



सत्यमेव जयते

**PARLIAMENT OF INDIA
RAJYA SABHA**

**DEPARTMENT-RELATED PARLIAMENTARY STANDING COMMITTEE
ON HEALTH AND FAMILY WELFARE**

SIXTY-SIXTH REPORT

**Action Taken by the Government on the
Recommendations/Observations contained in the
Fifty-Ninth Report on the Functioning of Central
Drugs Standards Control Organisation (CDSCO)
(Ministry of Health and Family Welfare)**

(Presented to the Rajya Sabha on 26th April, 2013)

(Laid on the Table of Lok Sabha on 26th April, 2013)



**Rajya Sabha Secretariat, New Delhi
April, 2013/Vaisakha, 1935 (Saka)**

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COMPOSITION OF THE COMMITTEE
(2012-13)

RAJYA SABHA

1. Shri Brajesh Pathak — *Chairman*
2. Dr. Vijaylaxmi Sadho
- *3. Dr. K. Chiranjeevi
4. Shri Rasheed Masood
5. Dr. Prabhakar Kore
6. Shri Jagat Prakash Nadda
7. Shri Arvind Kumar Singh
8. Shri D. Raja
9. Shri H. K. Dua
10. Shrimati B. Jayashree

LOK SABHA

- @11. Shri Ashok Argal
12. Shri Kirti Azad
13. Shri Mohd. Azharuddin
14. Shrimati Sarika Devendra Singh Baghel
15. Shri Kuvartjibhai M. Bavalia
16. Shrimati Priya Dutt
17. Dr. Sucharu Ranjan Halder
18. Mohd. Asrarul Haque
19. Dr. Monazir Hassan
20. Dr. Sanjay Jaiswal
21. Dr. Tarun Mandal
22. Shri Mahabal Mishra
23. Shri Zafar Ali Naqvi
24. Shrimati Jayshreeben Patel
25. Shri Harin Pathak
26. Shri Ramkishun
27. Dr. Anup Kumar Saha
28. Dr. Arvind Kumar Sharma
29. Dr. Raghuvansh Prasad Singh
30. Shri P.T. Thomas
- #31. Shri Chowdhury Mohan Jatua

* Ceased to be Member of the Committee *w.e.f.* 28th October, 2012.

@ Ceased to be Member of the Committee *w.e.f.* 9th January, 2013.

Nominated as a Member to the Committee *w.e.f.* 14th December, 2012.

SECRETARIAT

Shri P.P.K. Ramacharyulu, *Joint Secretary*

Shri R.B. Gupta, *Director*

Shrimati Arpana Mendiratta, *Joint Director*

Shri Dinesh Singh, *Deputy Director*

Shri Pratap Shenoy, *Committee Officer*

PREFACE

I, the Chairman of the Department-related Parliamentary Standing Committee on Health and Family Welfare, having been authorized by the Committee to present the Report on its behalf, do hereby present this Sixty-Sixth Report on the action taken by the Department of Health and Family Welfare on the recommendations/observations contained in the 59th Report of the Committee on “Functioning of Central Drugs Standards Control Organization (CDSCO)”.

2. The Committee had presented its 59th Report to both Houses of Parliament on the 8th May, 2012. The Ministry of Health and Family Welfare furnished an Interim Action Note (ATN) on the 12th September, 2012 and Final Action Taken Note on the 28th December, 2012 on the recommendations/observations as contained in the 59th Report of the Committee.

3. The Committee at its meeting held on the 23rd April, 2013, considered and adopted the Draft Report.

4. For facility of reference and convenience, observations and recommendations of the Committee have been printed in bold letters in the body of the Report.

