Recommendations of The Task Force on

Development of Manufacturing Capabilities in each Medical Vertical in Pharmaceutical Production

Department of Pharmaceuticals
Ministry of Chemicals and Fertilizers
Government of India

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Acknowledgements

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1. Department of Pharmaceuticals (DoP)
2. Ministry of Health & Family Welfare (MoHFW)
3. Drugs Controller General of India (DCGI)
4. All India Institute of Medical Sciences, New Delhi
5. Safdargung Hospital, New Delhi
6. Department of Biotechnology (DBT)
7. Pharmaceutical Export Promotion Council
8. Indian Pharmaceutical Alliance (IPA)
9. Indian Drug Manufacturers Association (IDMA)
10. Bulk Drug Manufacturers Association (BDMA)
11. Federation of Pharma Entrepreneurs (FOPE)
12. Organization of Pharmaceutical Producers of India (OPPI)
13. The Federation of Indian Chambers of Commerce and Industry (FICCI)
14. Confederation of Indian Industry (CII)
15. PHD Chamber of Commerce and Industry
16. The Associated Chambers of Commerce of India (ASSOCHAM)

Background

Availability of cheaper drugs, due to the Indian pharmaceutical industry in general and generic industry in particular, has contributed immensely in countering the disease burden in India. However, disease burden in India is still high and today India is facing a twin problem of pre-transition diseases i.e. diseases of under development as well as post-transition diseases i.e. diseases of affluence. This requires enhancing manufacturing capabilities of Indian pharmaceutical industry in various therapeutic categories, catering to different medical verticals like communicable diseases and non-communicable diseases, bio-pharma etc.

The communicable diseases are a major public health problem in the country. To control and eliminate various communicable diseases, specific national health programmes are being implemented in the country.

Around 2 million new cases and 0.2 million deaths due to tuberculosis are being reported every year in the country. Inspite of implementation of National Health Programme for control of TB, the Multi-Drug-Resistant Tuberculosis (MDRTB) and Extensively Drug-Resistant Tuberculosis (XDR-TB) are posing a great challenge to the programme. The drugs for treatment of TB including MDR and XDR are being manufactured and are available within the country. Yearly outbreak of Dengue and swine flu also poses a challenge for the government. There is a need to sustain both manufacturing and ready availability of these drugs along with research for new fixed drug combinations within the country.

Although in India, there is no regular system for collecting data on Non-Communicable Diseases (NCDs) but various reports suggest that India is experiencing rapid demographic and epidemiological transitions with a rising burden of Non-Communicable Diseases. NCDs cause significant morbidity and mortality both in urban and rural population and across all socio-economic strata in the country with considerable loss in potentially productive years (aged 35-64 years) of life. India leads the world with the largest number of diabetics and is sometimes referred to as the "diabetes capital of the world".

As per the WHO report, in India, NCDs are estimated to have accounted for 60 percent of all deaths in 2014, while 26 percent between the ages of 30-70 years have a probability of succumbing to one of the four diseases namely Hypertension, Cancer, Cardio–Vascular diseases and Diabetes. The report highlights the need to act immediately. It says that government must commit and set national NCD targets every year and implement policy and cost-effective interventions for prevention and control of major non-communicable diseases.

Availability of Blood products, Vaccines, Raw material/Intermediates, Fermentation based Antibodies & Vitamins, Monoclonal Antibodies, Recombinant-DNA products and

Regenerative Medicines play a key role in management of Communicable as well as Non-Communicable Diseases.

In view of the prevailing situation of communicable and Non-Communicable Diseases and to strengthen the disease management eco system, Department of Pharmaceuticals under the Ministry of Chemicals and Fertilizers was entrusted with the responsibility of a dedicated Task Force by the Prime Minister's Office to study the development of manufacturing capabilities in each medical vertical in pharmaceutical production .

Accordingly, the Department of Pharmaceuticals in December 2014, constituted a Task Force on "Development of Manufacturing Capabilities in each Medical Vertical in Pharmaceutical Production". The Major objective for constitution of the Task Force was to identify the gaps in production of drugs, vaccines, etc. in various therapeutic categories and to suggest remedial action.

Terms of Reference of the Task Force

The following were the Terms of Reference of the Task Force:

a) To identify focus areas for development of manufacturing capabilities in the respective medical vertical keeping in mind the specificities of each medical discipline.

b) Identify the gaps in domestic manufacturing in these verticals and suggesting ways to overcome them.

c) Identify the issues and support required from different government agencies and departments for achieving the manufacturing capabilities and filling the gap areas, if any, in each medical vertical.

d) Any other related issue which may come up during the Task Force meetings and which the Task Force may also like to include in the terms of reference.

Constitution of the Task Force

The constitution of the Task Force under the Chairmanship of Secretary (Pharma) was notified by the Department of Pharmaceuticals on 31.10.2014 as detailed below:

1. Secretary (Pharma) - Chairman
2. Representative of Secretary, Department of Health and Family Welfare
3. Representative of Drug Controller General of India
4. Representative of Secretary, Department of Commerce
5. Representative of Secretary, Department of Industrial Policy and Promotion
6. Director, National Institute of Pharmaceuticals Education and Research, Hyderabad
7. Representative of 2 NGO's working in Health Sector
8. Head of a Government Medical College in Delhi
9. Representative of Indian Pharmaceuticals Alliance (IPA), Indian Drug Manufacturers Association (IDMA) and Organization of Pharmaceutical Producers of India (OPPI).

Proceedings of theTask Force

The 1st meeting of the Task Force was held on 22.12.2014. In the meeting, it was decided to form the following three sub groups:

Sub Group 1: To look into issues related to Communicable Diseases

Sub Group 2: To look into issues related to Non-Communicable Diseases.

Sub Group 3: To look into issues related to Bio-Pharma, Prophylactics and OTC.

Composition of each subgroup was also decided as detailed below:

Sub Group on Communicable Diseases:

1. Chairman- Dr. R.S. Gupta, DDG(TB), DGHS
2. Member Secretary - IDMA
3. Co-opted Members, NGO's, Industry Associations

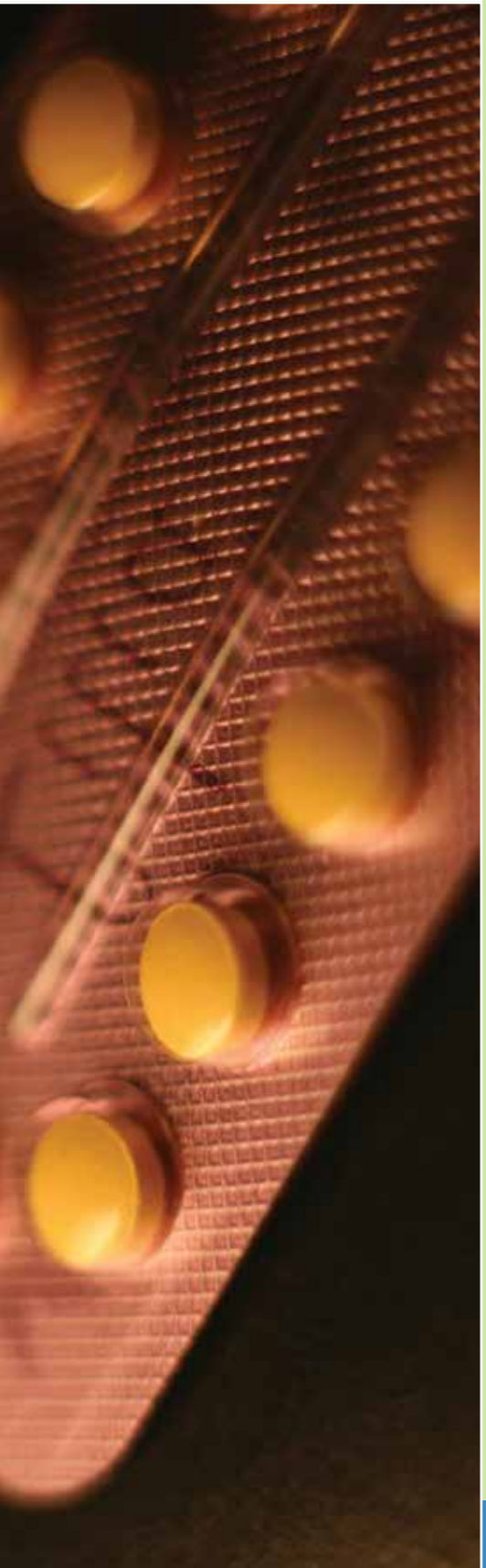
Sub Group on Non-Communicable Diseases:

1. Chairman - Dr. Mohd. Shaukat, DDG (NCD), DGHS
2. Member Secretary - OPPI
3. Co-opted Members, NGO's, Industry Associations

Sub Group on Bio-Pharma, Prophylactics and OTC:

1. Chairman - Dr. T.S. Rao, Scientist H, D/o Biotechnology/ Dr. Alka Sharma Director D/o Biotechnology
2. Member Secretary - FICCI
3. Co-opted Members, NGO's, Industry Associations

The 2nd meeting of the Task Force was held on 07.05.2015. Secretary (Pharma) reviewed the progress of all the three subgroups. The subsequent meetings of the Task Force were held on 01/07/2015, 31/07/2015 and finally on 05/10/2015.



An Overview on Various Diseases in India

The communicable diseases are a major public health concern in the country. The National Vector Borne Disease Control Programme (NVBDCP) is being implemented for control of Malaria, Dengue, Chikungunya and Japanese Encephalitis (JE) and elimination of Kala-azar and Lymphatic Filariasis.

The contribution of communicable diseases on the total disease burden in India is on the decline over a period of time. However, there are certain new infections and mainly zoonotic infections like Avian Influenza, NIPAH virus, EBOLA, Crimean Congo Hemorrhagic Fever (CCHF), Scrub Typhus etc. which are reported from time to time. Anti-Microbial Resistance (AMR) against various pathogens is also an emerging problem in India.

Around 1 million cases of malaria are reported annually through the public health system. 25,000-75,000 confirmed dengue cases are reported under NVBDCP annually in the country with case fatality ratio of <0.5%. Around 1,000 JE cases with a case fatality ratio of nearly 20% are being reported annually. Kala-azar incidence has been substantially brought down and is near to being eliminated but approximately 5,000 cases with few deaths are still being reported.

The Non-Communicable Diseases are surpassing the burden of Communicable Diseases in India. The existing public health system has a greater focus on Communicable Diseases. To address this need, a National Programme on Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS) was initiated by the Government in 2010, with a goal to reduce avoidable morbidity and premature mortality due to cancer, diabetes, cardiovascular Diseases (CVDs) including hypertension and stroke.

In India, the estimated deaths due to NCDs in 2008 were 5.3 million (World Health Organization (WHO) - NCD Country Profiles, 2011). The overall prevalence of diabetes, hypertension, Ischemic Heart Diseases (IHD) and stroke in India is 62.47, 159.46, 37.00 and 1.54 respectively per 1000 population. (Indian Council for Medical Research, 2006).

The cost implications of non-communicable diseases to society are multifold: direct costs to people with illness, their families and to the health care delivery system and indirect costs to society and to the government due to reduced productivity and intangible costs, i.e. adverse effects on quality of life. Heart disease, stroke and diabetes cause loss of billions of dollars to the national income each year in the world's most populous nation.

Summary of Key Recommendations

(A) COMMUNICABLE DISEASES VERTICAL

POLICY SUPPORT

1. Policies which restrict the distribution and availability of drugs for Communicable diseases should be reviewed to facilitate easy availability especially in Tier II/III cities and rural areas.
2. Quality control must be ensured and the available drugs should meet the prescribed standards.
3. List of APIs, which are in short supply or not manufactured in India may be drawn up and special incentives be offered to manufacturers to start manufacturing these APIs in India. List of these APIs should be reviewed periodically.
4. The government should make efforts to revive PSUs and assign PSUs the task of producing APIs that require large investments or special drugs usually termed as Orphan Drugs, those which cater to a very small population and hence may not be viable for the private sector to manufacture.
5. Government should consider to evolve a Cost Disadvantage Neutralization (CDN) mechanism as incentive that can be made available to the formulators procuring APIs from indigenous manufacturers by discontinuing the use of hitherto imported APIs.
6. Local manufacturers should be provided suitable handholding at least for initial two years, so that they can compete in overseas markets while entering into the export contracts.
7. Devise a Drug Indigenization Support (DIS) for the local Pharma companies to start indigenous production of critical APIs that are used particularly for NLEMs but are predominantly imported so far.
8. To stimulate demand for locally produced APIs, the Government should consider restricting import of certain priority APIs through amendment in the Foreign Trade Policy.

