National Conference on Inhouse R & D, Department of Scientific & Industrial Researh, Government of India, New Delhi, December 28, 29, 1989

IN HOUSE R & D - SOME POINTS TO PONDER

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Introduction

The substantial progress that Indian Industry has made in the last decades can be at least partly attributed to the strength of the technological skills of its R & D personnel. Although it is commonly said that India has the third largest contingent of scientists and engineers, it is now well recognized that the percentage of those actually engaged in real technological tasks is small. The investment of Indian Industry in R & D is also awefully small (less than 1%). In the light of these facts, the contribution of in-house R & D is significant indeed; it could be still better if appropriate investments and inputs are provided. This article will comment on those in relation to the Chemical Industry, especially the Drugs and Pesticides sectors with which the author has been intimately associated for several years.

Perspective plan for the Chemical Industry

The Chemical Industry in India constitutes an important and dynamic segment with good growth rate in production for local consumption but more significantly for exports. The export of plastics for example valued at Rs.129 crores in 1988-89 is expected to increase to Rs.400 crores by the end of the 8th plan. Exports of other chemicals and related products which are presently Rs.1280 crores can go upto Rs.14000 crores by 2000 A.D.

Realizing the need for formulating a perspective plan for the Chemical Industry, the Indian Government had appointed an apex committee to enunciate one upto the year 2000 A.D. This committee constituted four subgroups in the area of Inorganic chemicals, Organic chemicals, Dyestuffs and Pesticides. These committees had interactions with various experts and industry associations. They studied in detail the demand--supply pattern of each of the major chemicals and other important issues like growth rate, investments required in the industry, export potential,

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Contribution No. 14 from R & D Centre

the present technology, future upgradation and environment pollution. The role and contributions of R & D have been also considered.

Since the Chemical Industry is an essential one in the core sector, the perspective plan has continuing validity. We shall now look at the various opportunities for contribution by R & D in attaining the goals of this plan.

R & D assignments in Chemical Industry:

Inorganic Chemicals

The current status of technology in this group is mostly satisfactory; where necessary in specific cases, knowhow can be brought in. At the moment, caustic soda and calcium basic diphosphate seem to have export potential. The role of in-house R & D could be to improve the efficiency of plant operations through improved equipment designing, energy conservation, use of better materials of construction, effluent treatment and pollution abatement. Other specific R & D tasks could be (i) cost reduction in the process for sodium tripolyphosphate, (ii) development of liquid hydrogen manufacturing technology, (iii) development of new products like flame-retardant chemicals from phosphorus and inorganic catalysts such as Zeolites and those required in the manufacture of nitric acid.

Dyestuffs

The Indian Dyestuff Industry represents the highest development of chemical technology and R & D achievements and forms an important link in the chain of other essential chemical industries. It was thriving well until it was affected by internal demand recession; nevertheless this was offset by exports. Its production value is in excess of Rs.400 crores. The export component has been very high, amounting to Rs.215 crores in 1987-88. The target for 1988-89 at Rs.350 crores has been probably realized.

R & D has contributed in numerous ways - improvement in quality, yield and productivity, development of more economic alternative processes and of new products. Needs to be addressed in the future are producing newer and more economic dyestuffs with ease of application, higher fixation efficiency, fastness properties and superior colour yields.

R & D can also contribute to energy conservation and particularly pollution containment. It must be noted that the export performance of our dyestuff industry is probably helped by the less stringent (at least in practice) environment regulations in our country.

Organic Chemicals

Although drugs and pesticides (as also dyestuffs) should logically come under this group, they are discussed separately as they are relatively high technology, high value speciality chemicals. This group then is comprised of bulk, commodity chemicals used as basic building blocks and required in very large tonnage such as ethyl alcohol, acetic acid, acetone etc. Among these chemicals, some like phthalic anhydride and ethyl alcohol have been identified to have export potential.

The organic chemical industry has reached a size of near self-sufficiency in terms of technologies for most of the important chemicals. While for some of the chemicals technology has been developed by indigenous R & D, it has been imported for some others and absorbed by industry.

Some of the tasks identified for R & D work are:

i) Energy conservation or reduction in existing processes.

ii) Assimilation and improvement of imported technology.

iii) Continuation of efforts to increase yields and reduce raw material consumption and to substitute imports with indigenous materials.

iv) Development of catalysts such as those required in the manufacture of acetic acid, aniline, formaldehyde, pentaerythritol and phthalic anhydride.

v) Development of nonphosgene routes for polyurethene monomers and polymer alloys.

