
3. Experientia
4. Journal of Essential Oil Research
5. Journal of Chromatography
6. J. Pharmacy and Pharmacology
7. J. Nat. Products
8. Nature
9. Perfumer & Flavorist
10. Phytochemistry
11. Plants Medica
12. Science

Books

1. Spices and Herbs for the Food Industry
   By Y.S. Lewis (1984) U.S.$. 70.00
2. Source Books of Flavours
   By H.B. Heath (1981) U.S.$. 105.00

A National Library Exchange for Science Libraries may be considered by which the institutions can share and exchange scientific journals and books; NCST had published a Union Catalog listing the scientific periodicals subscribed to by the various sicence institutions in Kathmandu. There is need to update this Catalog and based on this a joint subscription policy could be considered.

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(b) Additonal Posts: The RDRL because of its excellent old holdings it could serve as a National Centre for Drugs and Natural Products. The freezing of all fresh appointments and new posts, inter-departmenetal transfers irrespective of descipline specialisation have also adversely affected the project execution. Drug development does need a minimal viable staff component to be able to cover all the stages of drug development from isolation of the product, pharmacological evaluation to developing suitable pharmaceutical formulation, preclinical toxicity, and human safety studies and large scale production. With the freeze on new posts it has not been possible for RDRL to have staff who could be trained in some of the specialized pharmacological and preclinical toxicology testing techniques, which has left a gap in the capability building in new drug development programme. Similarly there are some gaps in expertise in the Pilot Plant. It is suggested that the following additional posts should be created & allowed to be filled:

1. Pathologist - One
2. Haemotologist - One
3. Technician for Biology - Four
4. Chemical Engineer - Two
5. Analytical Chemist for Process Control Lab. - One

(c) Plant collection arrangements: With the reorganisation of the Department of Forestry and Plant Research, the Economic Mapping and Botanical Survey Section of the National Herberium & Plant Laboratory (NHPL) which used to carry out the plant collection work for RDRL should have to continue this work as the RDRL will have a continuous need for plant collection for its work on general screening and new essential oils is dependent upon new plant collections. Suitable arrangements need to be made between RDRL and NHPL to ensure that this plant collection work for RDRL will continue.

3. Royal Drugs Research Laboratory: For RDRL, it is most important that its scientific staff must develop self-confidence that "we can do it" and that: "nobody from outside can come and do the job for us,: we are ourselves competent to do the job". To this there is no short cut except determination and dedication, and hard and patient work. The senior staff must provide the

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leadership for this. This will create the self-relient outlook which is most essential for the laboratory's output. This is the challenge which RDRL has to meet. The scientific staff of RDRL is competent by any standard byt needs to develop the self-confidence. They must also be accountable and answerable for the confidence reposed in them.

(a) Pilot Plant, Godavary

(i) General: This certainly is a unique versatile facility established for the processing of plants in Nepal, consisting of concentration units, extractors, filters, spray drier etc. The equipment no doubt is larger sized than the usual run of pilot plants attached to R & D Lab. But viewed in the context that (a) this pilot plant facility was designed & ordered at a time when the HPPCL was not conceived; (b) except for the newly started HPPCL, there is no plant processing industry in Nepal and such a unit may be called upon to perform both R & D function as also carrying out actual commercial production, this large pilot plant facility would be in place; such facilities are not created again easily. It is a "National Facility" and should be used as such. Adequate mechanisms should be established for appropriate utilization of this facility both by HPPCL, and the private sector industry. A "Users Committee" should be formed consisting of representatives of the RDRL, HPPCL and Private Industries to work out the details of the procedures to be adopted. The possibility of continuous production in Pilot Plant of some products needed by HPPCL, RDL or SDVK on contract basis should be considered by RDRL; this will generate some funds and provide experience in running the pilot plant continuously.

(ii) Equipment modification: Some of the equipment is not optimally operative due to design inadequacy. Tournaire, the supplier have agreed to rectify these pumps and deficiencies and UNIDO has agreed to provide the funds for the same. Arrangements should be made to get this done at the earliest.

(iii) Process Contorl Laboratory: The Process Control Lab. equipment was ordered more than a year ago by UNIDO Hqs. but has not yet arrived. The Pilot Plant can not run properly without a functioning of Process Control Laboratory. It is unclear at what stage is this ecuipment held up. It is strongly urged that his equipment be procured without further delay.

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(iv) Boiler: With the difficulty likely to be experienced in getting enough quantity of Light Diesel Oil (LDO) for running the boiler, it is suggested that the smaller boiler filled at Thapathali should be shifted to Godavary and used in place as the larger boiler, which consumes much larger quantity of the oil.