NEW DELHI;
23rd April, 2013

Vaisakha 3, 1935 (Saka)

BRAJESH PATHAK
Chairman,
Department-related Parliamentary Standing
Committee on Health and Family Welfare

LIST OF ACRONYMS

AIIMS	– All India Institute of Medical Sciences
ATN	– Action Taken Note
APIs	– Application Programming Interface
CDSCO	– Central Drugs Standard Control Organisation
CMC	– Christian Medical College
DCG(I)	– Drugs Controller General (India)
DTAB	– Drug Testing Advisory Board
DCC	– Drugs Consultative Committee
DDC	– Deputy Drugs Controller
DMA	– Danish Medicine Agency
FDCs	– Fix Dose Combinations
GTB Hospital	– Guru Teg Bahadur Hospital
GCP	– Good Clinical Practice
GMP	– Good Manufacturing Practice
JIPMER	– Jawaharlal Institute of Postgraduate Medical Education and Research
KGMU	– King George’s Medical University
LHMC	– Lady Hardinge Medical College
LNJP	– Hospital Lok Nayak Jai Prakash Narayan Hospital
MAMC	– Maulana Azad Medical College
MCI	– Medical Council of India
NDACs	– New Drugs Advisory Committees
NLEM	– National List of Essential Medicines
PSURs	– Periodic Safety Update Reports
PGIMER	– Post Graduate Institute of Medical Education and Research
RML H	– Ram Manohar Lohia Hospital
SOPs	– Standard Operating Procedures
SSC	– Staff Selection Commission
UCMS	– University College of Medical Sciences
UPSC	– Union Public Service Commission
VMMC	– Vardhman Mahavir Medical College

REPORT

Introduction

(A) The Fifty-ninth Report of the Department-related Parliamentary Standing Committee on Health and Family Welfare (2011-12) on functioning of CDSCO was presented to the Parliament on May 8, 2012. It was conveyed to the Government immediately thereafter *vide* Rajya Sabha Secretariat Office Memorandum dated May 9, 2012 for implementation of the Recommendations contained therein. As per rules the Government was required to furnish details of action taken by them on the Recommendations contained in the Fifty-ninth Report to the Committee within three months from the date of presentation of the Report *i.e.* by August 7, 2012. The Government submitted its Action Taken Note (ATN), that on September 12, 2012.

(B) The Committee examined these action taken replies of the Government in-depth. Most of them were evasive, inconclusive, dilatory and vague. Most importantly, the replies were without any firm commitment about the implementation of Recommendations. During the course of its examination of the ATN the Committee also found that the Government, had constituted a three member expert committee to go into various irregularities, acts of omission and commission, dereliction of duty and collusive acts of the Organization pointed out in the Report. This expert committee set up immediately after presentation of the Report was required to submit its findings to the Government within two months. The Committee, however, observed that the said expert Committee had not submitted its findings to the Government even till the ATN was furnished to it. Consequently, replies to nineteen Recommendations of the Committee, mostly pertaining to gross irregularities, had not been furnished. These included Recommendation Nos. 7.14, 7.16, 7.31, 7.32, 7.33, 7.34, 7.35, 7.36, 7.37, 7.38, 7.41, 7.42, 7.43, 7.45, 7.46, 7.47, 7.49, 7.51 & 7.52.

(C) Taking cognizance of these serious deficiencies and shortcomings, Department of Health and Family Welfare was asked to submit the revised Action Taken Note before 30th December, 2012.

(D) The Department of Health and Family Welfare *vide* its Office Memorandum dated the 28th December, 2012 furnished its final action taken replies to the Committee. The present Report of the Committee is an analysis of these final actions taken replies of the Government to the Recommendations contained in the Fifty-ninth Report of the Committee.

Preliminary Submissions

As a part of the action taken replies the Government has made the following preliminary submissions:-

1. The Ministry of Health and Family Welfare in general agrees with the observations of the Hon'ble Committee. It regrets the delay in submission of this final Action Taken Report.
2. The Government had constituted a three member expert committee comprising Dr. V.M. Katoch, Secretary (Department of Health Research) and Director General, ICMR, Dr. P.N. Tandon, President, National Brain Research Centre, Department of Biotechnology, Manesar and Dr. S.S. Aggarwal, former Director, Sanjay Gandhi Post-graduate Institute of Medical Sciences, Lucknow under the following terms of reference and give its report:

To examine the validity of the scientific and statutory basis adopted for approval of new drugs without clinical trials as pointed out in the Report for further appropriate action in the matter.

To outline appropriate measures to bring about systemic improvements in the processing and grant of statutory approvals.

To suggest steps to institutionalize improvements in other procedural aspects of the functioning of CDSCO.

