NOTE

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3. R&D in identified formulations/drugs
   (a) Standardization, quality control, patenting & IPR issues
   (b) Limited safety and toxicity evaluation – identify centres and investigators
   (c) Limited clinical evaluation – identify centres and investigators
4. Evaluation of safety and efficacy data
5. Preparation of dossiers of effective formulations
6. Interaction with the Industry for manufacturing of selected formulations
7. Operational research of the selected products for implementation into health system
8. Publicity & awareness strategies to take the product to masses

Steps for Implementation of the Project

Step 1: Identify gaps in diseases and drugs:

India's century old heritage of traditional medical systems using natural products have been utilized for addressing preventive as well as curative aspects of health care in the country. Though India's pharma sector is well known in the production of synthetic as well as herbal products it has been realized that there are a large number of chronic diseases for which the modern system of medicine has no definite answer while the traditional medicine formulations and Homeopathic formulations have been effectively used for many centuries and it was felt that the strengths of these systems should be exploited to address the problems of health care to be beneficial not only to the diseases of developing countries but also to those of developed western world. A literature review of epidemiology would be taken (from the already available data with WHO / Public Health organizations) for various diseases prevalent around the globe and available treatment modalities to assess the adequacy of such therapeutic measures to solve the problem of illness and promotion of health in different countries. These may be either communicable or non-communicable diseases, modifiable identified risk factors for diseases or may also be related to reproductive health of the population. This exercise will identify the gaps in the knowledge system of health and diseases as well as the available therapeutic products in different systems of medical and health care so that corrective steps can be initiated by identifying the most effective therapeutic regimen.

Step 2: Brainstorming session on each disease condition – to identify formulations, Strengths & weaknesses and corrective measures:

Having identified diseases for which therapeutic products are inadequate, an exercise will be undertaken to have brainstorming session for each of these conditions which will not only identify the specific formulations used in various disease conditions but also will examine the strengths and weaknesses of such formulations by way of availability of the source material, method of preparation of the formulations, mechanism of action and the side effects, reported toxicity etc., once these are identified, it will be easier to identify appropriate measures which can be adopted in the preparation of the

specific formulations as per set norms in the classical texts or pharmacopoeia. A Task Force approach will be adopted involving the expertise available in both Ayurvedic as well as modern systems of medicine so that the synergy of different systems can be best adopted to come out with the best possible therapeutic product.

Step 3: R&D in identified formulations / drugs:

(a) Standardization, quality control, patenting & IPR issues:

For implementing a successful R&D programme for any product, it is essential to go through the process of standardization and quality control so that the product used for animal as well as clinical studies, have uniform standards and do not suffer from batch to batch variation. Further, finger printing of the ingredients will be made as per the latest technology available to ensure uniform standards in all the batches that are used for pre-clinical and clinical studies. Any formulation which has been subjected to standardization and quality control procedures can be patented and the intellectual property rights of the product will be preserved so as to give benefits to the system to which it belongs. This will help to protect the country from the bio-piracy and give an edge over the other products which have not gone through such standardization procedures. This will also give confidence to the pharma industry to procure the know-how from the various laboratories to bring out quality products which will have national as well as international market. Adopting GMP is the need of the hour for all manufacturing industries and the first step towards this is to prescribe standardization procedures and quality control methods.

(b) Limited safety and toxicity evaluation – identify centres and investigators

There are beliefs existing that Ayurvedic / herbal products are totally safe and without any side effects. It is also known that such beliefs are not always true and there are well known instances of toxicity due to Ayurvedic / herbal products. Hence it is essential that limited toxicity or total toxicological evaluation of the natural products needs to be done depending upon the type of formulation to ensure safety of the users in the long run. The type of the pre-clinical toxicology in relevant animal species will depend on the nature of the formulation. For example, whether these traditional formulations have been in long term use or new herbal formulations, each product will be examined by a team of experts who will decide on case to case basis the extent of toxicology evaluation which is required for each product. Specific centres which have the capability to carry out such studies will be identified along with Investigators who can be entrusted with this responsibility. Pre-clinical studies not only give information on the toxicity profile but will also give us information on the pharmacological activity to various products as well as mechanism of action in different animal models wherever possible if well planned studies can be designed for the same.