(b) Priclinical Toxicology Section: Priclinical toxicology testing is an essential part of any new formulation or new drug development activity. It has been intended to set up this facility at RDRL right from the beginning of the project. But due to non-availability of adequately trained staff it could not be done earlier. Now I understand staff is available who could be sent for training. As suggested else where this last part of the strengthening of RDRL should be taken up now; the member of staff of RDRL should first be sent for training preferably in the Expert's Lab. which should be followed by the Expert visit.

(c) Records & Reports: One of the essential components of scientific research is the recording of data and writing of scientific papers and reports based on this data. In the case of Institutes like RDRL an equally important aspect is the system of record keeping & storage of the records so that the information can be retrieved and referred to when needed. The data recording and report writing at RDRL needs upgrading which will greatly add to proper flow and dissemination of information. It is suggested that:

(i) Laboratory raw data recording should be standardised; it is best to have special laboratory experimental record notebooks with numbered page, and the senior scientists should ensure that all laboratory results are recorded in these notebooks.

(ii) The monthly & annual reports submitted by the scientists should have a standardised format and form a permanent record of the Institute.

(iii) Inter-departmental Flow of Information: All information passed on from one department to the other for further development such as from Phytochemistry or Technology to Pilot Plnat should be written in the form of a detailed report, with a copy to the DDG/Inch; at present very often the information is passed verbally or on slips of paper which is not adequate. Pilot Plant Head must insist in gathering a written report.

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(iv) Project Reports: For all completed projects a full Project Report incorporating all the techno-economic data should be prepared and kept in the Record Section or with the Head. This should be treated as codified information. The Institute should also prepare Non-Technical Note for each completed project which should be widely circulated so as to disseminate information about the completed projects, while the Project Report should be given as a part of the Technology Transfer arrangement.

(v) A properly furnished Technical Record Section should be established. Similarly a Sample Storage Section should be created, where samples of all plants collected and compound isolated or prepared should be stored.

(d) Choice of Projects: The Institute should have a balanced mix of new technology generation and product oriented projects. Suitable systems should be developed and adhered to for identification and selection of projects under either of these categories; efforts should be made not to allow adhoc project to be taken up. Each project should be discussed in an appropriate forum in the Institute before it is taken up. For product oriented project it is best if a user is identified before starting the project; and the user should be encouraged to sponser the project or be in some way connected with the execution of the project.

(e) Project Based Operation of R & D Work of RDRL: With a view to sharpen the multidesciplinary focus of R & D work, to make optimal use of the available resources and scientific staff and to time-schedule the work, project based working has been introduced for RDRL research and development work. All the scientific & technical staff is alloted to one or more of these projects. Each project has a Task Force, drawing in scientists from different desciplines with a Convener. The Task Forces are required to meet at least once a month to review and monitor the progress of work and plant future work. All the project group conveners form the Project Evaluation Cell with D-G as the Chairman which meets at frequent intervals to review and monitor the entire work of RDRL, and also to approve any new project to be started. This project based working of the R & D programmes provides a good instrument for the management to monitor the progress of the projects.

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(f) Inter-institutional Co-ordination: As one of the outputs of this project are the technologies for production of industrial products based on Nepal's medicinal & aromatic plants. Joint Co-ordination Committees (JCC) have been formed between Herb Production & Processing Co. Ltd. (HPPCL), Royal Drugs Ltd. (RDL) and Singh Durbar Vaidya Khana (SDVK) as these organisations are likely to undertake industrial productions based on technologies developed by RDRL (RDRL's output would be their input). This should lead to better utilization of R & D outputs. For each specific task, separate Task Force Committees have been formed with a Convener, who would convene the meetings and keep record of all the meetings and monitor the progress. It was decided that the JCC's would meet every 2nd month and the proceedings of each meeting would be minuted and circulated to the members for follow-up action which the Task Force Committees would meet more frequently. The need for continuing intimate co-ordination between RDRL and these organisations can not be enough emphasised, not only to utilize the R & D outputs of RDRL but also to share the common facilities for better utilization of the investment made. For example, HPPCL must make greater use of the Pilot Plant of RDRL and what RDRL pilot plant should not be reduplicated at HPPCL unless it is fully occupied. Similarly RDL should make fuller use of the formulation of pilot plant available at RDRL.

(G) R & D Projects

1. Essential Oils: The laboratory has special expertise & interest in this area. The R & D work in this project has progressed well both to identify new essential oils with economic potential as also to manufacture known products. In view of the great industrial potential of this area in Nepal, the work in this area should be enlarged. As blending of essential oils gives products with greatly enhanced value, RDRL along with HPPCL should initiate programmes in the art of blending & making perfumes. It is suggested that RDRL should in the near future submit a detailed project for financial assistance to UNIDO-UNDP to inlarge the scope of essential oil utilization in Nepal.