3. The three-member expert Committee that was required to submit its report within a period of two months took longer as it had to undertake comprehensive consultations with a large number of medical experts all over the country. The Committee submitted its report to the Government on 22.11.2012. A copy of the full report is being submitted to the Rajya Sabha Secretariat separately. The gist of its recommendations is as under:

(I) *Is there scientific validity of the statutory provision for allowing approval of drugs (already approved in countries abroad) without clinical trial in India?*

The overwhelming response of the selected medical professional community to this question was “conditional Yes”. The committee agrees with the same. However, this provision shall be applied only in highly selected cases and in a transparent and accountable manner. The committee recommends:

A select group should be constituted of knowledgeable medical professionals to:

Lay down the principles of determining the circumstances where such provision may apply, and

Lay down the procedure that should be adopted while applying this provision

The Committee has also given a list of names that can be considered for constituting this group.

A group of medical professionals and legal experts shall be constituted to *revise* the existing Rule 122A (2), Rule 122B (3) (1) and sub-clause (3) of Clause 1 of Schedule Y on the basis of guidelines and procedures evolved by the group constituted *vide* recommendation No. (i) above to provide for approval/licensing of drugs (already approved abroad from recognized countries) in India without clinical trial in India under exceptional circumstances only.

The CDSCO shall take appropriate steps to implement the revised statutory provisions and the guidelines and the procedures laid down by the expert group constituted under recommendation No. (i) above. For this purpose the CDSCO shall issue appropriate guidance to the Industry and the NDACs should lay down SOPs for implementation of the provision of providing approval/licensing of drugs in India without clinical trial in India. All future approvals/licensing of drugs without clinical trial in India should be regularly monitored.

All the 38 approvals granted under existing provisions, as identified by the Parliamentary Standing Committee (and CDSCO), *and also others, if any*, shall be re-reviewed by the respective newly constituted New Drug Advisory Committees as per revised provisions and the SOPs laid down by them. It would be prudent to take any action on already approved/licensed drugs, such as withdrawal of the approval etc., only after such a re-review. The NDACs may ask additional desired information from the manufacturers as deemed necessary. This should be carried out in a time bound fashion.

The Committee endorses the recommendations of the Parliamentary Standing Committee to be extra careful in approving the FDCs. The CDSCO should constitute a Committee of experts to lay down the *principles and procedures* to be adopted for approval of FDCs. The committee shall also review the *existing statutory provisions* for the approval of FDCs by the CDSCO and State Drug Authorities and recommend appropriate changes, if necessary. It should be a thorough and systematic exercise carried out with due diligence.

In India, to by-pass the price regulatory requirement, the use of FDCs is rampant. Once the rationale, principles and procedures for approval/licensing of new FDCs are laid down, all the existing FDCs may be re-reviewed in the interest of public health at large.

(II) *Measures to bring about systemic improvements in the processing and grant of statutory approvals*

(III) *Steps to institutionalize improvements in other procedural aspects of the functioning of CDSCO.*

In respect of (II) and (III) above, the Committee feels that a consultant/consultancy needs to be commissioned to review the structure of CDSCO based on the recommendations of the Mashelkar Committee.

4. **Steps taken to strengthen the drug regulatory system of the country:** A number of steps have been taken to strengthen the CDSCO during the last four years. While the CDSCO had a total strength of 111 posts in 2008 with 32 posts of Drug Inspectors, its strength has increased to 310 sanctioned posts with 169 posts of Drug Inspectors. Efforts are being made to further create additional posts in view of the increasing requirements of the organization and also to fill up vacant posts. The organization, which had only 12 Drug Inspectors in position in 2008, presently has 65 Drug Inspectors and selection of 90 more has recently been completed. Further, as against in 2008 when there was no Deputy Drugs Controller, now there are 14 Deputy Drugs Controllers.

In view of the constraints of staff due to delay in regular appointments, the Government has resorted to appointment of 234 persons in various categories, including 113 technically qualified personnel on contract basis so as to assist the organization in coping with the work load at the Head Quarters as well as Zonal Offices. Strengthening of zonal offices of CDSCO has also been done. During this period, two sub-zonal offices (Ahmedabad and Hyderabad) have been upgraded to zonal offices and three new sub-zones (Chandigarh, Bangalore and Jammu) have been set up. Now there are 6 Zones and 3 Sub-Zones of CDSCO in different parts of the country. The Ministry has already identified places for creation of three more Zones/Sub-Zones at Goa, Indore and Guwahati.