Some of the Centres which can be entrusted with this responsibility are as follows:

1. CDRI, Lucknow
2. ITRC, Lucknow

3. RRL, Jammu
4. IICT, Hyderabad
5. Dabur Research Laboratory
6. Zandu Pharmaceuticals
7. Banaras Hindu University, Varanasi
8. PLIM
9. HPL

(c) Limited clinical evaluation – identify centres and investigators:

Any drug development after pre-clinical evaluation leads to clinical evaluation to assess the efficacy of the formulation in the specific disease conditions for which it is to be prescribed. Although some of the formulations may be in use for different disease conditions, as per the traditional knowledge, a modern method of evaluation by joint efforts between the traditional practitioners and the modern physicians will give confidence to the consumers as well as prescribers about the efficacy as well as safety of the said product. This will also ensure global acceptance of our products as these have gone through the well established path of drug development. It is also possible during these studies to pick up side effects or adverse reactions that may occur during the administration of these preparations. It is necessary that such trials are conducted after a well designed clinical trial which is planned with the help of physicians and statisticians and following good ethical practices for clinical trials. Approval of institutional ethics committees and close monitoring by the monitoring team are the essential requirements for carrying out such trials in good centres by well established researchers who have commitment and expertise to conduct clinical trials. Evaluation of such trials will be done by both modern parameters as well as traditional methods of evaluating the outcome or their effectiveness of the administered drugs. The quality of life parameters which are the hallmark of traditional drugs can also be studied during these trials. The choice of centres and Investigators will depend on disease to be studied, availability of sufficient patients for trials and committed clinicians of both systems who are willing to abide by the clinical trial protocols and conduct the trial as per GCP requirements. Ethical guidelines for biomedical research on human subjects, released by the Indian Council of Medical Research in 2000 will be followed during the trial. Periodic monitoring of the trial will be made to assess the progress by a team of experts and necessary corrective measures will be taken as deemed necessary.

Step 4: Evaluation of safety and efficacy data:

Data generated by the pre-clinical and clinical evaluation has to be examined by a team of experts to validate the safety and efficacy of formulation. It will also ensure whether a standardized formulation has been used during the study. Recommendation of the expert group to take the product forward to attract the pharmaceutical companies is essential from the regulatory point of view. Once the phase III data is evaluated and the product is found to be suitable for commercial exploitation, marketing permission can be granted with adequate post marketing surveillance to pick up any adverse effects.

Step 5: Preparation of dossiers of effective formulations:

Products which have been found to be effective and safe by the above mechanism will now be ready for presenting to various national and international pharma companies for which suitable drug dossiers incorporating various parameters prescribed for natural products will be taken into consideration. The essential requirements to be incorporated in these dossiers are method of preparation, good agricultural & collection practices, full description of the plant material as per modern scientific parameters preferably by a taxonomist, pharamcognosy, chemical finger printing, standardization and quality control of the raw material, determination of microbial pesticides, heavy metals, production source of the finished product, batch to batch variation, stability study and shelf life. The dossier will also contain the total pre-clinical pharmacological and toxicological data, clinical data of various phases and the adverse effects detected, if any. At this stage dossier will be ready for transfer to the pharma industry for taking up further large scale manufacture of the drug.

Step 6: Interaction with the Industry for manufacturing of selected formulations:

Interested pharma companies will be invited to look at the dossier and data generated. After signing proper Memorandum of Understanding and Secrecy Agreement, the selected pharma companies will be encouraged to go ahead with large scale manufacture of the drug. In the Agreement, specific clause regarding marketing rights and profit sharing between the government and the industry will be specified to protect the interest of the product developers and the industry partners. It will also be beneficial to plan strategies to identify the industry partner from the beginning so that the products can be developed as joint ventures between the government departments and the pharma industry.