INFRASTRUCTURE

a) Fermentation Based API Manufacturing units require large capital investments. Also these industries have large requirements of power and steam. APIs based on Fermentation technology are currently not produced domestically due to its non-viability. Hence, these units should be given subsidized tariff for their power and steam requirements.

b) To facilitate the rapid transfer of technology, special API manufacturing zones for joint venture collaborations with international cooperation from API producing countries such as China and Italy, should be encouraged.

c) Encourage Public Procurement and Co-Operative Purchase Programmes for ensuring availability & affordability of drugs prepared in consultation with Communicable Disease Control Programme Managers.

SKILL DEVELOPMENT

1. Capacity building workshops should be organised for SMEs to assist them in obtaining WHO Prequalification status for the manufacture of both formulations and APIs.
2. NIPERs should assist in developing manufacturing capabilities of drugs used for Communicable Diseases.
3. NIPERs should facilitate in getting qualified and trained manpower for the various job functions for the pharmaceutical industry, namely research, production and quality control.

DUTY STRUCTURE

1. Import duties for APIs and key intermediates should be structured to protect the domestic manufacturers.
2. Concessional duties on imports of APIs should be withdrawn to provide level playing field to domestic manufacturers.
3. SMEs must be encouraged to invest profits in facility up gradation and tax exemptions as a percent of these investments may be allowed.

POLICY FOR PRICING

1. Reasonable price, mitigating the challenges faced by manufacturers & ensuring the availability , accessibility and affordability consistent with the National Pharmaceutical Pricing Policy (NPPP) issued by Ministry of Chemicals and Fertilizers (Deptt. of Pharmaceuticals) should be considered.

REGULATORY

1. To encourage manufacturing of APIs in India, procedures for obtaining Environmental Clearance (EC) should be simplified and Environmental Clearance for bulk drugs units should be accorded on a priority basis within a specified time period. State Pollution Control Boards should be sensitised that the manufacture of bulk drugs is of national importance and must not be delayed.

2. Quality control should be ensured and the available drugs should meet the prescribed standards, so as to control emergence of Anti-Microbial Resistance (AMR) against various pathogens.
3. Single Drug Formulations (SDF) should be available for patients to whom Fixed Drug Combinations (FDC) can not be given .
4. Government should facilitate the availability of land at reasonable prices.

RESEARCH & DEVELOPMENT

NIPERs should be mandated to develop efficient and economical process technologies for APIs and key intermediates which are of national importance (e.g. development of high titer cultures for the production of penicillins) and which are currently no longer manufactured in India due to non-viability.

(B) NON COMMUNICABLE DISEASES VERTICAL

POLICY SUPPORT

1. To increase Government spending on medicines to increase access to treatment for people suffering from NCD's.
2. Interest rates should be reduced as the margins in APIs' are very less.
3. Those who use domestic API should be given price incentives on finished products.
4. Cost of machines should be rationalized and competitively priced.

INFRASTRUCTURE

1. Supply and distribution system of medicine is weak and fragmented, which needs to be strengthened.
2. Efficient procurement and distribution of NCD medicines from the private players by the Government (Based on Tamil Nadu Medical Services Corporation (TNMSC)/Rajasthan Medical Services Corporation (RMSC) model).
3. Storage and distribution system needs qualitative improvement. The storage and distribution under required conditions (temperature, humidity, sunlight etc.) are not of desired standard, affecting quality of medicines.
4. Cheap power should be made available to Pharma Industries.
5. Public Sector should be strengthened to raise availability of essential NCD medicines and also to reduce cost of medicines.

6. Right infrastructure such as road, railway, airports and ports will encourage investors in establishing manufacturing units in India.
7. Government should encourage cluster-based development in the pharmaceutical sector to help in creating common facilities like common R&D centre, common testing labs, common effluent treatment plant, training centre etc. for development of SME.

DUTY STRUCTURE

1. Import duty on external suppliers of API should be levied. The external API suppliers should be registered by local authorities and their plants be also inspected.
2. Anti-dumping duty on key intermediates should be levied to protect domestic pharma industry.

REGULATORY

1. Government should facilitate faster environmental clearance, land acquisition and administrative clearances.
2. Price control is to be made effective for improving access to medicines for Indian patients.

SKILL DEVELOPMENT

1. Indigenous R&D should be encouraged.
2. Process R&D should be incentivized. Environmental technology deployment support should be made available.
3. Capacity building of pharma companies and also of regulators should be done by organizing workshops with international agencies like MHRA, EU, USFDA, etc.

(C) BIOPHARMA, PROPHYLACTICS AND OTC VERTICALS

POLICY SUPPORT

1. To create a vision document with short and long term plan for plasma industry in the country, as this industry is very challenging, demanding and has a very long-term effect on return on investments.
2. A policy should be made by government to encourage the voluntary collection of plasma "Source Plasma" in India for plasma fractionation.
3. To create a mechanism to allow use of the expired blood samples/excess plasma by the fractionation centers. This will take care of about 30% of the requirements.
4. To develop harmonized regulatory guidelines/ policy for stem cell research and clinical trials.

INFRASTRUCTURE

1. To set up accredited centralised contract manufacturing facilities for manufacturing, characterization and quality control of the cells (clinical grade) of clinical research.
2. There is also a need to create a mechanism of zone wise distribution of clinical grade stem cells for clinical research through cold chain.

SKILL DEVELOPMENT

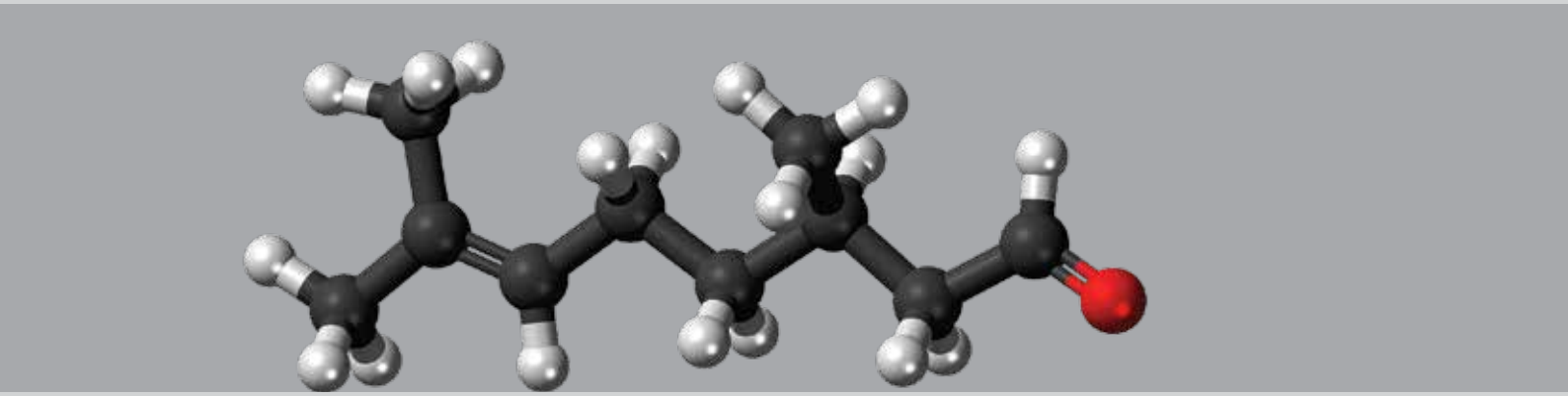
1. Set up centers to address issues of standards, proficiency testing and training of manpower of desired expertise in the area of regenerative medicines.
2. Some of the existing centers / labs can be roped in for the same.

POLICY FOR PRICING AND PROCUREMENT

1. Existing Vaccines under the NLEM & Price Control should be reviewed .
2. Toensure Vaccine Security in the Country, Vaccine Procurement should be in line with UNICEF Procurement system.
3. MOH&FW should enter into contracts with the approved manufacturers for a period of 3 years depending on the rates and capacities made available by the manufacturers and their past performance.

REGULATORY

1. Regulatory approval for importing different categories of Plasma/Fractions/ Intermediate and Paste.
2. Create a facilitative regulatory landscape for Plasma industry to grow and evolve, which would involve office of Drug Controller General of India (DCGI), National Institute of Biologicals (NIB), Department of AIDS Control (DAC), Indian Pharmacopeia Commission (IPC) and National Pharmaceutical Pricing Authority (NPPA).
3. There should be a Fast Track mechanism for grant of licence for manufacturing of the Vaccines, preferably a single window system.
4. Reduce the present approval timelines for biopharmaceutical products in order to expedite commercial manufacturing.
5. Validity of the import test license (form 11) and test license (form 29) should be increased from 1 year to 3 years .
6. To expedite the process of approval of translational research from various committees. Fast track approval process for unmet need and serious medical illness.
7. Need to streamline the procedure to get approval in the form 28 DA for formulation and filling of recombinant protein products.
8. Need to revisit the pathway and approval time for various approvals. Parallel submission and review of application is required for Review Committee on Genetic Manipulation (RCGM) and DCGI.



9. RCGM and DCGI offices should have a fixed window of time limit for each type of activity.

RESEARCH & DEVELOPMENT

1. The government should take the lead to provide speedy approval for basic and translational research in this area. This also includes creating a large animal model for preclinical studies before conducting clinical trials.

Conclusion

Enhancing access to safe and affordable medicines is crucial for addressing the burden of Communicable and Non Communicable Diseases(NCD). Cost-effective medicines to treat both types of diseases are available in India, yet they remain inaccessible and unaffordable to many who need them. Government needs to take up the responsibility to provide needed medicines in the public sector at affordable prices and in the required quantities. Scaling up manufacturing of medicines is not a hindrance for the robust Domestic Pharma Industry players in India.

Government should encourage Public Procurement and Co-Operative Purchase Programmes for ensuring availability and affordability of drugs prepared in consultation with Communicable Disease Control Programme Managers.

Government, in collaboration with the private sector, should give greater priority to treating chronic diseases and improving the accessibility of medicines to treat them. Important mechanisms for providing sustainable access to both type of diseases include the development and use of evidence based guidelines for the treatment, efficient procurement and distribution of these medicines to be in place for effective management of communicable and non communicable diseases.

On the regulatory side, government should facilitate faster land acquisition, environmental clearance, single window concept etc. to promote /enhance manufacturing capabilities.

Setting up Centers of Excellence to address issues of standard, proficiency testing and training of manpower of desired expertise in the area of regenerative medicines and much needed financial support in R&D will go a long way in discovery of new drugs. Facilitating citizens to gain access to affordable medicines shall be in line with the '**Make in India**' vision of Hon'ble Prime Minister of India.

Appendix 1

Report of the Sub Group on
Non Communicable Diseases under the DoP Task Force
on
Development of Manufacturing Capabilities in each Medical Vertical in Pharmaceutical production

Genesis of Subgroup

The DoP Task force on Development of Manufacturing Capabilities in Each Medical Vertical in Pharmaceutical production, in its first meeting on 22 December 2014, based on the major objective to identify the gaps in production of drugs, vaccines, etc. in various therapeutic categories, decided to form three Sub Groups on viz. 1) Communicable Diseases, 2) Non-Communicable Diseases and 3) Biopharma, Prophylactic and OTC.

Subgroup on NCD:

Chairperson:

Dr. Mohammed Shaukat, Deputy DG (NCDs)-DGHS

Member Secretary:

Organisation of Pharmaceutical Producers of India

Terms of References of Subgroup

- Identifying focus areas for development of manufacturing capabilities in each medical vertical in case of non-communicable diseases keeping in mind the specificities of each medical discipline.
- Identifying the gaps in domestic manufacturing in these verticals and suggesting ways to overcome them.
- Identifying the issues and support required from different government agencies and departments for achieving the manufacturing capabilities and filling the gap areas, if any, in each medical vertical.

List of members with background:

- **DGHS, Ministry of Health:** The Directorate General of Health Services, a repository of technical knowledge, is an attached office of the Ministry of Health & Family Welfare. The DGHS also renders technical advice on all medical and public health matters and in the implementation of various health policies and schemes.
- **Department of Pharmaceuticals:** The Department of Pharmaceuticals was created on the 1st of July in the year 2008 in the Ministry of Chemicals & Fertilizers, to provide greater focus for the growth of the high potential Pharmaceuticals industry.
- **CDSCO, Ministry of Health:** The Central Drugs Standard Control Organization (CDSCO) is the Central Drug Authority for discharging functions assigned to the Central Government under the Drugs and Cosmetics Act.