Drugs, Pharmaceuticals

Starting from humble beginnings around the time of independence, the Indian Pharmaceutical Industry has made tremendous progress in four decades. In 1988-89, the industry produced with a capital investment of Rs.750 crores, bulk drugs worth Rs.530 crores used in formulations of Rs.2690 crores. The export contribution was substantial -

Rs.243 crores of bulk drugs and Rs.157 crores of formulations, totalling upto Rs.400 crores; the projection for bulk drugs is Rs.425 crores for 1989-90. At the end of the 8th five-year plan, it is envisaged that formulations to the value of Rs.6,610 crores (at 1989 prices) will be produced from Rs.1,350 crores of bulk drugs. The ambitious target for 2000 A.D. is R.16,000 crores of formulations. The industry employs at least 2,00,000 persons directly and almost 10,00,000 indirectly in related or ancillary industries.

A large measure of credit for this performance must be given to the technologiclal prowess of the industry and the capabilities of its R & D, as well as to the Government's thrust for indigenisation and import substitution.

In-house R & D alone or occassionally with the assistance of CSIR Laboratories has provided process know-how for bulk drugs and formulations. Multinationals also brought in expertise and technology which have been assimilated, adapted and improved upon. Thus indigenous production based upon Indian R & D is reported for top-selling world class drugs.

Synthesis of complicated molecules requiring multistep processes, microbiological transformation products, semisynthetic antibiotics using immobilized enzymes and chiral molecules using conventional resolving agents is a spectacular achievement of the Indian R & D. A number of bulk drugs using GMP conditions are exported to the West. In fact India is the largest manufacturer of a few of these drugs.

In-house R & D can make more significant contributions in the future as follows:

i) International patents on 14 out of 15 top-selling drugs are expiring by 1995. We can take advantage of this by developing processes for those for which we still do not have one and increase our exports.

ii) Our prowess in process development is adaptive and imitative. Really innovative processes should be aimed at, which would be internationally patentable and can be exploited commercially.

iii) We should take advantage of modern developments in organic synthesis like high pressure chemistry and sonochemistry where applicable. Induction of optical activity using homogenous chiral catalysts or chiral

auxiliaries has to be contemplated on an industrial scale.

iv) In the exploitation of bio-technology, in-house R & D should still concentrate on fermentation reactions especially for antibiotics and chemicals like vitamin C and citric acid. Inspite of an early start, the expertise in this technology in the country is far from satisfactory. Use of 'natural or 'artificial' enzymes for organic reactions especially to produce chiral molecules from prochiral precursors is a laudable objective. While vaccines for diseases like Malaria, Filariasis and Leprosy could be pursued by both industrial and academic research, more sophisticated rDNA technology for esoteric, therapeutic peptides like tissue plasminogen activator is best left to the latter.

v) In the field of formulations, special R & D efforts are needed to introduce recent advances like trans -dermal patches, zero order delivery systems and liposome and antibody tagged preparations for targeted attack, bearing in mind, of course, that these should be cost effective.

Pesticides

The use of pesticides in India started on a small scale around 1948 by importing DDT for malaria control and then BHC for locust control. Pesticide use in agriculture was initiated for the first time in 1949. Indigenous production started in 1952 with the setting up of DDT and BHC plants in Delhi in 1954. From then the industry has made giant strides and contributed in a large measure to the green revolution. In 1986-87, the industry had an installed capacity for the production of 1,02,015 metric tonnes of pesticides for agricultural and public health purposes and produced 56186 MT at a capacity utilisation of 55%. The demand forecast for 1994-95 is 1,30,000 MT and for 2000 A.D. 1,52,000 MT. The turnover of the industry in 1988-89 was Rs.650 - 700 crores; it had an export component of around Rs.40 crores; import was of a smaller magnitude.

As in other fine chemical industries, the pesticides industry enjoys good technological strength due to the R & D capabilities. Due acknowledgement must also be given to the help it has obtained from CSIR laboratories. Thanks to these, today India is the largest manufacturer of basic pesticide chemicals among the Afro-Asian countries

barring Japan. Of the 126 pesticides registered in the country, 57 are manufactured locally, most of them based on indigenous technology. In fact, in one case, the country has the distinction of developing a non-lethal route to a herbicide which is exported successfully. R & D has also been able to take care of the needs of conventional formulations like emulsified concentrates, wettable powders, dusting formulations and in some cases granules.

Some of the identified tasks for R & D in the near future are:

i) Development of indigenous technologies for a few more pesticides like acephate, amitraz, newer synthetic pyrethroids, newer fungal imidazoles like propiconazole and potent sulphonyl urea herbicides like chlorosulfuron. R & D should specially concentrate on pesticides which are specific to pests (e.g. chitin synthesis inhibitor) and non-toxic to humans.

ii) Development of newer processes for existing pesticides with a view to minimise, if not, eliminate the strain on the eco system and hazards to humans, eg. non MIC route to methyl carbamates like carbaryl.

iii) Investigating and utilising our plant resources some of which have pesticidal properties.

iv) Initiate research in relevant biotechnological areas like biological control of insects and building up resistance to herbicides in treated plants.

v) Study and adaptation of modern formulation techniques which result in application of lesser quantities for achieving desired levels of control. Some developments are:

> Suspoemulsions, microemulsions, multiple emulsions, suspension concentrates, water-dispersible granules and controlled release formulations.