Step 7: Operational research of the selected products for implementation into health system:

Safe and effective products, once approved for marketing will also be subjected to operational research to study the acceptability by the population and ease of introduction into the health care system. The results of such research will give confidence to the public regarding use of the product as well as safety of the product. This will also help to understand the extent of use and decide the acceptability and affordability of the product. Integration into the national health care system of such affordable products will help in easy availability of safe and affordable drugs to the masses in the country.

Step: 8: Publicity & awareness strategies to take the product to masses:

It is essential to create a public awareness system and strategies so that the successful products can be provided enough publicity and visibility for large scale use as well as export potential to benefit the population of other countries. As the global demand for alternate/traditional system of medicine instead of the modern medicine is well evident through out the world, it will be possible to satisfy the needs of the people of the world. Thus the century old traditional knowledge of India can be harnessed to benefit the health and well being of the entire population of the world to bring back the glory to our traditional wealth of knowledge in the area of health & disease.

Milestones for Implementation of the Project (Time Schedule)

1. **Identify gaps in diseases and drugs**
   - Identifying – 2 month
   - Database, Epidemiologists, Public Health Specialists, AYUSH and Allopathic (Disease Specialists) Physicians.

2. **Brainstorming session on each disease condition – to identify formulations, strengths & weaknesses and corrective measures**
   - Brainstorming on selected diseases / conditions / issues (3 months for each one)
   - Task Force on specific diseases – 3-6 months
   - Constitution of Working Groups, documentation, meeting
   - Experts: Ayurvedic / Siddha / allopathic / Homeopathic / Unani physicians, pharmaceutical scientists, Dravyaguna experts, Ras Shastra experts, Pharmacologists.

3. **R&D in identified formulations/drugs**

(a) Standardization, quality control, patenting & IPR issues
   - Identifying - 2 month
   - Task force on specific issues - 3-6 months
   - Constitution of working group, documentation, meeting

Standardization and Quality Control could be carried out in the following institutions:

1. RRL, Jammu
2. NIPER, Mohali
3. CDRI, Lucknow
4. NBRI, Lucknow
5. IICB, Kolkata
6. IICT, Hyderbad
7. PERD, Ahmedabad
8. CCRAS, Chennai, Kolkatta
9. IMPCL Pharmacy, Mohan
10. GAU Pharmacy, Jamnagar
11. NIA Pharmacy, Jaipur
12. CCRAS Pharmacy, Kolkata
13. CCRUM Pharmacy
14. BHU/ Ayurvedic Pharmacy, Varanasi
15. BARC, Hyderabad
16. PLIM, Ghaziabad
17. HPL
18. IMPCOPS, Chennai
19. SM Siddha pharmacy, Erode

(b) Limited safety and toxicity evaluation – identify centres and investigators

1. Standardization and quality control: 6 – 13 months.
2. Safety evaluation - 12-24 months
3. Toxicology/Pharmacology : As per list 20 or more institutions

(c) Limited clinical evaluation – identify centres, Hospitals and investigators

Clinical evaluation - 12-36 months

1. AIIMS, New Delhi
2. PGI, Chandigarh
3. KEM, Mumbai
4. State Selected medical colleges
5. BHU, Varanasi
6. CCRAS Selected institutes
7. CCRUM Selected institutes
8. CCRH Selecred institutes
9. NIA, Jaipur
10. GAU, Jamnagar
11. Poddar, Mumbai
12. SPARC, Mumbai
13. Ayurvedic College, Thiruvanathapuram
14. Arya Vaidya Sala, Kottkkal
15. Nizam's Institute, Hyderabad
16. Osmania, Hyderabad
17. SGPGI, Lucknow
18. KGMC, Lucknow
19. Nair Hospital
20. UCMS, Delhi
21. MAMC, Delhi
22. Jamia Hamdard Delhi
23. Aligadh University
24. JIPMER, Pondicherry
25. CMC, Vellor
26. MMC, Chennai
27. Medical & Ayurvedic College – Bharati Vidyapeeth, Pune
28. Ayurvedic College, Hasan, Udipi,
29. Tilak Ayurvedic College, Pune.
30. Leading AYUSH Colleges identified by Department of AYUSH.

