ELISA AS DIAGNOSTIC TOOL PROSPECTS AND IMPLICATIONS

Editors:

S. VISALAKSHI
S. MOHAN

National Institute of Science, Technology and Development Studies, New Delhi

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A STUDY OF THE DIAGNOSTICS MARKET IN INDIA OPPORTUNITIES AND STRENGTHS

P.K. GHOSH

Director, Department of Biotechnology
CGO Complex, Block 2, Floor 7 & 8, Lodhi Road
New Delhi 110003

Indian population placed at 800 million in 1988-89[1] was about 18% of the world population (estimated at 4400 million). As against this share of global population of our country, the market share, both of the Indian Pharmaceuticals (Pharma) as well as of the Diagnostics were lower when compared with the corresponding world markets in monetary terms. It is evident from the following Table 1:

TABLE I. Pharma and diagnostic markets india *vs.* world

Year	India/World	Pharma market (US $ million)	Diagnostic market (US $ million)	Diagnostics market as % of Pharma market
1987	India	1822	15.4	0.85%
	World	117540	7710	6.56%
1990	India	2094	24.1	1.15%
	world	156450	10700	6.84%

Source: World Pharma and Diagnostic markets from various published sources. Indian figures worked out by taking the dollar to rupees exchange rates prevailing in 1987 and 1990.

The Indian Pharma market is not only small (1.55% only) but also equally insignificant compared to the corresponding world market. The Indian Diagnostics market bears a very small ratio of 0.85% to the Indian Pharma market, compared to the corresponding figure of over 6% on global basis. This would indicate that the diagnostic products in India have not yet come to the stage of wider usage. The small proportion of the Indian Diagnostics market is also to be viewed in the context of the

wide-spread Statutory Price Control imposed on the Indian Pharma market (which otherwise is also in a highly competitive environment), thereby Pharma prices are generally lower, while there is no Government price restriction or control currently on the sale of Diagnostics. This indicates a further diminished physical volume of diagnostics. The author thus considers the Indian Diagnostics market as dormant and nascent (though currently small), and holds potential for substantial expansion and growth in future.

During the last three years, much attention has been paid by the Government to promote the development of Diagnostics, specially the Immuno-diagnostics. Prior to this period efforts from the large Industries for entering into this sector were small. Moreover, a comparatively large number of small companies were in this business. Also the devices like the immuno-diagnostics and the nucleic acid probes were scarcely used in the Indian pathological laboratories and hospitals. This paper examines the current Indian market for the Diagnostics and extrapolates the future scenario to draw conclusion on the future potentials of this Industry.

There has been modest growth in the GNP at constant prices (1980–81 base), the growth rate being somewhat more than the rate of growth of population.[1] The population growth rate over the years has reduced to some extent. The quantitative index of industrial production has grown at compound rate of more than 7%. The total exports as well as imports have also grown over the years. All these macro-economic parameters depict a favourable climate for growth and expansion of business in general, and this would hold good for the Pharma and Diagnostics business as well. However, the per capita GNP during 1988–89 was only Rs. 4765 at current prices, and this is rather low. Therefore, one may think that a high level of sophisticated Diagnostics cannot be expected to be developed for percolation among the masses. It may, however, be mentioned that the top 10% of the Indian population has a share of 34% of the national income and the next 10% has another 16%.[2]

Thus, the top 20% has 50% of the national product to itself.. Compounded to this is the fact that practically the whole of this rich class is urban. Thus,20% of the current population which is about 160 million is the population sector which is the "real market" for the current sophisticated diagnostics in the private sector. This population is larger than that in many developed countries.

Besides the targeted population the budget for diagnostics is expected to be enhanced in Government hospitals, as more emphasis is going to be put on accurate diagnosis using sophisticated kits and tests. In this direction specially as the Defence and Railways, which employ very large

work force, lay its emphasis on accurate and quick diagnosis, the Government market shall substantially rise. Government budget for certain disease diagnosis specially for Acquired Immuno Deficiency Syndrome (AIDS) and Viral hepatitis (Hepatitis B) is going to increase substantially due to current deliberate emphasis by the Govt. to screen the blood samples or blood products in view of the potential dangers of spread of these diseases, specially through usage of contaminated blood and blood products. All such efforts would have profound effect in increasing the Government market substantially.

Medical Set up and Infrastructure

The following table indicates the number of hospitals and beds therein, in India as on 1.1.1987[3]:

TABLE -II Hospitals and beds therein

Particulars of hospitals and beds	Urban (Nos)	Rural (Nos)	Total (Nos)
Total number of hospitals:	6637	2966	9603
Total number of beds:	484494	89084	573578
No. of hospitals having more than 100 beds:	1065	148	1213

Of these 9603 hospitals, 4214 are in the Government sector (including Central, State Government and Local Bodies, etc.), 4454 in the Private sector and 935 belong to Voluntary Organisations. There were 125 Medical Colleges as of 1987-88[4].

The total number of doctors possessing recognised medical qualification under IMC Act was 331630 as on 1987[4]; besides, there are 9796 registered Dentists as on 1988[4]. The total number of qualified pathologist (Postgraduates) could not be correctly ascertained; however, based on the discussion with several doctors and pathologists, the numbers have been estimated at 2000 only as of now[6].