The Ministry has ambitious plans for capacity building for drug testing in the country during the Twelfth Plan. This includes upgradation of existing labs, setting up of new labs, setting up of Mini labs at ports of entry, commissioning of Mobile Labs, special labs for medical devices and cosmetics, etc. On skill development front, the CDSCO has been vigorously engaged in imparting comprehensive training to the staff of CDSCO at various levels. A separate training division has already been constituted and operationalized in CDSCO.

For attending to the area of Pharmacovigilance, which is already being done through the Pharmacovigilance Programme of India the Ministry aims at involving all medical colleges in the country in the programme.

The status of working of States' Drugs regulatory mechanism has been an area of concern as the enforcement of Drugs and Cosmetics Act is mainly done by them. The Ministry has given special attention to this deficient area. Considering the importance of making good quality drugs available to the public at large, in the Twelfth Plan it is proposed to strengthen the drug regulatory mechanism in the States/UTs through a specific scheme. This envisages augmentation of both the physical infrastructure and human resources. A new budget line has been opened and an initial token provision of Rs. 2 crore has been made in 2012-13 budget.

5. **Measures taken to streamline the process of new drug approval:** In order to streamline the process of drug approvals, 12 New Drug Advisory Committees (NDAC) and 6 Medical Device

Advisory Committees (MDAC) consisting of eminent medical experts from across the country have been constituted to advise the Drugs Controller General (India) in matters related to regulatory approval of new drugs, clinical trials and new medical devices. Two more Committees of Experts also advise the DCG(I) in matters related to regulatory approval of clinical trials for Investigational New Drugs (IND) and special biological products. Expert committee would be constituted to define policies, guidelines and lay down Standard Operating Procedures (SOPs) for approval of new drugs. The situation is still evolving and will be a continuous process.

6. **WHO National Regulatory Authority (NRA) Assessment (December, 2012):** A WHO-led team conducted a comprehensive review of the functioning of the National Regulatory Authority of India (CDSCO) and its affiliated institutions (including drugs testing laboratories) by its international experts drawn from eight different countries (USA, France, Sweden, Switzerland, China, Indonesia, Thailand and Iran) to assess whether CDSCO meets WHO published indicators for a functional vaccine regulatory system. WHO has established stiff benchmarks that define international expectations for a functional vaccine regulatory system. The regulatory functions of CDSCO and its affiliated institutions were assessed for compliance against the WHO indicators. In addition to the general framework for the system, the following regulatory functions were evaluated: marketing authorization and licensing; postmarketing surveillance including adverse events following immunization (AEFI); lot release by the national regulatory authority; laboratory access; regulatory inspections of manufacturing sites and distribution channels; and authorization and monitoring of clinical trials. WHO prequalification, which is a guarantee that a specific vaccine meets international standards of quality, safety and efficacy, is a prerequisite for manufacturers to supply to countries through United Nations procuring agencies. The WHO assessment concluded that the vaccine manufacturers in India continue to remain eligible to apply for Prequalification of specific products. The WHO assessment also concluded that the National Regulatory Authority of India, *i.e.*, CDSCO continues to be functional.

The Committee takes note of various steps initiated by the Government and action suggested on the Recommendations contained in its Fifty-ninth Report. It is, however, hugely disappointed to observe that inspite of the Government being afforded another opportunity to furnish conclusive responses on the various Recommendations of the Committee, has once again chosen to come up with half measures, vague and dilatory responses to say the least. As the subsequent analysis of the Committee will bear out that general agreement of the Government with the Recommendations of the Committee is mere platitude. The Government has done nothing concrete or conclusive even for the Recommendations and findings of the Committee, which directly concern the safety, and health of crores of our countrymen. The Preliminary Submissions, as is evident from its plain reading only, confirms the intent of the Government in staggering decisions and action on vital matters either by way of referring matters to committees after committees or evolving timeconsuming policies. The Committee deprecates this tendency of the Government in strongest terms.

The Committee would now deal with action taken by the Government on its individual Recommendations.