  Major functions of CDSCO are: Regulatory control over the import of drugs, approval of new drugs and clinical trials, meetings of Drugs Consultative Committee (DCC) and Drugs Technical Advisory Board (DTAB), approval of certain licences as Central Licence Approving Authority is exercised by the CDSCO hqrs. Confederation of Indian Industry (CII): CII is a non-government, not-for-profit, industry-led and industry-managed organization, playing a proactive role in India´s development process. Founded in 1895,

India's premier business association has over 7900 members, from the private as well as public sectors, including SMEs and MNCs, and an indirect membership of over 200,000 enterprises from around 240 national and regional sectoral industry bodies. CII works to create and sustain an environment conducive to the development of India, partnering industry, Government, and civil society, through advisory and consultative processes.

- **Federation of Indian Chambers of Commerce and Industry (FICCI):** A non-government, not-for-profit organisation, FICCI is the voice of India's business and industry. From influencing policy to encouraging debate, engaging with policy makers and civil society, FICCI articulates the views and concerns of industry. It serves its members from the Indian private and public corporate sectors and multinational companies, drawing its strength from diverse regional chambers of commerce and industry across states, reaching out to over 2,50,000 companies.

  Established in 1927, FICCI is the largest and oldest apex business organisation in India. Its history is closely interwoven with India's struggle for independence, its industrialization, and its emergence as one of the most rapidly growing global economies.

- **The Associated Chambers of Commerce & Industry of India (ASSOCHAM):** ASSOCHAM is a not for profit organization, facilitating reach of India to all businesses around the globe, for wanting to do business with India. ASSOCHAM initiated its endeavor of value creation for Indian Industry in 1920. It is also referred to as the "Chamber of Chambers" having in its fold more than 400 Industry Chambers, Trade Associations and serving more than 4,50,000 Corporate Members from all over.

- **OPPI:** The Organisation of Pharmaceutical Producers of India (OPPI) established in 1965, represents the research-driven pharmaceutical companies in India. OPPI is aligned with the nation's healthcare objectives and committed to facilitating dialogue and collaboration between the industry and allstakeholders.

- **IDMA:** The Indian Drug Manufacturers Association represents wholly Indian large, medium and small companies and State Boards in Gujara, Himachal Pradesh, Uttaranchal, Haryana, Tamil Nadu, West Bengal, Madhya Pradesh, Telanga, AP, Karnataka and Goa (under formation),

- **IPA:** The Indian Pharmaceutical Alliance (IPA) represents research based national pharmaceutical companies. Collectively, it accounts for almost 85 per cent of the private sector investment in pharmaceutical research and development. It contributes 60 per cent of the country's exports of drugs and pharmaceuticals and services about 45 per cent of the domestic market.

- **Pharmexcil:** The dynamic growth of Indian Pharma Industry, a knowledge based industry, and the recommendations of four major Pharma associations made the Ministry of Commerce & Industry to realize the need for separate export promotion council. Accordingly, Pharmaceuticals Export Promotion Council (PHARMEXCIL) was set up on 12.5.2004.

- **AIIMS / Safdarjung Hospital:** Premiere Hospitals of India and household names in India and abroad with people from all strata of society looking up to it to provide unbiased, affordable and quality healthcare.

- **PHDCCI:** PHD Chamber of Commerce and Industry, established in 1905, is a proactive and dynamic multi-State apex organisation working at the grass-root level and with strong national and international linkages. The Chamber acts as a catalyst in the promotion of industry, trade and entrepreneurship. PHD Chamber, through its research-based policy advocacy role, positively impacts the economic growth and development of the nation.

First meeting: The first meeting was held in OPPI Directorate at Mumbai on January 27, 2015. The meeting

was attended by the representatives from CII, FICCI and individual companies. The meeting concluded that to give our recommendations to DoP on terms of References, we should obtain data from AIOCD AWACs / IMS on NCDs and prepare a base paper for circulation amongst the group members for their inputs.

Second meeting: The second meeting of the Committee was held on July 08, 2015 at YMCA Conference Hall, New Delhi. The meeting was chaired by Dr Mohd. Shaukat Usta, Dy DG (NCD), DGHS. The meeting decided on following action items:

- The Chairman to write to organisations like BDMA for note on challenges faced by the Bulk Drugs Industry on production of API / Bulk Drugs and Excipients used in NCDs.
- IPA representative would provide a note if BDMA is not able to comment on any one of the aforesaid topics. IPA to also provide a note on the issue of quality.
- The Chairman would formally write to the NPPA/DoP to provide production details of drugs
- The Chairman would also formally write to DCGI on number of manufacturing units approved in India.
- Dr. Sandeep Bansal (Safdarjung Hospital) would provide the feedback from Clinicians on shortages of drugs used for NCDs, if any.

Burden of common Non Communicable Diseases:

India is experiencing rapid demographic and epidemiological transitions with a rising burden of Non-Communicable Diseases. NCDs cause significant morbidity and mortality both in urban and rural population and across all socio-economic strata in the country with considerable loss in potentially productive years (aged 35-64 years) of life. India leads the world with largest number of diabetics and is sometimes referred to as the

Disease1	India	World	India Share
Hypertension	139 mn	1 bn	14%
Cancer (deaths)	400,000	7,900,000	5%
Cardio – Vascular diseases	17,900,000	18,480,000	26.5%
Diabetes	65.0 mn	366 mn	16.8%

"diabetes capital of the world".

The Non-Communicable Diseases are surpassing the burden of Communicable diseases in India. The existing public health system has a greater focus on communicable diseases. To address this need, a National Programme on Prevention and Control of Cancer, Diabetes, Cardio vascular Diseases and Stroke (NPCDCS) was initiated by the Government in 2010, with a goal to reduce avoidable morbidity and premature mortality due to cancer, diabetes, cardio vascular Diseases (CVDs) including hypertension and stroke.

In 2008, out of the 57 million global deaths, 36 million deaths or 63% were due to NCDs, principally cardio vascular diseases, diabetes, cancers and chronic respiratory diseases. Nearly 80% of NCD deaths occur in low- and middle-income countries. It is projected that globally NCDs will account for nearly 44 million deaths by

[1]Hypertension and Diabetes statistics for 2011; Cancer and CVD statistics for 2008
Source: World Health Report, WHO 2010; WHO; International Diabetes Federation; www.diabetesatlas.org;
Express Healthcare (www.expresshealthcare.in);

2020. The leading causes of NCD deaths in 2008 were: cardio vascular diseases (17 million deaths i.e.48%of NCD deaths); cancers (7.6 million i.e. 21% of NCD deaths); respiratory diseases, including asthma and Chronic Obstructive Pulmonary Disease (COPD) 4.2 million and diabetes 1.3 million deaths. NCDs kill people at a younger age in low- and middle-income countries, where 29% of NCD deaths occur among people under the age of 60, compared to 13% in high-income countries. (Global status report on non-communicable diseases 2010).

In India, the estimated deaths due to NCDs in 2008 were 5.3 million (World Health Organization (WHO) - NCD Country Profiles, 2011). The overall prevalence of diabetes, hypertension, Ischemic Heart Diseases (IHD) and stroke in India is 62.47, 159.46, 37.00 and 1.54 respectively per 1000 population. (Indian Council for Medical Research, 2006).

Major risk factors to NCDs

Most NCDs are strongly associated and causally linked with following four major behaviour risk factors:

(i). Tobacco use

(ii). Physical inactivity

(iii). Unhealthy diet including high intake of salt (sodium chloride)

(iv). Harmful use of alcohol

The other risk factors include stress, lack of fiber in food, trans-fatty acids etc.

If the above behavioural risk factors are not being managed /modified, then they may lead to following biological risk factors:

(i). Over weight/obesity

(ii). High blood pressure

(iii). Raised blood sugar

(iv). Raised total cholesterol/lipids

The other non-modifiable risk factors such as age, sex and hereditary are also associated with the occurrence of NCDs. The major risk factor for the oral, Oro-pharyngeal and lung cancer is tobacco use.

Economic burden of NCDs

The cost implications of non-communicable diseases to society are multifold: direct costs to people with illness, their families and to the health care delivery system and indirect costs to society and the government due to reduced productivity; and intangible costs, i.e. adverse effects on quality of life. Heart disease, stroke and diabetes cause loss of billions of dollars to national income each year in the world's most populous nations.

Variable	Inpatient Care	Outpatient Care	Patients needing Surgical Care
Annual Family Income	48,000	48,000	45,000
Money spent on DM Investigations, Physicians fees and Medicine	6725	3050	5395
Expenditure on Hospitalization	5000	Nil	9000
Expenditure on Transport	300	200	200
Average Expenditure	7505	3310	13880
Proportion of Income spent on DM	17.5%	7.7%	16.3%

[2] Ramachandran JAPI 2007

Economic impact of diabetes: Direct costs

Cost borne by patients on Treatment of Diabetes both In-patient and Out-patient subjects (Cost / Year)[2]

With losses due to premature deaths due to heart disease, stroke and diabetes are projected to increase cumulatively, and India stands to lose 237 billion dollars during the decade 2005-2015. India also loses a substantial number of lives during the productive years of its citizens. The Potentially Productive Years of Life Lost (PPYLL) due to CVDs in the age group of 35-64 was 9.2 million in 2000 and is expected to rise to 17.9 million in 2030. This estimate is more than the combined estimated loss in China, Russia, USA, Portugal, and South Africa (16.2 million).

WHO also estimates that a 2% annual reduction in national-level chronic disease death rates in India would result in an economic gain of 15 billion dollars for the country over the next 10 years. Modelling studies have shown that the per-capita income in India would increase by 87% if the CVD mortality rate per annum declines by one percent whereas a three percent annual decline would increase per-capita income by 218% by the year 2030. Similarly, road traffic injuries are estimated to result in economic loss of $11,458 million (INR 550,000 million) or nearly 3% of GDP every year.

As per IMS MAT May 2015 data

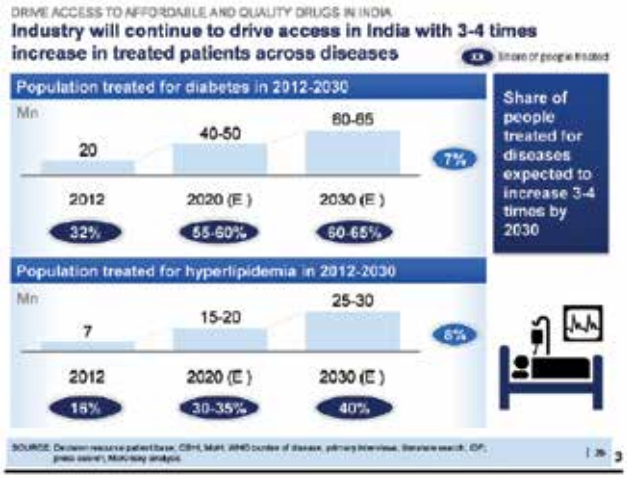
	Market Size in crores	% share to IPM	No of formulations	No of Brands
CVS	11,142	12	2015	3382
Diabetes	7245	8	5888	1143
CNS	5591	6		2644
Cancer	2200	2.3	1200	

Current availability of medicines for NCD's in India

Currently there are more than 10,500+ manufacturers in the country who produce NCD drugs.

As is evident from data above there are enough manufacturers and brands which are available for treating NCD's in India.

Population forecast for diabetes/hyperlipidemia 2012 – 2030



Currently 32% of total diabetic population in India are receiving some form of treatment. This number is anticipated to reach to 65% coverage by 2030.

[3] FICCI-Mckinsey Indian Lifesciences Vision 2030 report

In India, there is still opportunity to improve treatment penetration considerably, despite the low prices and strong set of initiatives taken by the industry. Capacity expansion for producing more NCD drugs is never a challenge for the Indian Pharmaceutical Industry.

The key mix of challenges to achieve the above numbers are in the areas of access as listed below (e.g. Weakness in Healthcare systems, fragmented and weak medicines supply and distribution systems, Quality of NCD medicines, Insufficient and unskilled pharmaceutical workforce availability) and awareness (e.g. gaps in understanding of consequences driving discontinuation of treatment) are key drivers for this.

In this context, we believe that through a set of concerted actions, innovative models and government support, industry can aspire to drive 3-4 times increase in number of treated patients across disease areas.

Increasing spend on medicines by Government is the Key factor to increase Access to treatment for people suffering from NCD's

State wise government spending on Drugs from 2001-02 to 2010-11 shows a dismal picture. The government spends only 50344 crores on procuring medicines.

In contrast, the excise collection from Liquor sale of Kerala state alone is 8000 crores+5 for the said year.

PHFI-ISID report *"Independent Evaluation of the NPPP2012 and DPCO 2013"* states that

"Access to medicines, can be accelerated by scaling up public spending on drugs. The current spending of governments (Both State and Central) must be scaled up from 1 percent to atleast 5 percent of GDP over 4 to 5 years"

TNMSC with a modest budget of 3506 crores serves 7 crore of its population by providing free medicines listed in its NLEM list since 1995. The government has to become the payor if it wishes to increase access to treatment for patients suffering from NCD's.