Taking all the above into consideration, it could be concluded that for sustaining a fairly moderate level of diagnostic market, the infrastructure is quite impressive.

Diagnostic Laboratories in the Country

As indicated earlier, there are 9603 hospitals in the country,most of which provide services for pathological examination of the body fluids of human. However, as mentioned above, most of the hospitals are situated

in the urban areas; the medical services are therefore disproportionately available to the people residing in the cities although a large portion of the population resides in villages. The hospitals primarily offer the simple and inexpensive services of examination of stool, urine , blood and other body fluids for chemical, microscopic and culture analysis; the Government hospitals usually offer such services free of cost to the visiting patients. Hospitals offering free services or charging nominal fees are often very crowded and it becomes quite a task to avail of the services by putting considerable effort and spending much time. Consequently, a large number of patients avail of the private services for such basic investigations; because of this many pathological laboratories have grown and flourished in cities in the private sector. Over the years, the market for the basic clinical investigations have thus grown to substantially visible levels. There is unfortunately however, no precise estimate of the numbers of such diagnostic laboratories in the country.

The author talked to a large number of representatives selling diagnostic kits and reagents as also a number of leading pathologists. Based on feed back information from such interviews, taking into consideration that 90% of the hospitals in the country have attached pathological laboratories, and having regard to the sale of reagents and kits by about a dozen of leading suppliers to the various pathological laboratories in the country, an estimate has been made based on intelligent assessment, taking into consideration the work-load of laboratories per day, about the probable number of laboratories currently existing in the country as indicated below:

TABLE III. Estimated number of pathological laboratories in the country and their daily work load

No. of Laboratories	Estimated daily work load (No. of Tests)
75 to 100	More than 400 upto 2000
325 to 400	More than 300 but less than 400
1300 to 1500	More than 150 but less than 300
2500 to 3000	More than 50 but less than 150
6300 to 7000	More than 10 but less than 50
2500 to 3000	Less than 10

Total 13000 to 16000 Say 14500

All these laboratories do at least some analysis of clinical chemistry tests. Most of these also carry out haematology total count, differential count, haemoglobin percentage, blood grouping, urine analysis, stool examination and pregnancy testing. A total of about 1500 laboratories

perform HBsAg test, which include clinical testing for hepatitis as well as screening of blood in blood banks. Around 500 laboratories including blood banks carry out HIV testing; this number is however, going to increase. About 1,000 laboratories do microbiological culture and antibiotic sensitivity tests. There are also about 500 laboratories which perform tests for hormones and steroids by non-radio isotopic methods and most common tests are for T3, T4 and TSH levels. Besides, there are about 150 laboratories which are engaged in RIA for hormones and steroids. Taking into consideration, these above number of pathological laboratories and considering on an average 250 working days per annum, the estimated total number of tests being carried out in the country currently has been placed at 220 to 260 million annually.

Incidence of Diseases in India

The growth of diagnostics market is related to the load of the incidence of diseases as well as to the medical facilities available for diagnosis. The status of general medical infrastructure including qualified manpower has been profiled previously. Table-IV indicates the common infectious diseases in the country. The diseases have been classified based on the causative agents which are of viral, bacterial, fungal, protozoal and helminthial origin.

TABLE IV. Common infectious/communicable diseases in India

VIRAL INFECTION

1. Influenza
2. Acute Respiratory Viral Infection
3. Herpes including Cytomegalovirus and chicken pox
4. Japanese Encephalitis
5. Hepatitis A
6. Hepatitis B
7. Hepatitis Non A Non B
8. Rotaviral gastroenteritis
9. Measles
10. Mumps
11. Rubella
12. Arboviral infection including dengue & KFD
13. Rabies
14. Poliomyelitis
15. Acquired Immuno Deficiency Syndrome (AIDS) (HIV–I and II)

TABLE IV. (Contd.)

BACTERIAL INFECTION

1. Streptococcal Infection
2. Staphylococcal Infection
3. Meningococcal Infection
4. Pneumococcal Infection
5. Typhoid and Paratyphoid fevers
6. Escherichiosis
7. Gonococcal Infection
8. Syphilis
9. Salmonella Gastroenteritis
10. Dysentery (Shigellosis)
11. Cholera
12. Infection by Klebsiella
13. Tetanus
14. Diphtheria
15. Pertussis (Bordetella)
16. Tuberculosis
17. Leprosy
18. Chlamydial Infections
19. Haemophilus influenzae
20. Infection by Pseudomonas aeruginosa and P. pseudomallei (melioidosis)
21. Gas Gangrene
22. Brucellosis
23. Food poisoning (Clostridium botulinum, C. fringens, etc.).
24. Actinomycosis

MYCOSES

1. Aspergillosis
2. Candidosis
3. Dermatomycosis
4. Coccidioidosis
5. Sporotrichosis
6. Chromomycosis
7. Cladosporiosis

PROTOZOAL INFECTIONS

1. Amoebiasis
2. Giardiasis
3. Malaria
4. Toxoplasmosis
5. Trypanosomiasis
6. Trichomoniasis
7. Leishmaniasis

HELMINTHIASIS

Nematodiasis

1. Filariasis
2. Ascariasis
3. Strongyloidiasis
4. Ankylostomiasis
5. Dracunculiasis
6. Trichocephaliasis
7. Enterobiasis

Trematodiasis

8. Fasciolopsiasis
9. Heterophyiasis
10. Clonorchiasis
11. Paragonimiasis
12. Schistosomiasis

Cestodiasis

13. Cysticerosis
14. Taeniasis
15. Hymenolepiasis
16. Taeniarhynchiasis

Diagnosis of many of these diseases can be accurately made by carefully observing the main syndromes. In certain cases, however, the syndromes are not adequately pronounced; their rapid and correct diagnosis would enable the starting of correct therapy which is important and essential in certain situations, as delay could cause severe complications.