CHAPTER-I

RECOMMENDATIONS/OBSERVATIONS IN RESPECT OF WHICH REPLIES OF THE GOVERNMENT HAVE BEEN ACCEPTED BY THE COMMITTEE

RECOMMENDATIONS/OBSERVATIONS

1.1 The Committee is of the firm opinion that most of the ills besetting the system of drugs regulation in India are mainly due to the skewed priorities and perceptions of CDSCO. For decades together it has been according primacy to the propagation and facilitation of the drugs industry, due to which, unfortunately, the interest of the biggest stakeholder *i.e.* the consumer has never been ensured. Taking strong exception to this continued neglect of the poor and hapless patient, the Committee recommends that the Mission Statement of CDSCO be formulated forthwith to convey in very unambiguous terms that the organization is solely meant for public health. (Para 2.2)

Action Taken

1.2 The functions of CDSCO emanate from the provisions of the Drugs and Cosmetics Act, 1940 and Drugs and Cosmetics Rules, 1945.

1.3 The preamble of the Drugs and Cosmetics Act, 1940 is to regulate the import, manufacture, distribution and sale of drugs and cosmetics. The quality control is exercised through the system of licensing and inspections as provided under the Act and Rules.

1.4 In the spirit of the recommendations of the Hon'ble Committee a Mission Statement of CDSCO has been formulated as under:

“To safeguard and enhance the public health by assuring the safety, efficacy and quality of drugs, cosmetics and medical devices.”

Further Recommendation

1.5 The Committee notes with satisfaction that the Government has at last formulated a Mission Statement, which is in consonance with the mandate of CDSCO. The Committee expects the Government to move beyond the formulation stage and formally implement this Mission Statement in letter and in spirit.

RECOMMENDATION/OBSERVATION

1.6 The Committee notes with serious concern that CDSCO is substantially under-staffed. Of the 327 sanctioned posts, only 124 are occupied. At this rate, what would be the fate of 1,045 additional posts that have been proposed is a moot point. If the manpower requirement of the CDSCO does not correspond with their volume of work, naturally, such shortage of staff strains the ability of the CDSCO to discharge its assigned functions efficiently. This shortcoming needs to be addressed quickly. Consideration can also be given to employ medically qualified persons as Consultants/Advisers (on the pattern of Planning Commission) at suitable rank. (Para 2.19)

Action Taken

1.7 The Government agrees with the observations of the Hon'ble Committee. Staff constraint

has always been the key factor in the functioning of the organization. The Ministry has been making continuous efforts at improvement in the situation. Though it has been attempted to take care of the constraint of medically qualified personnel through NDACs in some respects, the Ministry has already decided to consider engagement of highly qualified medical professionals in various therapeutic fields to assist the CDSCO in its core functioning.

RECOMMENDATION/OBSERVATION

1.8 The Committee also gathers that the average time taken for the completion of recruitment process is approximately 12 to 15 months. The Committee, therefore, recommends that to overcome the staff shortage, the Ministry should engage professionally qualified persons on short-term contract or on deputation basis until the vacancies are filled up. Due to the very sensitive nature of regulatory work, great care will need to be taken to ensure that persons employed for short periods did not and will not have Conflict of Interest for a specified period. (Para 2.20)

Action Taken

1.9 The Government agrees with the observations of the Hon'ble Committee. Delays in recruitment process do, however, take place as there are very time consuming procedures adopted by the recruiting agencies (UPSC and SSC) mandated by various Government instructions. These delays at times are beyond the control of the Ministry and despite the Ministry's efforts at expediting these recruitments, the situation has not improved. The Ministry would continue its efforts to expedite the recruitment process. However, to bridge the gap between the demands of the functioning of the organization and the availability of manpower, the Ministry has resorted to engagement of personnel on contract basis.

RECOMMENDATIONS/OBSERVATIONS

1.10 It is a matter of grave concern that there are serious shortcomings in Centre- State coordination in the implementation of Drugs and Cosmetics Act and Rules. This, the Committee notes, is despite the Ministry's own admission that Section 33P of the Drugs and Cosmetics Act contains a provision that enables the Central Government to give such directions to any State Government as may appear to it to be necessary for implementation of any of the provisions of the Drugs and Cosmetics Act and Rules made thereunder. The Committee understands that these provisions are meant to be used sparingly. However, there have been several situations which warrant intervention through Rule 33 P. Therefore the committee hopes that in future the Ministry would not be found wanting in considering the option of using Section 33P to ensure that provisions of central drug acts are implemented uniformly in all States. (Para 4.7)

Action Taken

1.11 The Ministry agrees with the observations of the Hon'ble Committee.

1.12 The issue of cancellation of licenses by the State Licensing Authorities for manufacture of drug formulations falling under the purview of the new drugs especially in respect of fixed dose combinations in the light of the observations made by the Parliamentary Standing Committee was discussed in the Drugs Consultative Committee in the meeting held on 20th July, 2012. It has been reiterated in the meeting that such license for new drugs for unapproved FDCs must not be granted by any State Licensing Authorities.