Other Key Challenges identified in Access to NCD Medicines: (Qualitative interviews)

If Capacity Expansion was not the hindrance in increasing access to NCD medicines, we interviewed our key members to understand the real challenges which cause this low penetration of NCD medicine even today in India. Based on our discussion the following have been highlighted

- **Weaknesses in health systems**

As many non-communicable diseases share common risk factors, they also share common health systems related constraints that limit access to needed essential medicines. These shared constraints also provide opportunities for intervention and treatment synergies. Effective medicines exist to address the burden of most non-communicable diseases. Many of these medicines are already listed in the National List of Essential Medicines 2011, as satisfying the priority health needs of the population. Nevertheless, NCD medicines are often unavailable in public facilities, and when these medicines are available in the private outlets even under DPCO 2013 stringent price control regime, prices are rarely affordable for the lower income population who need them for free. Low public sector availability of essential medicines is caused by a lack of public resources due to underfunding, inaccurate demand forecasting, and inefficient public sector procurement and distribution of medicines. This compels patients into the private sector, where medicines are relatively more available but costlier. High private sector prices are caused by a high manufacturer's selling prices, taxes and tariffs, and high mark-ups in the supply chain.

[4] PHFI-ISID report on evaluation of NPPP 2012

[5] http://www.thehindubusinessline.com/economy/the-alcohol-economy/article5436924.ece

[6] TNMSC website

- **Fragmented and weak medicines supply and distribution systems**

The Medicines supplies and distribution systems in India is highly fragmented. In many cases the public sector (government) role in supplies and distribution of medicines is rarely visible.

- **The challenge of quality of NCD medicines**

Medicine quality is also a problem especially in a diverse country like India. The number of recorded cases of falsified (counterfeit) medicines for chronic diseases is also increasing, for example through unregulated internet sales used by patients on chronic treatment. The storage and distribution under required conditions (temperature, humidity, sunlight etc.) are not of desired standard; affecting quality of medicines.

- **Challenges from the state of the pharmaceutical workforce**

Insufficient pharmaceutical workforce (in numbers and skill mix) remains a significant barrier to access to NCD medicines. Shortages in the pharmaceutical workforce already constrain the safe, effective, efficient and timely distribution of medicines. This poor state of pharmaceutical workforce further compounds the low level availability of medicines in the public sector.

- **Growing dependence on China for KSM/ intermediates:**

The lower cost and strong government support in China has led to increasing Indian imports of KSMs/ intermediates for APIs from China. China now accounts for nearly 60 per cent of India's total API/intermediate imports, up from 40 per cent back in 2004. This increasing dependence affects availability of essential medicines in the local market. Strengthening local industry to overcome this risk is therefore a critical need for making NCD medicine available at cheaper prices.

- **Price Control Regime**

Price control is being practised in India since 1979. But still the access to treatment remains dismal.

According to a new report by The IMS Institute India, price control is neither an effective nor sustainable strategy for improving access to medicines for Indian patients. The report goes on to state that "Primary beneficiaries of price controls have been high income patient populations, rather than the low-income targets"

It is essential that the government looks into the real root cause which is hampering Access to NCD medicines rather than limiting itself to finding aesthetic solutions for a deep rooted problem.

Key concerns related to Manufacturing in India

During our discussions certain concerns related to Manufacturing were listed by our respondents:

- Tough regulations and complexities related to land acquisition serve as a deterrent to the growth of the manufacturing segment
- Slow decision making and delay in environmental clearances
- Unethical administrative clearance/inspection also acts as a hurdle for the manufacturing sector
- Sub-optimal infrastructure such as road, railway, airports and ports discourage investors from establishing manufacturing units in India
- Power shortage is a long standing issue
- Limited cluster-based development in the pharmaceutical sector
- Lack of strict enforcement of regulations and quality measures for high quality product output

Key Recommendations from the group for improving Manufacturing in Pharmaceutical sector

The Pharma industry needs a policy that encourages cluster approach for funding and creating infrastructure.

Develop a couple of Pharma clusters that will help in creating common facilities like common R&D centre, common testing labs, common effluent treatment plant, training centre etc. for development of SME. Those who use domestic API should be given price incentives on finished products.

India should also participate in the development of global regulatory standards. Capacity building of not only the Pharma companies but also of regulators should be done by organizing workshops with international agencies like MHRA, EU, USFDA, etc.

Process R&D should be incentivized. Environmental technology deployment support should be available.

To make Indian Pharma industry competitive in API, the followings should be focused upon:

a) Cost of constructions should be reduced by reducing time delays

b) Cost of machines should be rationalized and competitively priced

c) Indigenous R&D be encouraged

d) Cheap power to be made available

e) Interest rates should be reduced as the margins in APIs' are very less

f) Import duty on external suppliers of API be levied

g) The external API suppliers should be registered by local authorities and their plants also be inspected

h) The time lines for approval of external suppliers should be on par with other countries

i) Need to work with international authorities to streamline regulatory burdens, prequalification

j) Anti-dumping duty on key intermediates should be levied to protect domestic Pharma industry

Conclusions:

Enhancing access to safe and affordable medicines is crucial for addressing the burden of NCDs. Cost-effective medicines to treat NCDs are available in India, yet they remain inaccessible and unaffordable to many who need them. Government has to take up the responsibility to provide needed NCD medicines in the public sector at affordable prices and in the required quantities. Scaling up manufacturing of NCD medicines is not a hindrance for the robust Domestic Pharma Industry players in India. However, challenges emanate from those that generally confront India's health system and those that are to do with the peculiarities of NCDs and the medicines needed to treat them. Government, in collaboration with the private sector, should give greater priority to treating chronic diseases and improving the accessibility of medicines to treat them. Important mechanisms for providing sustainable access to NCDs include the development and use of evidence based guidelines for the treatment of NCDs, efficient procurement and distribution of these medicines from the Private players by the Government (Based on TNMSC/RMSC model), establishment or the provision of viable financing models can be a few options to get started with.

Report

of

Sub-group on Communicable Diseases

(Ref : OM No. 31026/87/2014-PI-II dated 23rd June, 2015 of Department of Pharmaceuticals)

Task Force for Development of Manufacturing Capabilities in Pharmaceutical Production

September 2015

CONTENTS

1. Preamble

The communicable diseases are major public health problem in the country. To control and eliminate various communicable diseases specific national health programmes are being implemented in the country.

Around 2 million new cases and 0.2 million deaths due to tuberculosis are being reported in the country. Inspite of implementation of National Health Programme for control of TB, the Multi-drug-Resistant Tuberculosis (MDRTB) and extensively drug-resistant tuberculosis (XDR-TB) have been posing a great challenge to the programme. The drugs for treatment of TB including MDR and XDR are being manufactured and available within the country. There is a need to sustain both manufacturing and ready availability of these drugs along with research for new fixed drug combination within the country.

The National Vector Borne Disease Control Programme (NVBDCP) is being implemented for control of Malaria, Dengue, Chikungunya and Japanese Encephalitis (JE) and elimination of Kala-azar and Lymphatic Filariasis. Around 1 million cases of malaria are being reported annually through public health system. 25,000-75,000 confirmed dengue cases are being reported under NVBDCP annually in the country with case fatality ratio of <0.5%. Around 1,000 JE cases with a case fatality ratio of nearly 20% are being reported annually. Kala-azar incidence has been substantially brought down and to be eliminated but approximately 5,000 cases with few deaths are still being reported. Out of 255 filaria endemic districts, 222 districts have achieved elimination status but in remaining district, the MDA has to be continued. Among the six diseases, malaria, Kala-azar and Filaria have specific drug for treatment. Even after achieving elimination of Kala-azar and filaria, drugs for these diseases will continuously be required till eradication is being achieved. Malaria is outbreak- prone disease and continuous availability of drug is to be ensured. There should be mechanism for sustenance of production and uninterrupted supply of quality drugs.

Leprosy which was once considered to be eliminated is resurging with reported cases from various districts resulting in increased requirement of effective anti-leprosy drug. Chhattisgarh and Dadra & Nagar Haveli have still not achieved elimination. 60 percent of world-wide new cases are from India only. Such instance indicates that the provision of drugs has to be ensured even for the diseases which are eliminated.

Although incidence of HIV/AIDS is on decline, however, there is a continuous need of supply of ART drugs to keep the transmission low and also drugs to take care of opportunistic infections.

Acute Rheumatic Fever is still being reported and its one of the major sequel is rheumatic heart disease. Prophylaxis to prevent these cardiac manifestation/ complications is an effective preventive measure and availability of such drug needs to be ensured.

The communicable diseases like Leptospirosis are endemic in Kerala, Tamilnadu, Gujarat, Andamans, Karnataka, Maharashtra and Hepatitis B and C are also prevalent but under reported in India. Estimated prevalence for both Hep B & C ranges from 0.5% to 4% of the population. In such circumstances vaccines and drug for such diseases should be produced within the country in sufficient quantity for ensuring sustained supply at affordable cost. Acute Respiratory Infections (ARI), Acute Diarrhoeal Diseases (ADD), typhoid still continue to be a big problem.

The contribution of communicable diseases on total disease burden in India is on decline over the period of time, however, there are certain new infections and mainly zoonotic infections like avian influenza, NIPAH virus, EBOLA, Crimean Congo Hemorrhagic Fever (CCHF), scrub typhus etc. are reported from time to time. Anti-microbial Resistance (AMR) against various pathogens is also emerging problem in India.

In view of prevailing situation of communicable diseases, the Department of Pharmaceuticals under the Ministry of Chemicals and Fertilizers has timely visualized the need for a dedicated taskforce for development

of manufacturing in each medical vertical in pharmaceutical production. Further, this task force has rightly given due importance to the communicable disease by constituting a sub- group on communicable disease. This initiative will ensure that the country has the capacity for manufacturing quality drugs and vaccines at affordable price and reduce the dependency on importing high cost medicine and vaccine from other nation. In addition, this venture will ensure sustain supply and availability of drugs and vaccines for diseases which are eliminated/ in process of elimination. This is in line with the Government policy of "Make in India".

2. Background

The Task Force was constituted to focus on development of manufacturing capabilities in each medical vertical of Pharmaceutical production. The Task Force, in their meeting on 22nd December, 2014 decided to form sub-groups for Communicable diseases, Non-communicable diseases, and Biopharma, prophylactics, OTC, etc. Initially the subgroup for Communicable diseases was under Chairmanship of Dr R S Gupta, DDG(TB), Dte.GHS, which was later in June, 2015 amended to Dr A. C. Dhariwal, Director, National Vector Borne Disease Control Programme vide notification No. A.21020/02/2014-Admn.I dated 3rd June, 2015 of Dte.GHS (Annexure- i) with the following Terms of Reference:

a) To identify focus areas for development of Manufacturing Capabilities in each Medical Vertical in case of Communicable Diseases keeping in mind the specificities of each Medical discipline.

b) Identify the Gaps in Domestic Manufacturing in these verticals and suggesting ways to overcome them.

c) Identify the issues and support required from different government agencies and departments for achieving the manufacturing capabilities and filling the gap areas, if any, in each medical vertical.

The list of members of the Sub-group on Communicable diseases are at Annexure- iii.

The first meeting of the Sub-Group for Communicable Diseases under the chairmanship of Director, NVBDCP was held on 26th June, 2015. Dr Nichole Sequy from WR India, Dr Vandana Kalia from Deptt. of Scientific & Industrial Research (DSIR), Mr V K Tyagi from Deptt of Pharmaceuticals, Dr V S Salhotra from RNTCP, Dr Sila Deb, Deputy Commissioner, Child Health, MOHFW, Dr Somnath Karmarkar, from NCDC, Mr Ashok Madan from Indian Drug Manufacturers Association and Dr Sher Singh Kashyotia, Assistant Director, NVBDCP attended the meeting. Dr George Patani, Member Secretary of the Sub-group, could not attend the meeting as he was on travel duty to China. During the meeting, a note prepared by the IDMA was discussed in detail. The salient areas of discussion were

- Increasing production of APIs
- Tax incentives
- Removal of excessive price controls
- Encouraging Fixed Drug combinations
- Encouraging Innovations
- Assurance for Quality Control

The suggested recommendations were presented before the Secretary (Pharma) on 1st July, 2015. It was felt that the recommendations should be made more specific to the major communicable diseases and made as per the Terms of Reference.

Accordingly, the second meeting of the Sub-group was held on July 24, 2015 at Committee Room No. 1, India International Centre, Annexe, Max Mueller Marg, Lodi Estate, New Delhi 110003. This meeting was organized by IDMA and was attended by representatives of the Industry and Civil Society (VHAI), besides all other members. After detailed deliberations, recommendations were made which were presented before the Secretary (Pharma) on 31st July, 2015.