- many more institutions

4. **Evaluation of safety and efficacy data (third party evaluation)**

- Evaluation of safety/efficacy data – 3-9 months
- ICMR, DCG (I), AYUSH - CCRAS- CCRUM- CCRH, Department of Health,
- Department of Family Welfare

5. **Preparation of dossiers of effective formulations**

- Preparation of dossier - 3 months
- Consultants to be engaged for preparing dossiers

6. **Interaction with the Industry for manufacturing of selected formulations**

Industry interaction – partnership from step 1, 2-3 months, continuing exercise

Industries to be partners:

- Leading AYUSH Pharmaceutical Companies.

7. **Operational research of the selected products for implementation into health system**

- Operation research - 1-2 years
- ICMR, Ministry of Health & F.W., AIHPH, Kolkata, State Health Departments, University Medical, AYUSH Colleges.

8. **Publicity & awareness strategies to take the product to masses**

- Continuing process
- Print media, advertising, TV, Radio, posters, skits, street plays

Costing per formulation (product) for one disease condition – one or two products could be researched upon as per the expenses of AYUSH Department, ICMR, CSIR on various activities the tentative cost will be as follows:

S. No.	Activity Approximate	(Cost in lakh of Rs.)
1.	Identify gaps in diseases and drugs	10.00
2.	Brainstorming session on each (disease condition – to identify formulations, strengths & weaknesses and corrective measures)	10.00
3.	R&D in identified formulations/drugs	
	(a) Standardization, quality control, - patenting & IPR issues	100.00
	(b) Limited safety and toxicity - evaluation – identify centres and investigators	200.00
	(c) Limited clinical evaluation – -identify centres and investigators	250.00
4.	Evaluation of safety and efficacy data	100.00

5.	Preparation of dossiers of - effective formulations	25.00
6.	Interaction with the Industry -for manufacturing of selected formulations	25.00
7.	Operational research - of the selected products for implementation into health system	50.00
8.	Publicity & awareness - strategies to take the product to masses (Subject to actual)	200.00
	Total	**Rs. 970 lakh say Rs.10.00 crore**

For one product cost is = Rs.10 crore

Total cost for 12 products (12 x 10) = Rs.120 crore

Modus Operandi

The *"Golden Triangle Partnership" (GTP)* Scheme will have three major partners – Department of AYUSH (CCRAS- CCRUM- CCRH), CSIR and ICMR.

"Golden Triangle Partnership" project will be managed through the following committees:

Apex Committee: A policy making body for giving directions to the programme, chaired by Secretary, Department of AYUSH & will have DG, CSIR and DG, ICMR as other members. This committee will periodically take stock of the progress made and will suggest mid-course corrections. The Committee shall meet at least once in four months.

Steering Committee / Core Committee: will suggest the steps to be initiated at different stages and will closely monitor the Technical Advisory Committees. This committee will include three expert advisers/ representatives from each partner department. The meeting of this committee will be attended by members of all the three partners. The Committee shall meet at least once in three / four months.

Technical Advisory Committees (disease specific) for each of the discipline identified under the programme shall meet at monthly/ 2 monthly basis.

Task Force (Three Committee for Ayurveda / Unani / Homeopathy) for each Drug Development Programme, comprising of Investigators from different disciplines. Task force shall meet at 2 monthly basis.

1. All major policy decisions, however, would be taken on the overall direction and guidance of the Apex Committee i.e., Secretary (AYUSH), DG (CSIR) and DG (ICMR).
2. The GTP would work on the existing classical Ayurvedic formulations as well as new herbomineral combinations on the holistic approach to bring out validated products.
3. Department of AYUSH will take action on legal and regulatory issues.
4. Private drug manufacturing companies could also be associated in the project from the very beginning as partners for research and investment.