The incidence of many of these diseases in India is not precisely known, nor has any agency carried out detailed epidemiological studies. It is however, felt necessary to list out the important diseases to draw the attention of the planners to the fact that accurate diagnostic devices are required for many of these diseases, even to enable agencies to carry out the epidemiological studies. Currently, however simple to perform diagnosing devices are not available for many of the above listed diseases. Certain known biological methods of examination are laborious and time consuming; they are not suitable for field application. Rapid methods of diagnosis based on serology or other body fluid examination thus needs to be developed and standardised. Research is therefore required to be intensified and strengthened within the country in several disease areas.

Besides communicable diseases, a large number of noncommunicable ones have also started rising very fast and death rates due to these are on the increase. These include heart diseases, hypertension,rheumatic diseases, diabetes, cancer, etc. It is necessary that quick and much earlier diagnosis of these diseases is developed and made available to the society. Currently some of these are detected by the use of imported expensive test systems or kits.

The following Table–V indicates[5] some common diseases along with their incidence.

TABLE V. Estimated incidence of some common diseases in India

Diseases	Estimated Incidence (Nos. in million) 1990 AD	2000 AD
Communicable		
1. Tuberculosis	14	15
2. Leprosy	8	9.5
3. Amoebiasis	240	285
4. Diarrhoea(Total bouts/Year)	444	526
5. Typhoid Fever	40	48
6. Helminthiasis	320	340
7. Filariasis	42	50
8. Respiratory Tract Infection		
a) Upper Tract	80	95
b) Lower Tract	12	15
c) Combined	30	35

Table V. (Contd.)

9.	Malaria	40	19
10.	Veneral Diseases	47	61
Non communicable diseases			
1.	Heart diseases	26	38
2.	Hypertension	38	55
3.	Rheumatic diseases	3.5	4
4.	Anaemia	17.9	223
5.	Diabetes	19	25

No precise estimates are available on the incidence of Cancer and Hormonal diseases. Currently, there has also been wide-spread concern over the spread of AIDS, specially in the metropolitan cities, for which the incidence is not yet correctly ascertained.*

Accurate, speedy and timely detection and diagnosis of diseases is vital for any correct therapy. India has a high incidence of several diseases as partly depicted above. Compounded to this is the rapid growth of population. Early detection of pregnancy would greatly contribute towards the success of population control programme. The current births are placed at 24–25 million per annum[6]. The number of females in the reproductive age groups is estimated at 120–125 million. The estimated cases requiring detection and confirmation of pregnancies would therefore be quite high. In this connection, it is stated that a surprisingly large percentage of the eligible couples in this country are unable to bear children. Currently, such couples are estimated at 4 – 5 million. There could thus be a large demand for ovulation tests also. From the above, the current potential market for Diagnostics has been estimated by the author as under (Table -VI):

* The first AIDS case in India was detected in May 1986. Thereafter in the serosurveillance programme of the Government upto the period of 30th September 1991, nearly 1.13 million blood samples of various risk groups were analysed and 5879 cases were found to be seropositive to HIV–I infection, 85 numbers of cases of full blown AIDS were found. The surveillance had been intensified and currently there are 62 centres spread all over the country in 23 states. The states having maximum seropositives to HIV–I infection currently are Maharashtra, Tamil Nadu and Manipur. Recently HIV–II infection has also been noticed in Maharashtra and nearly 8 to 10% of the very high risk groups having HIV infection are identified to be having HIV–II infection. The AIDS situation has thus become alarming in India.

TABLE VI. Estimated potential number of tests currently required

Particulars		Estimated current No. of tests required (potential) per annum (Nos. in million)
1.	Early pregnancy	50 – 60
2.	Tuberculosis	15 – 20
3.	Leprosy	2 – 5
4.	Typhoid Fever	3 – 5
5.	Amoebiasis	20 – 25
6.	Diarrhoeal Diseases (Rota virus, E.coli, etc.)	5 – 10
7.	Filariasis	20 – 25
8.	Hepatitis B	3 – 5
9.	AIDS (HIV–I and II)	3 – 5
10.	Malaria	20 – 25
11.	Veneral Diseases	3 – 5
12.	Rheumatic Diseases	2 – 3
13.	Cancer	1 – 1.5
14.	Hormone Tests (Sex hormones, T3,T4, etc.)	1 – 1.5
15.	Ovulation Tests	1 – 1.5
	Total	**150 – 199**

Taking the selling price of one rapid test at about Rs.10 on the average, at manufacturers and suppliers level, the current potential market would work out to at least Rs. 1500–2000 million. This is besides the potential market for clinical chemistry. The potential for clinical chemistry is estimated at another Rs.500–600 million. Thus, the total potential market for Diagnostics could be about Rs. 2000–2600 million. The real market is, however, much smaller as indicated in the subsequent paras.