3. Gaps analysis and Recommendations

The gaps and recommendations have been discussed below as per the Terms of Reference (TOR).

TOR (a) - To identify focus areas for development of Manufacturing Capabilities in each Medical Vertical in case of Communicable Diseases keeping in mind the specificities of each Medical discipline

Focus areas for development of Manufacturing Capabilities in case of Communicable Diseases were identified as under:

i) Tuberculosis
ii) Malaria
iii) HIV/AIDS
iv) Influenza
v) Filariasis
vi) Kala Azar
vii) Leprosy
viii) Leptospirosis
ix) Sexually Transmitted diseases (STD)
x) Rheumatic Heart Disease (RHD)
xi) Hepatitis C
xii) Acute Diarrhoeal Diseases

TOR (b) - Identify the Gaps in Domestic Manufacturing in these verticals and suggesting ways to overcome them.

The drugs used for the treatment of the various diseases (verticals) were reviewed and their availability was discussed:

i) Tuberculosis				
Sr. No.	**Name of molecule**	**Formulation Production capacity in India**	**API Production capacity in India/ source of API import**	**Source of intermediates**
1	Isoniazid	Available	India/China	India
2	Rifampicin	Available	India/China	India
3	Pyrazinamide	Available	Available	Japan
4	Ethambutol	Available	Available	USA
5	Pyridoxine(Vitamin B6)	Available	China	China
6	Prothionamide	Available	China	NA
7	Ethionamide	Available	China	NA
8	Sodium - PAS	Available	Available	NA
9	Rifapentine	Available	Available	India
10	Cycloserine	Available	Available	NA
11	Capreomycin	Available	China/Korea	NA
12	Kanamycin	NA	China	NA
13	Moxifloxacin	Available	Available	China
14	Rifabutin	Available	Available	India
15	Ofloxacin	Available	China	India
16	Linezolid	Available	Available	India (limited)

17	Levofloxacin	Available	Available	India
18	Streptomycin	Available	China	NA
19	Delamenid	NA	NA	NA
20	Bedaquiline	Available	NA	NA
NA – Data Not Available				

Some of the notable observations of the discussions in the vertical of Tuberculosis are summarised below :

- The APIs and intermediates of a number of Anti-tubercular drugs are sourced from China.
- There is difficulty in sourcing Kanamycin , as there is no registered source with DCGI for in country supplies.
- Anti-tubercular drugs are required in fixed drug combinations as well as in single formulations due to sensitivity or intolerance to one of them. Second line drugs are required in single formulations.

ii) Malaria

Sr. No.	Name of molecule	Formulation Production capacity in India	API Production capacity in India/ source of API import	Source of intermediates
1	Chloroquine, Quinine, Amodiaquine, Mefloquine, Pyrimethamine	Available	Available	NA
2	Primaquine	Available	Available	NA
3	Artemisinin & derivatives(artemeter, artesunate)	Available	Available	China/Vietnam
4	Sulfadoxine + Pyrimethamine	Available	Available	India
5	Lumefantrine	Available	Available	India/China
6	Clindamycin	Available	China	China
7	Piperaquine	Available	Available	India/China
NA – Data Not Available				

- Since oral Artesunate monotherapy is banned, it should not to be available as single formulation. It should only be available in combination.
- Should be available in packings according to age groups
- Arterelone + Piperaquine, as an Indian product need to be registered with DCGI for Paediatric use.

iii) HIV/AIDS

Sr. No.	Name of molecule	Formulation Production capacity in India	API Production capacity in India/ source of API import	Source of intermediates
1	Acyclovir	Available	India/China	China
2	Didanosine	Available	Available	NA
3	Lamivudine	Available	India/China	India
4	Stavudine	Available	India/China (Major)	China/India

5	Zidovudine	Available	India/China	India/Korea
6	Efavirenz	Available	India/China	India/China
7	Indinavir	Available	Available	NA
8	Nelfinavir	Available	Available	NA
9	Ritonavir	Available	India/China	NA
10	Saquinavir	NA	Available	NA
NA – Data Not Available				

- There is shortage of paediatric combination of Anti-virals

iv) Influenza				
Sr. No.	**Name of molecule**	**Formulation Production capacity in India**	**API Production capacity in India/ source of API import**	**Source of intermediates**
1	Oseltamivir	Available	Available	China

The main Intermediate for Oseltamivir Phosphate is Shikimic Acid which is solely imported from China. This is mainly because this is derived from seeds of plant -Star Anise -that is grown predominantly in certain parts of China.

v). Filaria				
Sr. No.	**Name of molecule**	**Formulation Production capacity in India**	**API Production capacity in India/ source of API import**	**Source of intermediates**
1	Albendazole	Available	Available	India
2	Ivermectin	Available	Available	India
3	Diethyl carbamazine citrate	Available	Available	India

- There is no issue in the filaria vertical.

vi) Kala Azar				
Sr. No.	**Name of molecule**	**Formulation Production capacity in India**	**API Production capacity in India/ source of API import**	**Source of intermediates**
1	Liposomal Amphotericin B	Available	Germany/Japan	NA
2	Miltefosine	Available	Germany/USA	NA
3	Paromomycin	Nil	Italy	NA
4	Amphotericin B	Available	Germany/Japan	NA
5	Sodium stibogluconate	Available	Available	NA
NA – Data Not Available				

- Miltefosine and Liposomal Amphotericin B have poor availability

vii) Leprosy				
Sr. No.	**Name of molecule**	**Formulation Production capacity in India**	**API Production capacity in India/ source of API import**	**Source of intermediates**
1	Clofazimine	Available	Available	NA
2	Dapsone	Available	Available	NA
3	Rifampicin	Available	India/ China	China
4	Thalidomide	Available	India	NA
NA – Data Not Available				

viii) Leptospirosis				
Sr. No.	**Name of molecule**	**Formulation Production capacity in India**	**API Production capacity in India/ source of API import**	**Source of intermediates**
1	Penicillin	Available	China	China
2	Doxycycline	Available	China	NA
NA – Data Not Available				

ix) Sexually Transmitted Diseases				
Sr. No.	**Name of molecule**	**Formulation Production capacity in India**	**API Production capacity in India/ source of API import**	**Source of intermediates**
1	Penicillin	Available	China	China

x) Rheumatic Heart Disease				
Sr. No.	**Name of molecule**	**Formulation Production capacity in India**	**API Production capacity in India/ source of API import**	**Source of intermediates**
1	Benzyl Penicillin	Available	China	China
2	Penicillin V	Available	China	China

xi) Hepatitis C				
Sr. No.	**Name of molecule**	**Formulation Production capacity in India**	**API Production capacity in India/ source of API import**	**Source of intermediates**
1	Sofosbuvir	Available	NA	NA
NA – Data Not Available				

xii) Acute Diarrhoeal Diseases				
Sr. No.	**Name of molecule**	**Formulation Production capacity in India**	**API Production capacity in India/ source of API import**	**Source of intermediates**
1	Saquinavir	Available	Available	NA
NA – Data Not Available				

- Non availability of Zinc tablets/Syp for children due to lack of clarity of its regulatory status (Therapeutic or prophylactic).

Gaps in Domestic Manufacturing

I] Lack of API Manufacturing Capability: It was noted that a large number of APIs and intermediates required for the manufacture of formulations used in the treatment of Communicable Diseases are sourced from China. It was also informed to the group that the pipeline of APIs currently under review by WHO for pre-qualification indicate that China will surpass India in the number of units currently undergoing the pre-qualification process for the supply of APIs. It is recommended that a short list of APIs, as listed in Table 1, which are in short supply or not manufactured in India maybe drawn up and special incentives be offered to manufacturers to start manufacturing these APIs in India. This list maybe reviewed periodically.

II] Fermentation Based API Manufacturing Capability: It was noted that APIs based on Fermentation technology are currently not produced domestically due to its non-viability (TABLE 2). These units require large capital investments. Also these industries have large requirements of power and steam. Hence, it is recommended to provide these units with subsidised tariff for their power and steam requirements. Table 2 lists the fermentation based APIs which are no longer manufactured in India due to its non-viability.

TOR (c) - Identify the issues and support required from different government agencies and departments for achieving the manufacturing capabilities and filling the gap areas, if any, in each medical vertical.

1. Easy Availability at affordable cost:

Easy availability is essential. However, the outcome must be achieved in terms of an affordable price. It is recommended to encourage Public Procurement and Co-Operative Purchase Programmes for ensuring availability & affordability of drugs prepared in consultation with Communicable Disease Control Programme Managers.

Also, the success of the various national disease eradication programs have been attributed to the easy availability of the drugs through private, public and public-private (co-operative/NGO) distribution programs. Hence, it is recommended that all channels of drug distribution must be encouraged. e.g.. Oseltamavir, a drug used for the treatment of influenza was restricted for distribution to only those retail outlets having Schedule X license, hence sporadic shortages of the drug have been reported. It is currently proposed to change its classification from Schedule X to Schedule H1 so as to facilitate easy availability of Oseltamivir. It is recommended that policies which restrict the distribution and availability of drugs for Communicable diseases must be reviewed, to facilitate easy availability especially in Tier II/III cities and rural areas.

2. Assurance for Quality Control:

The issue of quality control cannot be compromised in view of emergence of Anti-microbial Resistance (AMR) against various pathogens. It is recommended that quality control must be ensured and the available drug must meet the prescribed standards.

3. Fixed Drug Combinations (FDC) Vs. Single Drug Formulations (SDF):

The support and encouragement for development of FDC Regime is already being done in NVBDCP, RNTCP, NACO and other communicable diseases wherever it is considered necessary after deliberation by experts and its effectiveness has been established in the public practice. e.g. a revision of the treatment protocol in the management of Malaria with Artemisinin based combination Therapy (ACT) for the treatment of falciparum malaria has resulted in the reduction of deaths due to malaria. For Elimination of Lymphatic Filariasis, the strategy of mass drug administration of Diethyl-carbamazine Citrate (DEC) to reduce the number of microfilaria carriers was changed to the co-adminsitration of DEC with Albendazole in 2007.

India has established a history of use of various fixed dose combinations and this knowledge must be used to improve disease management.

It is recommended that FDCs must be encouraged. However, SDF should also be available for patients in whom FDC cannot be given or different doses required.

4. Accelerated review of Bio-studies :

It is recommended that accelerated review of Bio-studies should be facilitated. However, the facilitation of accelerated review of bio-studies for treatment of communicable diseases involve certain issues which have to be addressed. The decisions in the following areas need to be expedited:

- Clinical Trials
- Approval of Ethical Committees
- Approval of Technical groups/Committees
- Process details, time taken and identifying the impediments in the process of approval.
- Review of protocols for the administration of combination therapy for the management of communicable diseases in children must be placed on a high priority.

5. Support innovations in packing technology for easy transport, shelf life, storage, response and compliance:

Support for innovations in packing technology is recommended to facilitate easy transport, storage of pharmaceuticals, better compliance and response to the therapy. However, issues of safety, impact on pharmaco-dynamics, and cost-effectiveness needs to be addressed and types of innovations need to be identified for support at present or expected innovations. The committee has taken cognizance of New Drug Delivery System (NDDS) including Sustained Release, Extended Release formulations, trans-dermal delivery mechanisms, site-specific release formulations etc which definitely add to the effective healthcare delivery. The production capability for manufacture of most of such innovative formulations is sufficiently developed. However, with regular obsolescence, sustained efforts need to be ensured to take care of newer patterns of diseases and medications evolving globally.

6. Price Controls should be rationalized and affordable:

While it is important to ensure the availability, affordability and accessibility of Quality Drugs, it is accepted that price controls should be rationalized by removal of excessive price control on medicines and impractical implementation of laws for price control, such as recalling stocks from the market, which hinders free availability in the market and may result in inaccessibility of drugs in rural, remote & hard to reach areas. But the price cannot be left merely on market forces to make medicines unaffordable & unavailable to the needy persons. It is recommended that reasonable price, mitigating the challenges faced by manufacturers & ensuring the availability & accessibility on affordable price consistent with the National Pharmaceutical Pricing Policy (NPPP) issued by Ministry of Chemicals and Fertilizers (Deptt. of Pharmaceuticals) should be considered.

7. Incentives, Technological up-gradation & Changes in Duty Structure to encourage "Make in India" for manufacturers of APIs:

Dependance on imports from China in supply of APIs has been noted as an extremely weak link in our supply chain. Almost 80% of the WHO prequalified suppliers of formulations are manufacturers from India. However, the current pipeline of new manufacturers involved in the WHO pre-qualifiation process indicate that the number of API prequalified suppliers from China will far outnumber the current number of API suppliers and our dependence on China for the supply of these will increase even further. Hence, it is important that more domestic API manufacturing capacity is developed.