5. The Department of AYUSH (CCRAS- CCRUM- CCRH) will share resources for various R&D activities to be carried out through various ICMR, CSIR and other institutions.
6. The GTP will function in the Mission Mode, keeping the five year target in view for development of drugs of national importance.

Steering Committee:

The Steering Committee will comprise of the following members and the committee will meet every two months to approve the projects, release of funds and assess the progress of work.

1. Concerned Technical Advisor
2. Director of the concerned Council
3. Director of National Institute of the concerned ASHU system
4. Head, R&D Planning Division, CSIR
5. Head, Technology networking & Business Development, CSIR
6. Director, Indian Institute of Integrative Medicine, Jammu
7. Director, Indian Institute of Chemical Technology, Hyderabad
8. Senior DDG, ICMR
9. D.D.G., ICMR
10. Chair in Clinical Pharmacology, ICMR/ HOD, Pharmacology, AIIMS
11. One renowned scientist nominated by Secretary (AYUSH)

Note: Any other subject experts may be called as special invitee as per requirement from time to time

Secretarial Assistance: Work on the project will be done in a Mission Mode manner and each Council will have one Consultant in each system i.e. Ayurveda, Homeopathy, Unani with consolidated salary @ Rs.25,000/- p.m. and one Computer Data Operator with salary @ Rs.6,000/-. They will assist the technical advisers for the implementation of this project.

Funding:

- ⇒ Three partners will provide funds from their department's existing schemes/existing heads of research/drug/standardization/clinical trials/toxicological studies etc.
- ⇒ The estimated cost for developing drugs for one identified area is Rs.10 crore. Therefore, the total budgetary requirement over a period of 5 years will be in excess of Rs. 120 crores.
- ⇒ For GTP, Department of AYUSH will route the funding through involved Councils as per the approval of Steering Committee. For this purpose, CSIR, ICMR and Research Councils of AYUSH will submit the actual expenditure required for the activities carried out by them.

During the 11th plan, all the partners will contribute in GTP. Money could be routed through the Research councils/Institutes. Ayush share will be Rs. 75 crore. CSIR and ICMR will also contribute some amount. CSIR and ICMR will spell out their share soon after discussing with competent authorities.

Note: No additional funds for Development of Pharmacopoeial Software, Development of Research Council Labs as per NABL/GLP and Fundamental and Basic Research in ASHU disciplines can be taken from GTP component. However, project related infrastructure/equipment etc. could be supported.

Release of funds: Financial allocations for GTP project activities will be done through the Research Councils/Institutions of the three partner departments or directly to the project implementing institutions on annual basis. Tentative cost of various activities is indicated under the table of costing. This will be as per the norms of DST/CSIR/ICMR etc.

Funds allocations for GTP for 10th Plan:

2005-06 - Rs.15.00 crore, 2006-07 - Rs.20.00 crore

Rasa kalpas (Herbo-mineral preparations) Projects under Golden Triangle Partnership (GTP) Scheme:

- Safety Evaluation of following 8 (eight) most widely used Bhasmas / Rasakalpas (Herbo-mineral & metallic preparations) and more are to be identified.
    1. *Kajjali*
    2. *Rasa manikya*
    3. *Rasa sindoor*
    4. *Basant kusumaksr Rasa*
    5. *Arogyavardhini Vati*
    6. *Mahayogaraja Guggulu*
    7. *Mahalaxmivilas Rasa*
    8. *Makardhwaja*
- Standardization / Drug development of prioritized disease conditions is under progress at CSIR.

Participation of AYUSH Industry in Drug Development under GTP Scheme:

Areas of interest as one disease – one industry and one Council to develop/standardize the drug and taking Drug Development under GTP Scheme.

In the Project Screening Committee meeting for Golden Triangle Partnership (GTP) scheme held on 06-03-07 at Dept. of AYUSH and ICMR is advised for taking up the Drug development project for HIV / AIDS with the involvement of CCRAS, CCRUM, AIIMS and AYUSH Industry.

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