The potential market for the diagnosis of ailments and physiological conditions of the body estimated at Rs.1500–2000 million is based on the principles of immunology. Such tests would be based on antigen to antibody binding principles which would be presented as tests like Latex Agglutination (LAT). Enzyme-Linked Immunosorbent Assay (ELISA), Radio Immuno Assay (RIA), Immunofluorescence (IF), Indirect Hemoagglutination (IHA), Visual colour change (VCC), etc. Several tests would also be based on Nucleic Acid Probes (NAP). The current actual market for Immunodiagnostics and Nucleic Acid probes (current real market for probes is almost non-existent)is, however,only about Rs. 100 – 110 million as indicated later. The author thus concludes that this market has not yet been adequately harnessed by the Industry.

An Analysis of Current Real Market of Diagnostics

The diagnostics market in real terms during the last 3 years has been placed by the author as under (Table-VII) which also indicates the pharmaceutical market during the corresponding year. The figures of diagnostics market are projections made by the author based on feed back from the representatives of the leading companies in the business as shown in Table VII.

TABLE VII. Diagnostics and pharma market in India

Year	Diagnostics market (Rs. Million)	Pharma market (Rs. Million)	Diagnostics market as % of Pharma market
1987	200	23500	0.85
1988	235	26900	0.87
1989	320	31900	1.00
1990	410	35600	1.15

It will be seen from the above that the Diagnostics market is increasing fast and is growing at a rate of more than 25% per annum.

The share of different classes of products as projected by the author during 1989 is placed below (Table -VIII):

TABLE VIII. YEAR – 1989.

Classes of Products		Turnover Value (Rs. million)	Turnover Value as % of total
1 *Clinical Chemistry including enzyme based, non-enzyme based determinants and related small instruments*		152	47.5
2 *Infection disease testing:*			
– Hepatitis B	18		
– Streptococci	5		
– Veneral diseases	3		
– Malaria	3		
– Rubella,Mumps and			
– Measles	4		
– Amoebiasis	1		
– Toxoplasmosis	0.5		
– Hepatitis A and C	0.5		
– Others	2.0		
	37.0	**37**	**11.6**

TABLE VII (Contd.)

3. *Physiological status of body fluid and non-infectious disease testing:*			
– Early Pregnancy	34		
– Immune diseases including rheumatoid factor	20		
– Cancer markers	12		
– Hormone estimation	10		
– Others including ovulation, allergies, etc.	5		
	81	81	25.3
4. Haematology including blood grouping, blood banking and coagulation		50	15.6
Total		**320**	**100.0**

It will be seen that clinical chemistry tests comprise the bulk of the market. The area is comparatively competitive and prices are comparable among the competitors. The infectious diseases detection market is currently small and comparatively non-competitive. The testing kits are usually imported and are proprietory in nature. The products are highly priced. The market has not yet grown adequately. The market has not even been adequately promoted. The market for Hepatitis B and AIDS tests mostly belong to Government. So far, bulk of the AIDS kits within the country have been obtained through the WHO. The Government infrastructure for blood screening is however being strengthened. It is anticipated that within a short period from now, the market for both these kits shall shoot up suddenly and substantially both in the Government sector as well as in the private sector as soon as the Government infrastructure is strengthened and as the programmes on public awareness are intensified. Among the non-infectious disease testing systems and others early pregnancy detection tests are becoming increasingly popular. The market is also becoming highly competitive. Incidentally, this is currently the largest of the immuno diagnostic market and the demand is increasing steadily. Tests for the detection of immune diseases, cancer, hormones including sex hormones, corticosteroids and thyroid hormones, as well as those for ovulation are proprietory and highly priced. The market is not yet competitive.

This is also true for haematology tests although substantial indigenous capability for blood grouping sera has been developed. The current unit prices of common tests both in the area of clinical chemistry as well as rapid modern methods have been dealt with separately in subsequent paras.

Major Diagnostic Companies And Existing Production Base:

The diagnostics market is substantially held by a handful of companies whose number will not exceed 25; the total number of companies including the traders may however, be around 100.

Major companies having substantial hold in the market are the following:

1. M/s. Ethnor Ltd. (Ortho Diagnostic system), Bombay
2. M/s Span Diagnostics Pvt. Ltd., Surat
3. M/s. Miles India Ltd., Baroda
4. M/s. Boehringer Knoll Ltd., Bombay
5. M/s. Hoechst India Ltd.(Behring Diagnostics),Bombay
6. M/s. Ranbaxy Diagnostics, Delhi
7. M/s. Bhaba Atomic Research Centre, Bombay
8. M/s. Abbot Laboratories SA, USA(Through M/s.D.P. Medical Diagnostics Pvt.Ltd., Bombay).
9. M/s. Decruz Corporation , Bombay
10. M/s. Sri Krishna Kesab Laboratories, Ahmedabad
11. M/s. J.Mitra & Co.,Delhi
12. M/s. Stangen Laboratories , Hyderabad.
13. M/s. Sigma Laboratories, Bombay
14. M/s. Accurex, Bombay
15. M/s. High Tech., Bombay
16. M/s. Trans Asia, Delhi
17. M/s. Wellcome Diagnostics UK(Through M/s Anand Brothers & Co. Bombay)
18. M/s. Technicon, USA (Through M/s. Blue Star Ltd, Bombay)
19. M/s. Intercare India Ltd, Calcutta
20. M/s. NR Jet Pharmaceuticals Ltd, Bombay.