The hurdles and suggestions to encourage manufacturing of APIs in India are listed below:

a) It is recommended to facilitate the Availability of land at reasonable prices

b) On obtaining land, manufacturers take 3-4 years to obtain Environmental clearance (EC). Existing manufacturers have to obtain Environmental Clearance again either to augment capacity at the same location or to change product profile, although there is no increase in loads of emissions or hazardous waste generated, from that permitted at the time of commencement. Hence, it is proposed that the procedures for obtaining Environmental Clearance must be simplified and EC for bulk drugs units must be accorded on a priority basis within a specified time period. State Pollution Control Boards must be sensitised that the manufacture of bulk drugs is of national importance and must not be delayed.

c) High cost of Power and Steam must be subsidised, especially for Fermentation based industries where these utilities form a major cost component. It is recommended that the PSUs be revived to manufacture APIs and key Intermediates where the investment is large and competition from China is intense due to Government subsidies.

d) It is recommended that CSIR/NIPERs be mandated to develop economical process technologies (including development of High Titer cultures required by the Fermentation Industries) for the manufacture of these APIs. These technologies developed maybe transferred to these PSUs or SMEs in cases where the economies of scale are much smaller.

It is recommended to review the Import duty structure of the various intermediates and APIs. It is observed that international competition reduce the costs of key intermediates and once a monopolistic situation is reached, the cost of the intermediates is increased to ensure that the Final API cost is unviable leading to stoppage of manufacture. It is recommended that that import duties for these APIs and key intermediates be structured to protect the domestic manufacturers. Concessional duties on imports of APIs too must be withdrawn to provide level playing field to domestic manufacturers.

This recommendation is in line with government policy, 'Make in India ' and 'Single Window Clearance'. Facilitation of availability of land, environmental clearance & augmentation of capacity is recommended. The intention is to encourage the production of essential Active Pharmaceutical Ingredients (API's).

Special API manufacturing zones for joint venture collaborations: To facilitate the rapid transfer of technology, special API manufacturing zones for joint venture collaborations with international cooperation from API producing countries such as China and Italy, must be encouraged, where the hurdles highlighted as above must be addressed for speedy execution and implementation. This will also align well with the MAKE IN INDIA program currently promoted by the Government of India.

Among the incentives for local production, the Government may consider to evolve a Cost Disadvantage Neutralization (CDN) mechanism as incentive that may be made available to the formulators procuring APIs from indigenous manufacturers by discontinuing using hitherto imported APIs. The quantum of CDN may be worked for each imported API taking into consideration among other things, the difference between the landed cost and price at which the domestic manufacturers could offer a particular API. Such quantum may be periodically reviewed/ adjusted based on the global prices' scenario for respective APIs. The CDN may be offered for at least first two years of commencement of local production of any specific API. Such a system will stimulate local demand for the locally manufactured APIs vis-à-vis imported APIs.

Besides CDN for local formulators to offset their possible competitive disadvantage, the local manufactures may be provided suitable handholding at least for initial two years so that they can compete in overseas markets while entering into the export contracts. In addition to the conventional export incentives already available, the Government may devise a Drug Indigenization Support (DIS) to the local Pharma companies that start indigenous production of critical APIs that are used particularly for NLEMs but are predominantly imported so far.

As an indirect measure to stimulate demand for locally produced APIs, the Government. may consider restricting import of certain priority APIs through amendment in the Foreign Trade Policy. Such APIs may be allowed to be imported by the Actual Users based upon the Essentiality etc against a Special Import License issued by the DGFT.

Certain duty exemptions hitherto available to many APIs being considered critical for some national health programmes etc need to be reviewed and may be done away with. Such steps will also encourage local production.

8. Promotion of Pharma PSUs. :

The govt. should make efforts for PSUs to be revived and assigned the task of producing APIs that require large investments or special drugs usually termed as Orphan Drugs, those which cater to a very small population and hence may not be viable for the private sector to manufacture.

9. Existing Incentives should be utilised by the industries:

The several tax incentives are already available to manufactures and maximum benefits should be availed by them. To encourage SMEs involved in pharmaceutical manufacturing to upgrade their facilities, SMEs must be encouraged to invest profits in facility upgradation and tax exemptions as a percent of these investments may be allowed.

10. The role of NIPERs:

The role of the various NIPERs and their assistance must be sought in developing manufacturing capabilities for manufacturing drugs for Communicable Diseases. The first objective for developing institutes like NIPERs was to train qualified and trained manpower for the various job functions for the pharmaceutical industry, namely research, production and quality control. In addition the NIPERs may be mandated to develop efficient and economical process technologies for APIs and key intermediates which are of national importance (e.g. development of high titer cultures for the production of penicillins) and which are currently no longer manufactured in INDIA due to non-viability. The commercial manufacture of the above mentioned products, developed with technology at the various NIPERs may be licensed out to the PSUs or to SMEs depending on the investments required for the manufacture.

11. Capacity building workshops be organised for SMEs to assist them in obtaining WHO Prequalification status for the manufacture of both formulations and APIs.

Table 1 : Availability of Drugs used in the treatment for Communicable disease in India

Sr. No.	Name of Disease	Name of molecule	Formulation Production capacity in India	API Production capacity in India/ source of API imported	Source of intermediates
1.	Tuberculosis	Isoniazid	Available *Micro Labs *#Macleods Pharma *#Lupin Ltd # Strides Arcolab #Svizera Labs #Cadila Pharma	Available ◊Calyx Chemicals India ◊Second Pharma, China	India
		Rifampicin	Available # Strides Arcolab #Svizera Labs #Macleods Pharma #Lupin Ltd	Available/China ◊Lupin ltd India ◊Sandoz P. Ltd India	India

		Pyrazinamide	Available *Cadila Pharma *Micro Labs *#Macleods Pharma #Lupin Ltd # Sandoz Pvt ltd #Svizera Labs # Strides Arcolab	Available ◊Calyx Chemicals India ◊Anuh Pharma India ◊Lupin ltd India	Japan
		Ethambutol	Available *Cadila Pharma *#Macleods Pharma #Lupin Ltd # Sandoz Pvt ltd	Available ◊Lupin Ltd India)	USA
		Pyridoxine (Vitamin B6)	Available	China	China
		Prothionamide	Available *Lupin Ltd *Micro Labs	China ◊Pen Tsao Chem China	NA
		Ethionamide	Available *Lupin Ltd *Micro Labs *Macleods Pharma *Cipla Ltd	China ◊Pen Tsao Chem China	NA
		Sodium - PAS	Available *Macleods Pharma	Available	NA
		Rifapentine	Available	Available	India
		Cycloserine	Available *Macleods Pharma	Available ◊Shasun Pharma India	NA
		Capreomycin	Available	China / Korea ◊Zhejiang Hisun Pharma China	NA
		Kanamycin	Availability is scarce	China	NA
		Moxifloxacin	Available *Macleods Pharma *Cipla Ltd *Ranbaxy Lab	Available ◊Zhejiang Hisun Pharma China	China
		Rifabutin	Available *Lupin Ltd	Available	India
		Ofloxacin	Available *Macleods Pharma *Cipla Ltd *Micro labs	China	India
		Linezolid	Available	Available	India (Limited)
		Levofloxacin	Available *Macleods Pharma *Cipla Ltd *Micro labs	Available ◊Zhejiang Langhua Pharma China	India
		Streptomycin	Available	China	NA
		Delamanid	NA	NA	NA
		Bedaquiline	Available	NA	NA

2.	Malaria	Quinine & Salt Chloroquine, Amodiaquine, Mefloquine, Pyrimethamine	Available # Strides Arcolab #Ipca labs #Ajanta pharma #Cipla Ltd	Available	NA
		Primaquine	Available	Available	NA
		Artemisinin and derivatives (artemeter, artesunate)	Available # Strides Arcolab #Ipca labs #Ajanta pharma #Cipla Ltd	Available ◊Mangalam Drugs India ◊Sequent Scientific India ◊Ipca Laboratories India ◊Mylan Labs India ◊Sanofi-Aventis, Italy	China/Vietnam
		Sulfadoxine + Pyrimethamine	Available	Available	India
		Clindamycin	Available	China	China
3.	Leprosy	Corticosteroids	Available	China	NA
		Clofazimine	Available	Available	NA
		Dapsone	Available	Available	NA
		Rifampicin	Available # Macleods Pharma # Lupin Ltd # Strides Arcolab # Sandoz Pvt ltd #Svizera Labs	Available/China ◊Lupin Ltd India, ◊Sandoz Pvt Ltd India	China
4.	Dengue	----------	----------	----------	----------
5.	Leptospirosis	Doxycycline	Available	China	NA
6.	Filariasis	Albendazole	Available	Available	India
		Ivermectin	Available	India	India
		Diethyl carbamazine citrate	Available *Eisai Co, Ltd - Japan	Available	India
7.	Kala Azar (Leshmaniasis)	Sodium stibogluconate	Available	Available	NA
		Paromomycin	Nil	Italy	NA
		Amphotericin B	Available	Germany/Japan	NA
		Pentamidine Isothionate	Nil	Nil	NA
		Miltefosine	Available	Germany/USA	NA
8.	Anti Retro Virals	Aciclovir	Available	Available/ China (minor)	China
		Didanosine	Available	Available ◊Mylan Labs India)	NA
		Lamivudine	Available *# Macleods Pharma *#Mylan labs *#Hetero Labs *#Aurobindo Pharma *# Strides Arcolab *#Ranbaxy Lab *#Cipla Ltd #Pharmacare Ltd #Emcure Pharma	India/China ◊Laurus Labs India ◊Mylan Labs India ◊Shanghai Desano Chem China ◊Shijiazhuang Lonzeal Pharma China	India

		Stavudine	Available *Bristol-Myers Squibb *# Macleods Pharma *#Mylan labs *#Hetero Labs *#Aurobindo Pharma *# Strides Arcolab *#Ranbaxy Lab *#Cipla Ltd #Pharmacare Ltd #Emcure Pharma	China (major) India (minor)	China (major) India (minor)
		Zidovudine	Available *# Macleods Pharma *# Mylan labs *# Hetero Labs *#Aurobindo Pharma *# Strides Arcolab *# Ranbaxy Lab *# Cipla Ltd	India (major) ◊Sequent Scientific India ◊Mylan Labs India ◊Zhejiang Langhua Pharma China ◊Shanghai Desano Chem China	India (major) Korea (minor)
		Efavirenz	Available *Emcure Pharma *# Macleods Pharma *#Mylan labs *#Hetero Labs *#Aurobindo Pharma *# Strides Arcolab *#Ranbaxy Lab *#Cipla Ltd	India (major) China (minor) ◊Mylan Labs India ◊Shanghai Desano Chem China	India (major) China (minor)
		Indinavir	Available	Available	NA
		Nelfinavir	Available	Available	NA
		Ritonavir	Available *#Mylan labs #Hetero Labs #Aurobindo Pharma #Cipla Ltd #Emcure Pharma	Available ◊Mylan Labs India ◊Shanghai Desano Chem China	NA
		Saquinavir	Available	Available	NA
9.	Influenza	Oseltamivir	Available *Cipla Ltd *Strides Arcolab *Mylan labs	Available ◊Mylan Labs India	China
10.	Sexually Transmitted Diseases (STD)	Penicillin	Available	China	China
11.	Rheumatic Heart Disease (RHD)	Benzylpenicillin	Available	China	China
		Penicillin V	Available	China	China
12.	Hepatitis C	Sofosbuvir	Available	NA	NA
13.	Acute Diarrhoeal Disease	Zinc	Available *Alkem Labs	◊Dr Paul Lohmann Germany	NA

Footnotes:-
* Name of Indian company manufacturing Single dose formulation, listed in WHO Prequalified list of Medicinal Products.
\# Name of Indian company manufacturing Combination formulation, listed in WHO Prequalified list of Medicinal Products.
◊ Name of the company listed in WHO Prequalified API List (Published on 15 July 2015). NA - Data Not available

Table 2: Current Status of some Fermentation-based API Units(Source: Journey Towards Pharma Vision 2020 – An IDMA Initiative).				
Sr. No.	**Name of Bulk Drug**	**Producers**	**Production commenced in**	**Present status**
1	Penicillin G/V	Alembic, Sarabhai, IDPL,JK Torrent, Ranbaxy, Standard	In early 60's	Plant stopped
2	Streptomycine	Alembic, Sarabhai, IDPL	In early 60's	Plant stopped
3	Tetracycline	Sarabhai, IDPL, Pfizer	In early 80's	Plant stopped
4	Oxytetracycline	Sarabhai, IDPL, Pfizer	In early 80's	Plant stopped
5	Kanamycin	Alembic	In early 70's	Plant stopped
6	Erythromycin	Alembic, Themis, IDPL, Standard	In early 80's	Partially in operation for captive production for safety.
7	Rifamycin	Themis^, Lupin^^, San-doz^^	Late 80's	Closed^,Captive^^
8	Gentamycin	HAL, Themis	Late 80's	Closed
9	Sisomycin	Themis	Late 80's	Closed
10	Vitamin B12	Themis, Alembic, MSD	Early 70's	Closed
11	Cephalosporin 'C'	Alembic	Early 90's	Closed
12	Lovastatin	Themis, Biocon, Kreb	Early 90's	In operation
13	Pravastatin	Themis, Biocon, Mylan	Late 90's	Closed
14	Griseofulvin	Glaxo	Late 80's	Closed
15	Cyclosporine A	Biocon, Mylan	Late 90's	Closed
16	Bleomycin	Themis	Early 90's	Closed
17	Mitomycin 'C'	Themis	Early 90's	Closed
18	Citric acid	Citurgia, Citric India, Themis	Early 80's	Closed
19	Ephedrine	Malladi, Embio	Early 80's	In operation
20	Ascorbic Acid	Sarabhai, Jayant, Vitamin	Early 80's	Closed

Subgroup on Biopharma, Prophylactic and OTC

The second meeting of the subgroup on Biopharma, Prophylactic and OTC was held on July 14, 2015 at FICCI, New Delhi under the chairmanship of Dr. Alka Sharma, Director, Department of Biotechnology who has taken over from Dr. T. S. Rao after his superannuation. A follow up of meeting was held on August 26, 2015 with various stakeholders to discuss the identified areas.