1.13 The State drug licensing authorities had also been issuing licenses of drug formulations along with the brand names which were not as per the provisions of the Drugs and Cosmetics Rules.

1.14 The Ministry has used the provisions under section 33P of the Act in the past. In order to take care of these aforesaid issues, the Ministry has again issued statutory directions under section 33P to the State Governments on 1.10.2012 on the following issues:

1. Not to grant licenses for manufacture for sale or for distribution or for export of new drugs, except in accordance with the procedure laid down under the said rules *i.e.* without prior approval of the Drugs Controller General (India).
2. To grant/renew licenses to manufacture for sale or for distribution of drugs in proper generic names only.

1.15 Copies of the two letters dated 1.10.2012 of the Ministry containing the said directions are enclosed at **Annexures-I** and **II**.

Further Recommendation

1.16 The Committee notes that the Government, albeit belatedly, has now started invoking Rule 33 P to issue directions to the State Governments in connection with the implementation of the Drugs and Cosmetics Act and Rules. It has in pursuance of the Recommendation of the Committee issued statutory directions to State Governments on October 1, 2012 under Rule 33P on two issues. The Committee while appreciating the action taken by the Government on its Recommendation feels that had the Government shown similar alacrity in resorting to Rule 33P in the past, things would not have come to such a sorry pass. It, therefore, considers the continued inaction of the Government and reluctance to resort to Rule 33 P in the past as inexplicable.

RECOMMENDATIONS/OBSERVATIONS

1.17 The documents submitted by the Ministry show that even in large developed countries with well developed drug regulation such as US the adverse reactions are not detected by spontaneous reports from doctors in practice. All major side effects were detected in large scale controlled, focused Post-Marketing Phase IV trials involving thousands of patients such as SCOUT on anti-obesity drug sibutramine (now banned) and the RECORD trial on rosiglitazone (now banned). Therefore to expect that any spontaneous reports from medical profession, either in private practice or even institutions (medical colleges, large hospitals) will pick up hitherto unknown side effects in India is not realistic. There is hardly any alternative but to take immediate cognizance of serious adverse drug reactions reported from countries with well developed and efficient regulatory systems. The health and lives of patients in India cannot be put to risk in the hope of detecting ADRs within the country. (Para 8.7)

1.18 The Committee feels that since the chances of picking up unknown serious adverse effects of drugs being marketed in the country are remote, therefore CDSCO should keep a close watch on regulatory developments that take place in countries with well developed regulatory systems in the West and take appropriate action in the best interest of the patients. (Para 8.8)

Action Taken

1.19 It has since been decided that whenever a drug is banned due to adverse drug reactions in countries with well developed and efficient regulatory system *viz.* USA, UK, EU, Australia, Japan and Canada, the manufacture, import and marketing of such drugs would be immediately put under suspension till the safety of the drug is examined and established in the country.

1.20 The DCG (I) has been adequately sensitized in this regard.

Further Recommendation

1.21 The Committee is happy to note that finally pragmatism and concern for public good has prevailed and the Ministry has decided to suspend marketing approval of all drugs prohibited for sale in the US, UK, EU, Australia, Japan and Canada for safety reasons. The Committee is of the firm conviction that drugs not approved for use or approved for extremely restricted use in countries with robust regulation should also be brought under the purview as has been done by the World Health Organisation. It is a well-known fact that drug manufacturers simply do not submit applications for the approval of new drugs to robust regulators to avoid rejection by other agencies/countries. It is precisely for this reason that several manufacturers, in spite of the huge potential of marketing drugs in the US, avoid entering the US market. As once a drug is rejected in the US, it becomes highly impossible to get approval even in countries with poor drug regulation. The Committee is also confident that now when the Ministry has adopted, albeit, belatedly this global best practice in drug regulation, it would immediately apply it on two burning cases *viz.* Analgin and Buclizine.