Several new entrants holding substantial potential for future growth are the follwing :

1. M/s. Cadila Laboratories Ltd.(Diagnostics Division), Ahmedabad.
2. M/s. Lupin Diagnostics Ltd., Bhopal
3. M/s. Infar India Ltd., Calcutta
4. M/s. Pharmacia United,. Bangalore
5. M/s. Rallis India Ltd., Bombay
6. M/s. Merck Diagnostics, Bombay
7. M/s. Amarsham Ltd., UK. (Through M/s Star Ltd., Bombay)

Production facilities with matching R&D investment has been made only by few companies. Based on the feed back information from the representatives of various companies, the following compilation has been made about the companies specialising in production of diagnostics in the country alongwith their specialities (Table IX).

Prices of diagnostic tests:

While the immunodiagnostic tests and nucleic acid probes are devices of modern origin, the clinical chemistry tests are comparatively older but are

Table IX. Major Producing Companies with Specialisation in Product Areas

Sl.	Companies	Specialisation in product areas
	M/s.Ethnor Ltd, (Ortho Diagnostic System)	— Blood Grouping Sera — IHA tests — Clinical Chemistry — Latex Agglutination
	M/s. Span Diagnostics, Surat	— Latex Agglutination tests — ELISA kits for Hepatitis B — Clinical Chemistry
	M/s. Hoechst India (Behring Diagnostics), Bombay	— IHA tests — Latest Agglutination tests — ELISA kits for Hepatitis B
	M/s. Miles India, Bombay	— Urine test strips — Blood Glucose test strips — Clinical chemistry
	M/s. Bhaba Atomic Research Centre, Bombay	— All Radio labelled products
	M/s. Ranbaxy Diagnostics, Delhi	— Latex Agglutination tests — ELISA tests
	M/s. Cadila Laboratories Ltd., Ahmedabad	— ELISA kits for Filariasis — Blood Grouping
	M/s. Trans Asia, Delhi	— Clinical Chemistry
	M/s. Lupin Diagnostic Ltd., Bhopal	— Immunoglobulins & conjugates — ELISA Tests — Particle agglutination tests
	M/s. NR Jet Pharmaceuticals Ltd., Bombay	— Clinical Chemistry — Latex immuno assays

M/s. Boehringher Knoll Ltd., Hyderabad	— Clinical Chemistry — Serological products
M/s. Accurex Diagnostics, Bombay	— Clinical Chemistry
M/s. J. Mitra & Co., Delhi	— Clinical Chemistry

Source: Based on Market Studies by the Author.

relatively much more in use.. As a result, the clinical chemistry tests are in a more competitive environment than the other modern testing devices. Moreover, most of the tests require bulk of simple reagents and chemicals which are manufactured by a large number of small companies. The eventual result is that many clinical chemistry tests are comparatively much cheaper than the modern immunodiagnostic or other tests.

The following table would indicate the comparative prices per test of various classes of products currently available (1990) in the Indian market. The prices are based on information obtained from the current price lists of some important companies; these do not include special prices which the manufacturers or traders offer on special purchases. The table is illustrative only and not exhaustive.

TABLE X Unit Prices of Clinical Chemistry Tests as well as Immunodiagnostics Tests of Leading Companies.

Particulars	Companies Marketing	Prices per test (Rupees)
A. Clinical Chemistry		
(i) Blood glucose	Ranbaxy	0.50
	Ortho	0.55
	Span	0.60
	Miles	0.60
	Boehringer	0.80
	Technicon	1.00
(ii) Blood urea	Ortho	3.00
	Span	3.40
	Srikrishna	3.50
	Miles	3.50
	Ranbaxy	3.80
	Technicon	5.00
	Boehringer	6.00
(iii) Uric acid	Span	5.00
	Ortho	5.40
	Miles	6.10

TABLE X (Contd.)

Particulars	Companies Marketing	Price per test (Rupees)
(iv) Blood grouping Sera **	Span	5.50
	Sri Krishna	6.50
	Ortho	9.00
(v) Cholesterol	Span	3.50
	Ortho	3.80
	Ranbaxy	3.80
	Sri Krishna	4.00
	Miles	4.00
	Technicon	5.00
	Boehringer	6.00
(vi) Triglycerides	Miles	11.50
	Span	12.40
	Ranbaxy	13.00
	Technicon	14.00
	Ortho	14.50
	Boehringer	16.00
(vii) Haemoglobulin — Total count	Miles	2.00
	Pharmacia	6.00
	Technicon	8.00
—Differential count	Pharmacia	7.00
	Technicon	10.00
(viii) SGOT/SGPT	Span	4.00
	Ranbaxy	4.95
	Ortho	5.50
	Miles	5.50
	Boehringer	11.00
	Technicon	12.00
(ix) Electrolyte Na/K	Boehringer	5
	Miles	5
	Pharmacia	5
	Technicon	5
	Abbott	6
(x) Urine Glucose and protein	Span	0.80
	Miles	1.00
	Boehringer	2.00