2. Other Group of Natural Products: As suggested in the last report RDRL should consider developing technology for natural products of economic value even beyond drugs and essential oils, provided a user can be identified, who are prepared to

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sponser the work. These could include spices, gums, resins & colouring matters. R & D studies should also be undertaken on the utilization of Agriculture bye-products and waste-products; a few suggestion for this are given below:

(a) Wool fat: for cholesterol and lanolin.
(b) Sugarcane presmud: for carnauba wax and phytosterols.
(c) Rice bran oil: for vit E concentrate.

Before any work is undertaken a feasibility report should be prepared on the location & quantities of the waste/byeproducts available, their quality, and the market of the products. And only if the study shows economic viability should R & D work be undertaken. It would be useful to try to associate private or public sector industry with this work right from the beginning.

3. Standardisation of Ayurvedic Products: As a part of this project very useful work has been done to fix pharmacognostic standards for identification of about 100 more commonly used Ayurvedic drugs and Vol. I - III concerning 20 plants in each volume have already been published & the fourth volume is getting ready. It will be useful to translate those books into Nepalese, which will provide guidance to Ayurvedas physicians to correctly identify these plants.

There is need to take up more work to develop standards for quality control assay of Ayurvedic drugs. No doubt most Ayurvedic drugs are mixtures of many chemical constituents but the modern instrumental analytical techniques and spectroscopic methods offer adequate scope for this to be done. In cases when the active ingredients are known GLC/HPLC methods based on % of the active constituent could be developed. In other cases a GLC or HPLC finger print or a spectroscopic profile could be standardised. In still either cases are bioassay method may be developed. Unless the quality control methods are developed, the batch to batch reproducibility in production can not be assured.

4. Essential oil and fixed oil from Cinnamomum Glaucescens (Sugandh Kokila) berries:

The identification of Sugandh Kokila berries as a source of an economically useful essential oil and fixed oil has been one of the important outputs of this project. Although the essential oil from these berries is being commercially produced by HPPCL, the fixed oil is not yet being commercially produced.

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Unless an integrated project is developed incorporating both the essential oil, the fixed oil and lauric acid and the glycerel (or any other alcohol made therefrom) the full economic potential of this industry can not be projected. There is need to form a crash task-force between HPPCL and RDRL to work on this project intensively to work out fully the techno-economics and if necessary a private industry may also be associated with the task-force.

5. Production of Rosin, Turpentine and products derived therefrom: It is gratifying to note that on basis of earlier exploratory work carried out at RDRL, Nepal Rosin & Turpentine Ltd. has decided to sponsor a project on the production of rosin and rosin-based products at RDRL. This is a very noteworthy development and should be fully supported and promoted. The staff of RDRL should try to adhere to the time-frame that would be jointly decided for the project components, so that greater confidence is built up between the partners.

6. Diosgenin from Dioscorea: The world situation has changed substantially regarding the use of diosgenin as the starting material for steroid industry, since this project was initiated more than four years ago, and steroid industry world over is shifting to alternative methods. It is, therefore, most important that this project should be finalised without further delay and techno-economic parameters optimised. There after if the price of diosgenin is within the international price range, commercial production may be undertaken. The project should be terminated thereafter.

7. Other Outputs

7.1&2. Workshop for Equipment Maintenance & Glass Blowing: The equipment maintenance and glass blowing are very useful National facilities established at RDRL and other laboratories should be encouraged to make use of these facilities both for the maintenance of their instruments and repair of glass apparatus as also to get their people trained in these essential laboratory maintenance techniques. It would be very useful to hold the proposed workshops. In view of the non-availability of gas the glass blowing work has been at a standstill. It is proposed to hold these workshops in the first quarter of 1990 by which time gas is likely to be more freely available and which will also give enough time to do

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preparatory work for the workshops. In the meantime brochures should be prepared and widely circulated to prospective users, institutions & agencies informing them of the establishment of these facilities at RDRL.

3.4.5 Workshops for sales promotion, raw material procurement and managements of raw material based industry: These workshops fall more within the perview of the objectives of the HPPCL. RDRL should of course be intimately involved in conducting these workshops.

8. Project Inputs

a. Training

(a) Toxicology Training: In the budget 2 m/m of expert's visit are provided. The expert's visit will be more beneficial if some initial training of one of member of the RDRL staff in preclinical toxicology preferably in the Expert's Lab. is arranged. This will also help the RDRL to establish and equip the Toxicology Lab. before the Expert's visit, and the Expert's time will be more gainfully spent in making the Lab. at RDRL operational and will be able to run some actual Lab. experiments. It is suggested that the 2 m/m provided for Toxicology Expert may be re-appropriated as follows:

- 2 m/m Training
  and after the RDRL Toxicology Lab. is ready.
- 1 m/m Expert's visit.