1.22 Furthermore as this salutary mechanism has been put in place in India, the Committee going a step further would also like the CDSCO to mandatorily go into the regulatory status of drugs in countries with robust regulation. And any drug which is relevant to the needs of the countries like the US, Canada, UK, EU, Australia and Japan, if not cleared there should be subjected to intense scrutiny both when it is being considered for approval as also when their continued marketing is being reviewed. The Committee would appreciate a decision in the matter within fifteen days of presentation of this Report to the Parliament.

RECOMMENDATIONS/OBSERVATIONS

1.23 In most cases, most of these experts whether appointed by CDSCO or DTAB are from Delhi. The following facts reveal this pattern:

- Rimonabant was referred to a committee of six experts, all from Delhi.
- Levonorgestrel: Four out of five from Delhi.
- Letrozole: Four out of five from Delhi.
- Sibutramine: All five from Delhi.
- Rosiglitazone: All five from Delhi.

A review of membership shows that one expert sat on 5 of the 6 committees. One wonders whether expertise on drugs is confined to Delhi. (para 8.10)

Action Taken

1.24 As regards one expert, namely Dr. Y.K. Gupta who attended five of the six committees, it may be mentioned that Dr. Y.K. Gupta is Professor and Head, Department of Pharmacology, AIIMS, New Delhi. Dr. Gupta has wide experience and expertise in the relevant field. Being based in Delhi and considering his standing, he was invited for attending most of those meetings.

1.25 However, henceforth, such committees will be constituted with experts from across the country in light of the observation of the Hon'ble Committee.

1.26 The DCG(1) has been adequately sensitized in this regard.

Further Recommendation

1.27 **The Committee notes with satisfaction that the Ministry has finally veered towards the idea of constituting committees with experts from across the country. The Recommendation of the Committee was basically to highlight that the Delhi centric composition of these committees was depriving them of the sage advice and expertise of the immense talent present in Government medical colleges spread across the country. In this age of specialization and super specialization in various disciplines and sub disciplines of medical science it is, in any case, not very sensible to confuse expertise with hierarchy.**

RECOMMENDATION/OBSERVATION

1.28 The Committee strongly recommends that with some 330 teaching medical colleges in the country, there are adequate number of knowledgeable medical experts with experience who can be requested to give their opinion on the safety and efficacy of drugs. The need is to make such consultations very broad based so as to get diverse opinion. The opinions, once received, can be put in public domain inviting comments. Once the experts know that their opinions will be scrutinized by others, including peers, they would be extra cautious and give credible evidence in support of their recommendation. (Para 8.11)

Action Taken

1.29 The Ministry agrees with the observations of the Committee. Efforts would be made to make such consultations as broad-based as possible. The opinions of the experts would also be put on the web-site. The DCG(I) has been adequately sensitized in this regard.

Further Recommendation

1.30 **The Committee is happy to note that the Ministry has appreciated the nuances of this recommendation of far reaching import and decided to implement it. It would, however, like the Ministry to take immediate steps to commence the implementation proper of this measure to derive its maximum benefit for the general public without any further loss of time.**

RECOMMENDATIONS/OBSERVATIONS

1.31 Unfortunately some State Drug Authorities have issued manufacturing licenses for a very large number of FDCs without prior clearance from CDSCO. This is in violation of rules though till May, 2002, there was some ambiguity on powers of the State Drug Authorities in this respect. However the end result is that many FDCs in the market have not been tested for efficacy and safety. This can put patients at risk. (Para 9.2)

1.32 To remove such unauthorized FDCs from the market, the Central Government can either issue directions under Section 33P to States to withdraw the licences of FDCs granted without prior DCGI approval or the Central Government can itself ban such FDCs under Section 26A. (Para 9.3)

1.33 The Committee was informed that DCGI has been requesting State Drug Authorities not to issue manufacturing licences to new FDCs and suspend licences of unauthorized FDCs issued in the past. However in exercise of powers under Section 33P specific directions have not been issued. The Ministry failed to provide any coherent reason for lack of action under this Rule. The Ministry informed the Committee that even if Section 33P was invoked, there was no provision to take action against States if directions were not carried out. If considered necessary, the Ministry

may examine the possibility of amending the law to ensure that directions under Section 33P are implemented. (Para 9.4)