B. Special Tests including Immunodiagnostics with formats (Latex,ELISA etc.)

(i) Early pregnancy detection:		
Latex	Span	9.00
	Ortho	9.25
		11.75 (Higher sensitivity)
	Ranbaxy	10.00
	Srikrishna	11.60
ELISA	Srikrishna	25.00
	Span	22.00
	Wellcome	38.00
Others	Ortho	48.00 (Card,Single step)
	Span	40.00 (do)
	Abbot	40.00 (Card,three steps)
	Ranbaxy	33.00 (Cup)
	Span	26.00 (Cup)
	Intercare	25.00 (SPIA)
(II) Hepatitis—B		
Latex	Span	8.00
	Ortho	9.50
	Srikrishna	10.00
ELISA	Behring	13.00
	Ranbaxy	12.00
	Ortho	10.00
	Span	10.00
	Abbott	15.00
	Wellcome	23.00
	Pharmacia	12.00
	Infar	20.00
RPHA	Span	6.00
	Boehringer	7.00
(iii) HIV ELISA	Span	25.00
	Ortho	25.00
	Ranbaxy	20.00
	Abbott	28.00
	Wellcome	32.00
	Pharmacia	28.00
	Infar	22.00
(iv) T_3/T_4 ELISA	Span	22.00
RIA	Pharmacia	16.00

** Prices are per ml of blood grouping sera

B. Special Tests including Immunodiagnostics (contd.)

Particulars	Companies Marketing	Prices per test (Rupees)
	BARC	9.00
(v) TSH ELISA	Span	25.00
	Boehringer	33.00
	Miles	28.00
	Ranbaxy	40.00
	Abbott	25.00
RIA	Pharmacia	16.00
	BARC	10.00
(vi) FSH ELISA	Boehringer	55.00
	Abbott	30.00
	Infar	50.00
RIA	Span	15.50
	Pharmacia	16.00
	BARC	12.00
(vii) LH ELISA	Boehringer	55.00
	Abbott	30.00
	Infar	50.00
RIA	Span	12.00
	Pharmacia	16.00
	BARC	12.00
(viii) PRL ELISA	Boehringer	65.00
	Abbott	35.00
RIA	Span	27.00
	Pharmacia	24.00
	BARC	20.00
(ix) Glyco haemoglobin	Boehringer	90.00
	Span	37.50
	Pharmacia	55.00

The table shows clearly that the Clinical Chemistry tests are comparatively cheaper. It also shows that there is more variation in the prices of speciality tests including the immunodiagnostic tests, than clinical Chemistry tests. One of the reasons for more variations in the prices of speciality tests is that several internationally reputed manufacturers are exploiting their proprietory brand image and are keeping prices higher.

Government intervention and promotion

Realising the value of early diagnosis and also having regard to the scientific infrastructure already developed within the country and also taking into consideration the basic scientific work carried out in several laboratories, the Government of India felt the need to harness the infrastructure for the indigenous development of simple, easy-to-use, inexpensive, sensitive and specific immunodiagnostic testing kits. The work was assigned to the Department of Biotechnology (DBT) in 1987. The author was and is currently a part of the administrative infrastructure looking after the promotion of the immunodiagnostic market in the country through indigenous research.

The DBT is working to promote research in diagnosis of diseases relevant to India in various R&D laboratories in the country. The diseases on which emphasis have been laid are Tuberculosis, Leprosy, Filariasis, Typhoid Fever, Viral hepatitis, Diarrhoeal diseases; Amoebiasis, Malaria, Leishmaniasis, Toxoplasmosis, Brucellosis, Streptococcal infection, Aspergillosis, Schistosomiasis and certain types of cancer. The Institutes being funded are National Institute of Immunology, N.Delhi; All India Institute of Medical Sciences, N. Delhi; Post Graduate Institute of Medical Education & Research, Chandigarh; Institute of Research in Reproduction, Bombay; Mahatma Gandhi Institute of Medical Sciences, Wardha; Institute of Chemical Biology, Calcutta; Trivandrum Medical College, Trivandrum; Cancer Research Institute, Madras; Hindustan Antibiotics Ltd., Pune etc.

As a number of Institutes have been working earlier also on developing system for diagnosis, a country-wide review was undertaken by the DBT on the status of work done in various laboratories and their commercialisability through industries. This review revealed that the knowledge-base developed in certain Institutes were ripe for producing workable commercial kits for early diagnosis of Filariasis, Amoebiasis, Typhoid fever, Malaria, detection of pregnancy and blood grouping.

Industries were contacted by the DBT with a view to commercialise these technologies. In cases where the Institutes had directly contacted the industry and sought the help of DBT, the Department had closely coordinated the interaction to facilitate the transfer of technology to the Industry. Several industries have shown interest in such interactions. As a result of interventions by the DBT, an agreement was signed between Mahatma Gandhi Institute of Medical Sciences, Wardha and M/s. Cadila Laboratories Ltd., Ahmedabad for manufacture and marketing of Filaria kits. The kit was released in the market in September, 1989. Subsequently,

more agreements were signed; one between Ranbaxy Laboratories, Delhi and National Institute of Immunology (NII), N. Delhi for introducing early pregnancy detection kit, one between M/s. Rallis India Ltd., Bombay and NII, N. Delhi for introducing kits for the detection of Typhoid fever and Amoebic Liver Abscess; one between NII and Cadila for blood grouping sera and the other between M/s. Karnataka Antibiotics & Pharmaceuticals Ltd., Bangalore and Astra-Research Centre, Bangalore alongwith Indian Institute of Science, Bangalore for early detection of malaria (Table XI). The early pregnancy detection kit has already been introduced by Ranbaxy in the market. Many more agreements are in the offing.