(b) Microbiological Drug Assays: In the Drug Quality Control Department there is need to strengthen the section on Microbiological Bioassays by providing further training. No provision for this has been made in the original budget. However, in the budget line for Planning Consultant for 1988-89 there will be some saving. It is suggested that this saving may be used to provide for this training.

- 2 m/m training in Microbiological Assays in a Govt. Drug Control Laboratory.

(c) Other training components provided are given below & should be completed soon:

Fellowships

- Equipment maintenance - 1
- Glass Blowing - 1

Expert's Visit

- 1 m/m Chemical Engineer.

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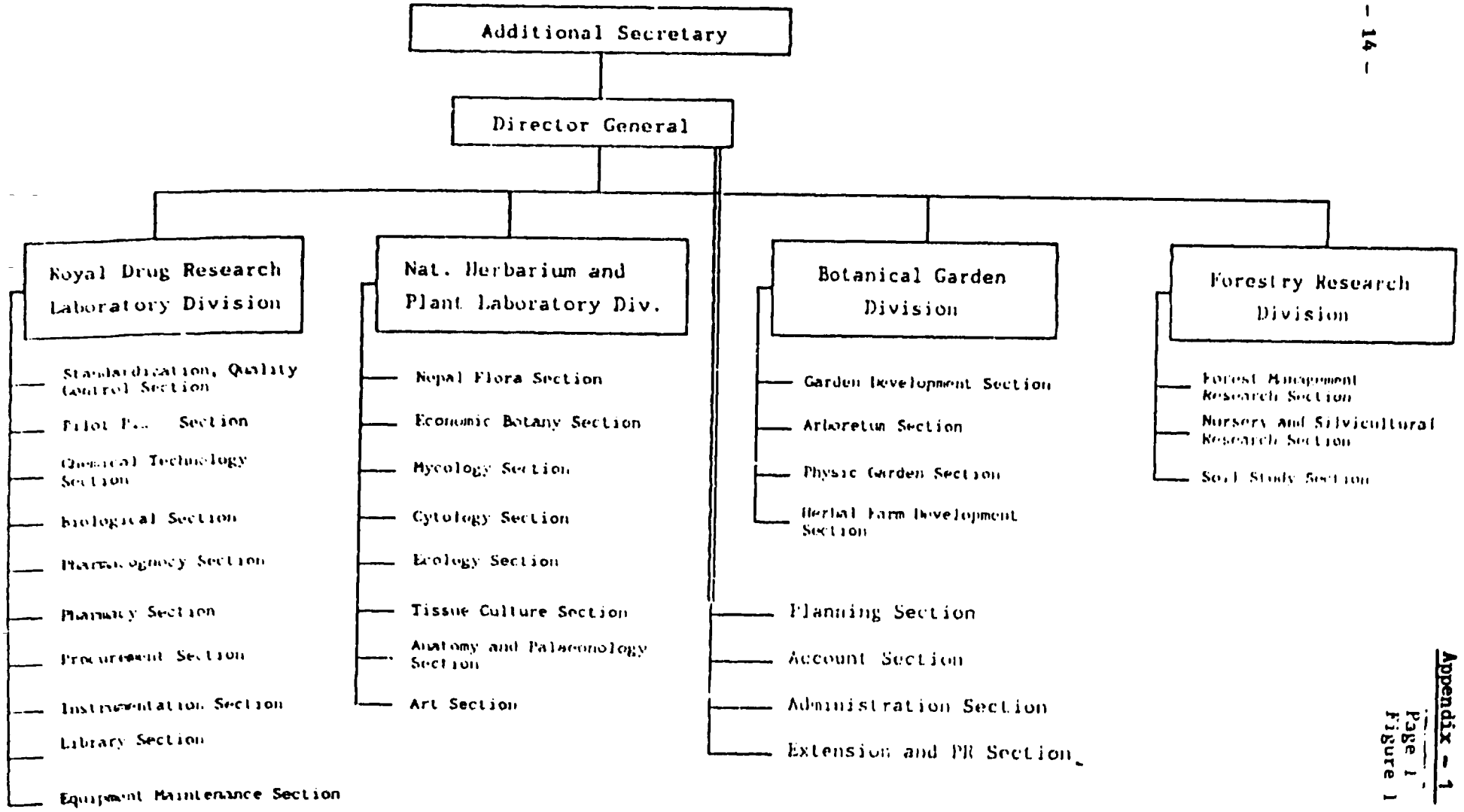

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