<u>From development to discovery research - a plea</u>

The demands of a large country like ours with a vast population, in terms of human health needs and agricultural crop protection are large, diverse and in some cases specific. On the other hand, our industries in these areas are quite advanced and backed up with necessary skilled R & D people and infra structure. It is time therefore to consider, diverting our attention slowly from development to discovery research.

Basic research for new drugs :

The international cost of developing of a new drug is very high (Rs. 50-100 crores), but the market itself is very large (Rs. 1,70,000 crores in 1987). There is reason to believe that development costs of a new drug in India need not be that high. Our efforts will become viable if a new discovery is aimed at serving local needs as well as capturing a share of the world market. We have some of the skills and expertise needed for the task but others can be acquired. Additional investments may be needed. Of the three important institutions engaged in this research, two are in the private sector and the third is a CSIR laboratory. A few others in the private sector have been closed down for various reasons. New incentices to private industry and possibly a few more institutions in the private sector are needed. Collaboration among them will bring down the costs. In any event, licensing to or co-development with a multinational group is indispensable for the success of this venture which will involve filing international patents and world-wide marketing.

Five major areas are suggested for this kind of undertaking on the basis of national relevance and international importance :

Antibacterials/antiinfectives - $ 13.6 billions.
12% of the world market in 1987;more than Rs.
400 crores in India in 1988 at about 20% of the market.

Cardiovascular agents - $ 16 billion.

Nonsteroidal antiinflammatory agents - $ 5.3 billion

Antiulcers - $ 4.6 billion
Zantac alone sold for $ 1.48 billion in 1987 and now sales are in excess of two billion.

Anticancers - $ 3.9 billion.

Apart from these, malaria, fialariasis and leprosy are local problems needing attention. Fertility control is also a major issue.

Basic research for new pesticides

The discovery and development of a new pesticide is just as costly and time consuming as a drug and entails a similar multidisciplinary approach. Nevertheless such an undertaking will be worthwhile in India because of a large and growing market and specific needs of plants under our agro-climatic conditions. Additionally, these can be targeted at a worldwide market of twenty billion dollars.

Success of the approach will again involve investments in the private and public sector and collaborative efforts among these and will require further, penetration of the international market through multinational companies, with appropriate patent protections.

In the context of development of both new pesticides and drugs, we should well bear in mind the success of Japanese science. Although a relatively late comer in the field of new drugs, Japan has the greatest number of introduction of new chemical entities as drugs (14/52 in 1988). Many of these have been licensed to multinationals. Similarly, Japan has had resounding success in developing new pesticides like fenvalerate, MTI 500 and Cartap.

Measures to give new fillip to in-house R & D

The following will go a long way to strengthen Indian R&D which will lead to increased contribution :

i. New tax incentives/grants to private industry to start and sustain R & D activities, especially basic research for new molecules. Even pricing policies and control mechanisms need to be looked at freshly to ensure adequate profitability for affording such investments.

ii. Removal of import duty on R & D equipment and reasonable quantities of fine chemicals - In house R & D laboratories get much less money for purchase of equipment compared to CSIR laboratories or funded university professors.

iii. Centrally funded library facilities and information retrival systems in industrial belts. These have become unaffordable to individual R&D units.

iv. Adequate monetary compensation for industrial scientists- this is now lagging behind CSIR pay scales.

v. More wide-spread recognition of achievements of R & D scientists in terms of honours (there are very few, none equivalent to the Bhatnagar Prize), fellowships (equivalents of FASc or FNA), enlistment to committees (fewer get into these compared to University or CSIR scientists) and enrollment into foreign delegations or exchanges.

vi. More widespread exchanges among in-house R & D scientists, academic and CSIR people and visiting lecturership at graduate/post graduate schools.

Acknowledgements : The author is grateful to Shri H. Krishnamurthy and Dr. P.V. Arur of Hidustan Organic Chemicals for making available a preview summary of the Perspective Plan for Chemical Industry and to the latter (Dr. P.V. Arur) for interesting discussions. He also wishes to acknowledge help received from Mr. Prasad Chandran, Searle India, Dr. A. Venkateswarlu, Atul Products and Shri R.D. Joshi, OPPI who provided draft reports of the subgroups concerned respectively with pesticides, dyestuffs and pharmaceuticals.