TABLE - XI MOUs Signed Between Institutes & Industries

— Early pregnancy detection.
— Filariasis detection
— Hepatic Liver Abscess detection
— Typhoid Fever
— Malaria
— Blood Grouping Sera

Source: Department of Biotechnology, Govt. of India, New Delhi.

Based on the research leads already achieved at several Indian Institutes, it is expected that sensitive, reliable and in-expensive kits for the early detection of the following diseases may be developed and marketed through purely Indian research efforts during the next 5 years (Table XII):

TABLE XII Diagnostic Tests in The Pipe-line: 1991.

— Tuberculosis including Tubercular meningitis
— Leprosy
— Hepatitis A
— Hepatitis B
— Encephalitis
— Leishmaniasis
— Rotaviral gastroenteritis
— Acquired Immunodeficiency Syndrome
— Streptococcal Infection
— Escherichiosis
— Shigellosis
— Aspergillosis
— Candidosis
— Toxoplasmosis
— Filariasis
— Schistosomiasis

Source: Department of Biotechnology, Govt. of India, New Delhi.

There are a number of areas where indigenous capability does not exist yet e.g. detection of AIDS. Realising this, on request from the Ministry of Health, the DBT took up the task of bringing the current contemporary technologies from abroad. In the first phase, after evaluating nine internationally reputed kits through the assistance of the Indian Council of Medical Research (ICMR), Delhi and after discussing with three companies whose kits were found to be satisfactory in ICMR evaluation, recently one company has been selected for the setting up of basic manufacturing facilities in India for the production of AIDS kits: More companies shall be evaluated in future in similar ways for inducting contemporary technologies from abroad.

The appropriate agencies in the government would also examine issues related to duties on finished kits and raw materials required for their production. The intention is to rationalise the process so as to promote indigenous production of kits in the country with a view to make abundant availability of kits at reasonable prices.

Discussion and issues for consideration:

(i) Diagnosis of a disease by a method—be it microscopic, cell culture, serological or other biological methods—gets established initially through the clinicians. The clinicians are to be first convinced about the efficacy of the tests. At this stage, all the established methods of promoting a drug formulation in pharma business as are used by the manufacturers and the marketers for establishing initial market entry are also used for promoting the new diagnostic tests. These include dissemination of product information and literature, exhibition of efficacy results, arranging seminars, arranging periodic demonstration of tests by mounting experiments at hospitals and laboratories, regular visits of influential clinicians to constantly keep them updated, liberal sampling of products to hospitals and pathological laboratories,establish linkages between the clinicians and the pathological laboratories, offering attractive trade discounts etc., and at the same time maintaining efficient distribution chain and keeping continuously high quality standards of product performance. Once the tests are established among the clinicians, their role gets thinned down and the controlling authority of the product market gets transferred to and starts getting tuned in the hands of pathologists. At this stage if more than a manufacturer exists , the acceptability depends largely on how the pathologist reacts to each of these tests. Scientific merits of the tests including sensitivity, specificity and simplicity no doubt play significantly important role in the choice; however, other business practices

and the comparative advantages may score over scientific and other merits. New entrants in the diagnostics business would have to keep these aspects in mind.

(ii) Setting up of pathological laboratories in India does not require any permission under Drug Act. Any person desirous of setting up a laboratory can do so and start the business just by obtaining a trade licence from the State authorities, like starting any other business activity. This status is very disadvantageous from the point of view of quality checks and the requirements of maintaining minimum standards. All such standards are self-driven and it is for the individual owner to decide how he would like to maintain standards. This situation needs a change, keeping the interests of the patients in view; the current situation does not either guarantee accuracy of the test results nor any legal responsibility on the laboratory performing the tests.

(iii) All diagnostic products including kits are classified as drugs under the current Drugs Act of the country even though most of the tests are in-vitro ones. These products may fall under the Schedules C/C-I of the Act. While there is adequate in-country capability of checking the quality of the products and reagents used for chemical analysis of parameters of body fluids, there is inadequate infrastructure in the country, to check the quality of Immunodiagnostics. There is no Government laboratory to draw samples and check the quality nor there is yet adequate consolidated expertise. Interestingly, for many tests even the standards are not known; consequently, it would not be possible to design and mount experiments for quality checking of products. This situation has resulted in the introduction of all sorts of tests in the market by imports. As per the current law, the trader/supplier has to obtain a certificate from the manufacturer about the quality of the product and that is the end of it. The cold chain which has to be consistently maintained countrywide as well as at the cargo handling facilities at the airports is also a problem. The need for the quality check in India before use cannot thus be over-emphasised. Therefore, Government quality controlled laboratories need to be set up without delay; during the intervening period certain existing institutes in the country may be suitably equipped and may be attached to the quality control authorities of the Drug control Administration for enabling atleast random checking of the efficacy of the marketed products.