The Department of Pharmaceuticals, GoI constituted a Task Force in December 2014 on *"Development of manufacturing capabilities in each medical vertical in pharmaceutical production"*. **The Terms of Reference of the Sub-group provided by Department of Pharmaceuticals are:**

1 Identifying focus areas for development of manufacturing capabilities in each medical vertical Prophylactics, Vaccines and Over The Counter (OTC) drug keeping in mind the specificities of each medical discipline.

2. Identifying the gaps in domestic manufacturing in these verticals and suggesting ways to overcome them.

3. Identifying the issues and support required from different government agencies and departments for achieving the manufacturing capabilities and filling the gap areas, if any, in each medical vertical.

Ms. Shobha Mishra Ghosh, Sr. Director FICCI welcomed the representatives with an update on the subgroup formed by Department of Pharmaceuticals. The list of participants is annexed.

Dr. Alka Sharma set the context of the meeting by suggesting the group focuses on the "Terms of Reference" provided by DoP and come out with key recommendations pertaining to manufacturing. She observed that the previous recommendations were more related to 3rd Terms of Reference and towards regulatory bottlenecks and did not specify the areas where India needs to strengthen its manufacturing of Biopharma and Prophylactic products. She mentioned that the first subgroup meeting was held in February 2015 under the Chairmanship of Dr. T. S. Rao, Advisor, Department of Biotechnology, the recommendations emerging out of discussion during themeeting was submitted to Department of Pharmaceuticals. In the recent meeting held in DOP on July 1, 2015, the Secretary, DOP, Dr. V. K. Subburaj had reviewed the progress of the Subgroup. The Subgroup conveyed that no additional inputs have been received on the draft recommendations made in its 1st meeting. However, some of the members of the Task Force requested for the copy of the recommendations to provide their comments on recommendations.Hence it was suggested that a meeting should be organized by inviting members from other association and Industry for wider perspective for finalising the recommendations of this Sub-group.

Dr. Eswara Reddy, Joint Drug Controller of India, CDSCO said that the objective of this Task Force is to improve the manufacturing capabilities and availability of drugs in India. He agreed with Dr. Alka Sharma to re-frame the recommendations as per the Terms of References. Then, the participants of the Sub-group deliberated upon "Terms of Reference" on Biopharmaceuticals and Over the Counter drugs.

A. Biopharmaceuticals:

The Terms of Reference were discussed in detail by the participants and the recommendations emerged for biopharmaceuticals are as follows:

I. Terms of Reference: Identifying focus areas for development of manufacturing capabilities in each medical vertical Prophylactics, Vaccines and Over The Counter (OTC) drug keeping in mind the specificities of each medical discipline.

After detailed discussion, the sub-group was in consensus that the manufacturing capabilities for the following 7 areas need to be strengthened:

1. Blood products
2. Vaccines
3. Raw material/Intermediates
4. Fermentation based Antibodies & Vitamins
5. Monoclonal Antibodies
6. Recombinant-DNA products
7. Regenerative Medicines

II. Terms of Reference: Identifying the gaps in domestic manufacturing in these verticals and suggesting ways to overcome them.

After detailed discussion,the recommendations emerged on the identified areas are as follows:

1. Blood Products/ Plasma Derived Medicinal Products (PDMP)/ Plasma Protein Therapy (Blood Products):

India produce Blood products (PDMP) like Albumin and IVIG from local (Indian Plasma) but the demand of Albumin is so high that India is always on short supply, while IVIG scenario is still better. The clotting factors like Factor VIII, IX and Fibrinogen is 100% imported. While hyper-immune products (Anti D, Tetanus Immunoglobulin Hepatitis-B Immunoglobulin, and Rabies Immunoglobulin are also 100 % imported or prepared from imported bulk. This creates a huge demand and supply with factor of;

- Availability
- Affordability
- Safety

There is an increase in whole blood collection from 3. 6 lakh units in 1997 to 14.76 lakh units last year through a six fold increase in blood donation camps across the state, production of plasma has also increased to the tune of 2 lakh litres annually. It was suggested that there is a need to manage the blood effectively in order to increase the supply of plasma.

The production of albumin depends on the unit's capacity to produce albumin. The shortage of human albumin is also due to price control.

Further, the subgroup discussed that there is a need to identify:

- Total requirementof the blood product and its availability in India
- Changes needed in regulatory system for blood banks, and plasma products – DCGI, IP, NIB, State FDA, etc

- What policies should government make to improve the availability of plasma products in India
- The gaps and measures to fill the gap
- Indigenous manufacturing capabilities
- Quantity of blood products imported
- Technology used should be in line with international standard

The industry members shared that India has only 6 manufacturers of blood products. They are:Reliance, Virchow, Intas, Hemarus, Bharat Serums and PlasmoG.

A list of manufacturing site approved for import of blood product in India from CDSCO website is annexed. A list of manufacturers, list of marketers, Import Data and Export from FICCI is also annexed.

Recommendations:

- Create a vision document for plasma industry for the country, as this industry is very challenging, demanding and have very long-term effect and ROI.
- A policy should be made by government to encourage the voluntary collection of plasma in India
- DAC department of AIDS Control needs to be involved as they are nodal agency in recommending blood bank products and needs to work with DCGI, NIB and IPC
- To create a mechanism to allow use the expired blood samples/ excess plasma by the fractionation centres. This will take care about 30% of the requirements.
- Regulatory approval for imparting plasma Kit.

2. Vaccines: Since vaccines are one of the fastest growing segments of Biopharmaceutical Industry, it is necessary to facilitate manufacturing with full support from the government of India. PSUs had also played an important role in the National Immunisation programmes. Some of the PSUs which were closed by the Government on the grounds of not complying with the WHO GMP.

The Key Challenges (a) The introduction of new vaccines is an increasingly complex as well as costly activity (b) Supply chain management is a critical component for the successful delivery of immunization services and (c) Immunization programmes are often adversely impacted by certain issues such as demand forecasting, financial and procurement management, storage and transportation, human resources, maintenance and campaigns.

It was discussed by the subgroup that there is need to identify: total requirement and availability of vaccines in India;Indigenous manufacturing capabilities;Identify the gap and measures to fill the gap;what policy should government make to increase the manufacturing;

As of today, all the primary vaccines which are in the Immunization Programme of GOI, sufficient manufacturing capacities are available from various Companies in the Public Sector as well as Private Sector. The primary vaccines such as BCG, Hep-B, DPT, TT, OPV ---- are being procured through Open Tenders by GOI. Any reported shortages in the past were on account of delay in procurement process by the Govt or delay in supplies by few Companies who after having taken the orders being L1 did not supply within the requisite Delivery Schedule.

The Vaccine prices in India are reasonable. In the past few years Newer vaccines such as Pentavalent Vaccine have been licenced by Indian manufacturers and the same is available all over India. Infact, 3 WHO Pre-qualified Vaccine manufacturers are supplying Pentavalent to GOI against GAVI assistance through UNICEF and since the time of introduction there has been no reported shortage at all.

Newer Vaccines such as Rota, Japnese Encephalitis, HPV, Pneumo, Pentavalent& Hexavalent (containing IPV) are all under different stages of Clinical Trials with various Indian manufacturers and they should be available in the next 2-3 years in sufficient capacities at reasonable rates. Infact, one Indian manufacturer is already licenced for Rota Vaccine.

Further, DCG(I) had convened a meeting with Vaccine manufacturers on 15th January' 2015 to Fast Track the Vaccine segment and three Working Groups were formed i.e. 1st Group: to address as how the business of Vaccines/Biologicals can be increased globally. 2nd Group was incorporated to speeden up the licensures/ make suitable changes keeping in consideration the present scenario of the difficulties being faced by the Vaccine Industry and 3rd Working Group was formed to address difficulties being faced by Vaccine Industry w.r.t. Post Approval Changes introduced in Dec' 2008 and now suggest the changes to be incorporated.

Recommendations:

The recommendations emerged are as follows:

(a) There should be Fast Track mechanism for licensure of the Vaccines, preferably a single window system. Presently, from the pre-clinical stage to licensure, it almost take 5-6 years for a vaccine to be manufactured.

(b) The Govt. should procure the vaccines for Immunization Programme not only on the basis of L1 but on the basis of past performance, Quality and also Capacities available with the manufacturers so as to avoid any shortage.Ministry of Health and Family Welfare, Vaccine Procurement should be in line with UNICEF Procurement system wherein ministry should enter into Contracts with the approved manufacturers for a period of 3 years depending on the rates & capacities made available by the manufacturers and their past performance. This will ensure Vaccine Security to the Country.

(c) The indigenous vaccines being made in the Country are already being offered at low prices as compared to foreign vaccines but by putting few of them in the Price Control it leads to less margins to the manufacturers. Vaccine Industry is very Capital Intensive Industry and Manufacturers have to invest regularly in upgrading the GMP's etc. In any case, the GOI procures vaccines through Open Tenders and since the Manufacturer's quote low prices to get the award of Tender having Price control on Vaccines which are under National Essential list of Medicines does not achieve any purpose, hence Price Control is not required.Hence the existing Vaccines under the NLEM & Price Control should be removed and no Vaccines in future should be added under Price Control. Documents on Vaccine Pricing and Procurement by Institutions and Regulatory Pathway for Licensing of Human Vaccines in India are annexed.

3. Raw material/ Intermediates

The Sub-group felt that most of the raw materials are imported in India. Cost of raw material is also pushing up the cost of biologics.

- The CII has shared the BCG report on India's dependent on China for API (annexed).
- IDMA sharedthe report (annexed).

4. Fermentation based Antibodies & Vitamins:

Dependence on fermentation based antibodies and vitamins on import from China. Based on the discussion held, the group felt that this category includes: For e.g: 6–Aminopenicillanic acid (6–APA) and its predecessor, Penicillin–G (Pen–G), were identified as key advanced intermediates in fermentation– based products. These intermediates—which are highly dependent on imports, with China accounting for more than 90 percent of the supply—form the base for most of the semi–synthetic penicillins (SSPs). Moreover, 6–APA constitutes a significant value of the final API (almost 75 p ercent of the value for amoxicillin).

5. Monoclonal Antibodies:

India has manufacturing capabilities for monoclonal antibodies, but the success rate is not up to the mark. It was discussed that there is a need to identify the type of monoclonal antibodies which is imported in India and what government should do to increase the manufacturing.

1. Most mammalian cell culture required for large scale manufacture of monoclonal antibodies require satellite supporting activities such as –
    - Cell bank characterization
    - Virus clearance studies
    - Media and feed manufacturing
    - High productivity Cell line development

India lacks the above and therefore Indian Manufacturers are dependent of outside CROs for the above – this leads to heavy burden on cost on outsourcing and logistics.

2. Regulatory delays that affects "First-to-File" status globally. This deprives the Indian Biosimilar Companies of a global reach and leadership.

3. Speedup of Regulatory approvals through a variety of improvements suggested by FICCI in the past.

6. Recombinant- DNA Products:

The group recommended thatthere is a need to strengthen the manufacturing capabilities for r- DNA product. The group also recommended to streamline the regulatory framework in this area with defined timeline.