(iv) As the diagnostic tests are varied and include specialised knowledge in several branches and as there is no standard operating

procedure (SOP) for testing as well as quality checking of these products, it is necessary to select a panel of experts (POE) at national level to develop SOP, provide feed back market information of satisfaction using the kits and advise Government on the steps to be taken for introducing newer tests. The panel should also have experts to study the market demand and should take steps to promote the concepts of newer diagnosis by organising training, demonstrations and quality control workshops. They should also prepare manuals and disseminate necessary information to the professional bodies like the Indian Medical Society , the Indian Immunology Society, etc. as also to the Drug Control Authorities.

(v) As more testing systems using the procedures of immunology and nucleic acid probes are getting introduced into the market and as these tests are often associated with the usage of sophisticated and complicated equipments, the training of technicians on newer diagnostic machines is of greater importance. The need for the maintenance and repairs of instruments performing such tests is also increasing. This situation is getting further aggravated in view of the non-existence of manufacturing bases of such machines in the country. While setting up of factories for manufacturing the machines is a long drawn affair, the minimum one could do is to obligate the setting up of maintenance, repair and training facilities by each party marketing kits when these are linked with usage of specialised equipments. Besides other advantages, this would create many job opportunities.

(vi) Many diagnostic tests require radio-isotopes, very few of which are being produced within the country. Bhaba Atomic Research Centre (BARC) controls the distribution and the use of radio immuno assays(RIA)in the country. However, the market is still mostly controlled by foreign companies, who supply RIA probes at exorbitant prices. Moreover, due to their short life, there is enormous problem in coordinating and scheduling their supplies. With a little attention and effort many such RIA probes could be made inhouse. BARC could study the market and evolve methods for enabling us to import-substitute and simultaneously develop indigenous capabilities.

(vii) Cold chain is an infallible infrastructure for the success of the immunodiagnostics and nucleic acid probe tests. As currently most of the products are imported, the airport refrigerators and cold rooms are utilised during the entry of the products into the country . However, very often the importance of continuous preservation in cold condition is not appreciated

and such products are stacked in room temperature outside the cold room for several days. One can imagine the risks of deterioration of such products in adverse preserving conditions. It is thus necessary that there is close liaison among the concerned authorities including the customs as also the suppliers so as to minimise the exposure of the products to adverse climatic conditions. This situation shall be very relevant to the Indian producers also as the market grows and the consumption increases within the country, and as the need for wider distribution arises throughout the country. The design of appropriate package, the choice of coolants, the reliability of transport, specially the airways, and the availability of refrigerators at the consumer's end are factors which would decide the successful dissemination of the products throughout the country.

(viii) Diagnostic business in clinical chemistry is highly competitive and the prices per test are comparatively less expensive. For immunodiagnostic tests including Latex, ELISA,RIA, SPIA, etc., the manufacturers have been enjoying proprietory brand advantages and products are relatively highly priced (Table X). As the market grows and as the real competition increases in the marketplace, it is anticipated that the general business trend shall be on reducing the unit prices and introducing newer and effective systems in keeping with the needs of the customers. This is when the proprietory advantages of brands shall give away to the cost effective products; thus situation shall however come into play not before another 5 years as the Indian market is just developing on rapid and modern testing methods.

(ix) The country does not yet have adequate number of skilled technicians. The profession is still dominated by the low paid technicians. Moreover, the profession is believed to be potentially hazardous and therefore, many do not like to choose this as a career. The net result is shortage of skilled work force and the consequent difficulties in modernising existing laboratories using automated systems. The situation shall however improve as we move along, and as the market grows further to sustain a higher turn-over and enable investors to make more profits so as to enable them to recruit more numbers of well-paid, skilled technicians.

(x) Most of the testing systems and formats available in the market require a laboratory to perform the tests. Testing formats usable by the patients for self-testing have just started coming in, namely the early detection of pregnancy or the self monitoring of sugar in urine or even in blood. There is clear scope for introducing such products in the market

specially for the detection of certain situations like blood in fecal matter, blood sugar, urine parameters, certain communicable diseases and of course early pregnancy. This is also intimately connected with the knowledge level of the users and therefore public programmes in creating awareness in these directions would go a long way.

(xi) The R&D base in the industry in the area of modern diagnostics is almost non-existent; only few companies have established some infrastructure during the recent years. The research base which is expected to be a blend of modern microbiology, immunology, hybridoma technology, genetic engineering, protein and oligonucliotide chemistry, polymer science, separation technology including various types of affinity chromatography, microscopy including EM etc., has not yet been set up by any industry. The modern techniques of rapid diagnoses need a fairly good research base to sustain a technology procured from elsewhere; for innovation and new product development, the base has to be even stronger. As the setting up of modern laboratories with good infrastructure in many of these areas would need substantial investment and as the diagnostics market is very small in India, the investors would not find it really attractive to set up elaborate R&D infrastructure except the bare minimum that would be needed to sustain products, the technologies of which have been procured from outside sources. Indian companies may not thus be able to come out with innovative or improved versions of current products through their own efforts. However, they could take advantage of the modern infrastructure already set up by the Govt. at several premier institutes in the country by establishing linkages with them. There are already many existing methods for establishing such linkages like buying semifinished R&D results having potentials of being developed into products and technologies usable by the industry; sponsoring specific innovative or even developmental projects at institutes etc. Creation of such linkages among the industries and institutes are foreseen as major events during the next couple of years.

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