7.Regenerative medicines:

The group felt that there is a need to focus on regenerative medicinekeeping in view its potential therapeutic applications. The group discussed this area in detail and felt that:

Currently majority of the institution, hospitals and Industry are conducting both early translational research (basic and preclinical studies) and late translational research (pilot studies and randomised controlled trial). At present there is a gap in understanding of requirements of standards to be followed for manufacturing, characterization, quality control, manufacturing and distribution etc of stem cells. Though, this area has been addressed in the regulatory guidelines formulated by the government, there is a need to have clear and articulated set points on the issues related to research, production , pilot scale/ studies etc.

The government is addressing this through interministerial approach. Based on the discussion, the recommendation emerged are as follows:

a) To set up accredited centralised contract manufacturing facilities for manufacturing, characterization and quality control of the cells (clinical grade) of clinical research. In the initial phase, 2-3 centres can be identified to take up this task; having the basic infrastructure. This will help in reducing the cost and the time of completing the task. Later on, after gaining experience, more centre can be established or adopted.

b) Set up centres to address issues of standard, proficiency testing and training of manpower of desired expertise in the area of regenerative medicines. Some of the existing centres/ labs can be roped in for the same.

c) There is also a need to create mechanism of zone wise distribution of clinical grade stem cells for clinical research through cold chain.

d) To develop harmonized regulatory guidelines/policy for stem cell research and clinical trials.

e) The government should take lead to provide speedy approval for basic and translational research in this area. This also include creating large animal model for preclinical studies before conducting clinical trial.

f) To expedite the process of approval for translational research from various committees. Fast track approval process for unmet need and serious medical illness.

III. Terms of Reference: Identifying the issues and support required from different government agencies and departments for achieving the manufacturing capabilities and filling the gap areas, if any, in each medical vertical.

After detailed discussion,the recommendations emerged are as follows:

a) Regulatory bottlenecks: The recommendations made by the Sub-group in its first meeting were discussed and it was recommended by the industry to reduce the present approval timelines for biopharmaceutical products in order to expedite commercial manufacturing.

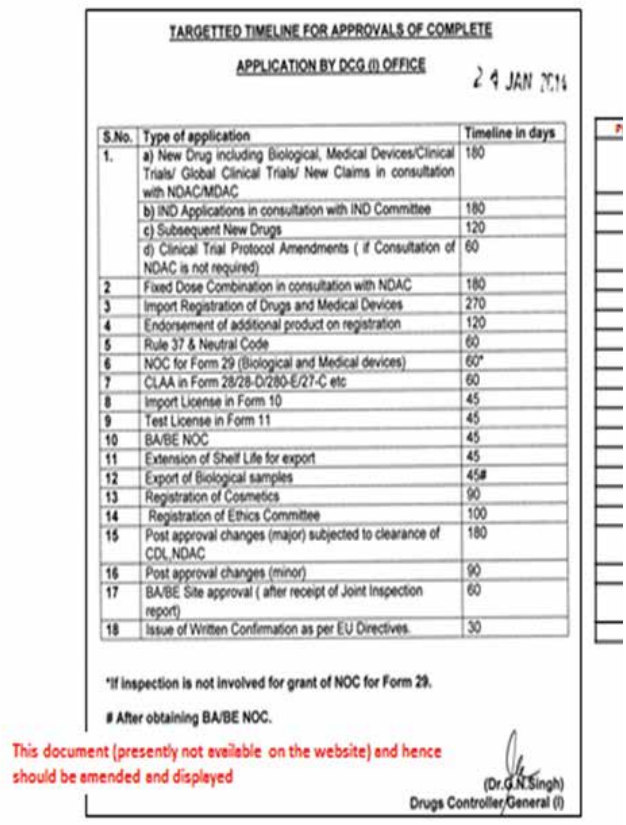
b) Test Licensing:It was recommended that the validity of the Import test license (form 11) and test license (form 29) should be increased to 3 years

c) Need to streamline the procedure to get approval in the form 28 DA for formulation and filling of recombinant protein products.

d) Facilities that handle only the purified recombinant proteins (and not recombinant organisms - GMOs or LMOs). The procedure needs to be streamline to get approval.

e) Ministry should revisit the pathway and approval time for various approval. Parallel submission and review of application is required to RCGM and DCGI.

f) RCGM and DCG(I) offices should have a fixed window of time limit for each type of activity.



TARGETTED TIMELINE FOR APPROVALS OF COMPLETE APPLICATION BY DCG (I) OFFICE

29 JAN 2014

S.No.	Type of application	Timeline in days
1.	a) New Drug including Biological, Medical Devices/Clinical Trials/ Global Clinical Trials/ New Claims in consultation with NDAC/MDAC	180
	b) IND Applications in consultation with IND Committee	180
	c) Subsequent New Drugs	120
	d) Clinical Trial Protocol Amendments (if Consultation of NDAC is not required)	60
2	Fixed Dose Combination in consultation with NDAC	180
3	Import Registration of Drugs and Medical Devices	270
4	Endorsement of additional product on registration	120
5	Rule 37 & Neutral Code	60
6	NOC for Form 29 (Biological and Medical devices)	60*
7	CLAA in Form 28/28-D/280-E/27-C etc	60
8	Import License in Form 10	45
9	Test License in Form 11	45
10	BA/BE NOC	45
11	Extension of Shelf Life for export	45
12	Export of Biological samples	45#
13	Registration of Cosmetics	90
14	Registration of Ethics Committee	100
15	Post approval changes (major) subjected to clearance of CDL,NDAC	180
16	Post approval changes (minor)	90
17	BA/BE Site approval (after receipt of Joint Inspection report)	60
18	Issue of Written Confirmation as per EU Directives.	30

*If inspection is not involved for grant of NOC for Form 29.

After obtaining BA/BE NOC.

This document (presently not available on the website) and hence should be amended and displayed

(Dr.G.N.Singh)
Drugs Controller General (I)

g) Pre-submission advice procedure (which is recently introduced) will help address such issues. CDSCO should facilitate the procedure at a minimal time.

h) To conduct RCGM and NDAC meetings at regular intervals.

i) As per D&C act every r-DNA product is considered as new drug and hence its every new indication is also a new drug and therefore needs approval from DCGI's Office. Additionally Guidelines on Similar Biologics Approval mentions it as extrapolation of efficacy & safety results to other indications (with conditions to be fulfilled – unless those are evaluated by DCGI's office) and does not have mention as automatic extrapolation. In case of similar biologics, while granting the approvals for additional indications, it is very important to ensure the patients' safety. Hence, automatic extrapolation for additional indications for similar biologics should not be recommended in view of the patient's safety. CDSCO Guidelines on Biosimilar is annexed

B. Over the Counter Drugs:

The Sub-group discussed the details of Over The Counter (OTC) and based on the discussion held, the recommendations emerged for OTC are as follows:

i. Industry has proposed the Inclusion of definition of OTC Drugs in Amended Drugs and Cosmetic Bill 2015.

ii. The Ministry of Health should review the schedule-H periodically.

iii. It was recommended that, DCGI should cleanly state that whether the drug is prescription or non-prescription at the approval stage and available in the CDSCO website.

iv. Government should make awareness program with respect to OTC.

v. CDSCO website should have a separate tab providing all information and details regarding the OTC

vi. OTC drugs are used by consumers for symptomatic relief in minor day to day ailments. These drugs are used for short term, often duration of use lasting 5-7 days. Further such drugs are consumed on not more than 2-3 occasions in a year. This means OTC drugs do not pose significant economic burden on the consumers as compared to Prescription drugs, which are consumed for longer durations. In view of this OTC drugs should be kept out of price control. OTC drug with a unit dose price up to Rs 5 should be kept out of price control to accommodate new formats, innovations.

vii. E- commerce of OTC drugs

Recommendations:

- FICCI OTC Taskforce group prepared the document on Effect of Pricing Policy on OTC Drugs
- Recommendations for E- Commerce of OTC Drugs emerging out from FICCI & CII Report: (annexed)

Key Recommendations:

1. Intermediaries (i.e. generic e-Commerce marketplaces) which are not designed for the sale of prescribed medicines and who prohibits the sale of prescribed drugs on their site, guidelines may be issued to all the state FDA to follow the Information Technology Act 2000 and The Information Technology (Intermediary Guidelines) Rules, 2011 and aforesaid notifications dated 18.03.2013 and notify Intermediary about the listing/ offer for sale which may be contravention of the law. Intermediary should act within the time stipulated under Information Technology Act 2000 and The Information Technology (Intermediary Guidelines) Rules, 2011.

2. Drugs regulator shall make available the names of manufacturers, importers and the brand names of all the drugs and medicines whether prescribed or not approved or licensed by the drugs regulator on

its website and such information shall be updated periodically. It is further proposed that the list of all licensed pharmacist should also be made available and updated on the regulator's website.

3. Drugs regulator shall engage in consumer education series to educate consumers to buy prescribed drugs only on the prescription of a licensed medical practitioner.

4. Suggestive Guidelines for Reinforcing Due Diligence for those Intermediaries who wants to specifically allow sale of prescription drugs are as follows:

   - Orders of scheduled drugs should require a valid prescription of a registered medical practitioner
   - Orders should be processed from a physicallicensed premise
   - Orders should be dispensed by a Registered Pharmacist in a licensed premise
   - In a market place model there should be a team of Qualified Pharmacist and Pharmacologists for Validation of Prescription. The email id and phone no should be accessible for the users to report any adverse effect or solve any drug related query.
   - There should be no listing and sale of Schedule X drugs and other risky drugs (Schedule H-1). There should be adequate checks and balances in place to prevent sale of any schedule X drugs.
   - It should be clearly mentioned to the user that the platform is a market place and their order will be processed by a local licensed pharmacy. The details of the pharmacy should be shared with the users using Email and SMS
   - Create a Prohibited Products program : A Prohibited Products Program can be made up of (1) the Prohibited Products Classifier, which is the technology behind the program, (2) up-front seller vetting, (3) seller investigation and enforcement, (4) ongoing monitoring of the regulatory landscape, and (5) ongoing manual audits.

i. Prohibited Products classifier:

a) The Prohibited Products Classifier (PPC) is an automated tool which can be used to monitor all products sold on such sites. The tool can search the product catalogue, identify products that match a set of keyword-based rules. It uses machine learning technology to determine if the product should be allowed on the site.

b) Products flagged by the tool can then manually reviewed by a dedicated team that works 7 days a week to confirm that the product is actually restricted and not a false positive. Intermediaries should perform this extra step because the rules cast a broad net when searching the site for products that may be illegal or otherwise violate the policies, which means lot of legitimate products are picked up during the sweep by an automated tool.

ii. Seller Vetting

a) In addition to searching the catalogue for problematic products, a number of measures to be implemented to vet the sellers. For instance, a machine learning model can be used to identify sellers that are more likely to sell products that violate the policies. In certain categories, such as Health & Personal Care, Beauty and Grocery, pre-approval is required for all new sellers. The pre-approval process can be discussed in more detail separately.

iii. Enforcement against sellers

a) In addition to removing a seller's listings of restricted products, audits of third-party sellers can be performed and enforcement action against seller accounts with multiple violations to be taken, such as removing their selling privileges.

iv. Monitoring of regulatory developments

a) Monitoring a variety of sources to keep up to date with regulatory developments and to update the set of PPC rules to reflect these developments.

v. Manual audits:

a) Manual audits of the site to be conducted regularly in order to ensure that the PPC rules are correctly identifying products that should be restricted, and are not incorrectly removing products that are appropriate for sale.

vi. Regular correspondence with FDA and other regulators:

The Intermediaries to partner with the DGCI and FDA in their investigations by providing information about third-party sellers and products on our site.

vii. When the gaps are identified in the rule coverage (for example through an audits and FDA contacts), the existing rules can be updated and, when needed, create new rules to address these gaps

5. Marketers with licences for online sale must not have track record of fraud , lineage with Manufacturing firms, Manufacturing companies mustn't hold licenses to sell , and relatives and group companies must also be denied online marketing licences
6. Entrepreneurs with court cases, legal notices, bad moral conduct must not be issued online drug selling licenses
7. The punishment for breach of conduct must be fool proofed with a cyber security policy that will report breach of conduct. The cyber security
8. E-Prescription directly from Doctor to Pharmacy with a valid digital signature with every prescription should be the only right future model proposed, which can tackle all & every risks of dispensing
9. Include the Ministry of Broadcasting and Information among the other Ministries
10. The Ministry of Health must take responsibility to Patient Health and must have owness of the issues related to the same, and as policy power is distributed the patient will be under high risk
11. A task force for e-records creation Management must be formed for smooth transition into a safe online medicine dispensing system
12. Adoption of norms from US FDA /UK FDA must be included in the guidelines

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