1.34 It is also possible to ban FDCs, not authorized by CDSCO by invoking Section 26A which empowers the Central Government to ban any drug to protect public health. The Committee was informed that the Government has not evoked Section 26A either so far. No explanation was offered for not using powers under Section 26A. (Para 9.5)

1.35 The Committee was informed that the issue regarding grant of Manufacturing Licenses for unapproved FDCs by some State Drug Authorities were first deliberated in 49th DTAB meeting held on 17 February, 2000 *i.e.* 11 years ago. It is a matter of great concern that even after a lapse of a decade, no serious action has been taken. (Para 9.6)

1.36 The Committee is of the view that those unauthorized FDCs that pose risk to patients and communities such as a combination of two antibacterial need to be withdrawn immediately due to danger of developing resistance that affects the entire population. (Para 9.7)

Action Taken

1.37 The issue of cancellation of licenses by the State Licensing Authorities for manufacture of drug formulations falling under purview of the new drugs especially in respect of fixed dose combinations in the light of the observations made by the Parliamentary Standing Committee was discussed in the Drugs Consultative Committee in the meeting held on 20th July, 2012. It has been reiterated in the meeting that such license for new drugs for unapproved FDCs must not be granted by any State Licensing Authorities.

1.38 Earlier, in 2007, direction was issued to the State Drug Controllers to withdraw the 294 FDCs which were licensed without approval of DCG(I). However, the manufacturers Association got stay order from the Madras High Court. The matter is still *sub-judice*.

1.39 The Ministry has, however, again issued statutory direction under section 33P to the State Governments on 1.10.2012 to refrain from granting new drugs licensing including FDCs without approval of DCG (I).

1.40 In the light of the observations of the Hon'ble Committee:

- (i) Action in respect of the aforesaid 294 FDCs will be taken after the outcome of the court case in Madras High Court;
- (ii) In respect of other FDCs licensed by the State Licensing Authorities before 1.10.2012, *i.e.* the date of issue of direction under section 33P, without the permission of DCG(I), it has now been decided that the DCG(I) will ask all the State Drugs Controllers to ask the concerned manufacturers to prove the safety and efficacy of such FDCs before the CDSCO within a period of 18 months failing which such FDCs will be considered for being prohibited for manufacture and marketing in the country. As regards the new FDC, if any, licensed by the States Licensing Authorities after 1.10.2012 without approval of DCG(I), the same will be considered for being prohibited from manufacturing and marketing in the country.

Further Recommendation

1.41 **The Committee derives satisfaction from the fact that at last in pursuance of its Recommendation the issue of manufacturing licenses to unauthorized FDCs has been centre staged after more than eleven years and discussed in the Drugs Consultative Committee meeting held on 20 July, 2012. It further notes with satisfaction that the Ministry has**

issued statutory direction under Section 33P to State Governments on 1 October, 2012 to refrain from granting drug licenses including FDCs without the approval of DCG (I). The Ministry has also indicated its intention to take action against the 294 FDCs which are a subject of litigation in Madras High Court based on the outcome of the case. Furthermore, in regard to FDCs licensed by the State Authorities before 1 October, 2012, the State Authorities have been asked to direct the manufacturer concerned to prove safety and efficacy of such FDCs before the CDSCO within a period of 18 months or invite prohibition for manufacture and marketing. The Committee feels that 18 months is too long a period for the purpose of proving efficacy and safety of these products. As in the eventuality of these being harmful or less advantageous to health and well being of public can cause incalculable damage in this long interregnum. The Committee therefore strongly recommends that this period should be curtailed to nine month *i.e.* up to 30 June, 2013 without fail.

RECOMMENDATIONS/OBSERVATIONS

1.42 The Committee feels that though the Ministry is forming NDACs, which are given very important powers, there is no transparent procedure for the selection of experts of such Committees. The Committee also recommends that institutions from which experts are chosen should be from different parts of the country. (Para 10.2)

Action Taken

1.43 The 12 New Drug Advisory Committees so far constituted consist of medical specialists from Government medical colleges and reputed institutes across the country as under:

- AIIMS, New Delhi
- PGIMER, Chandigarh
- JIPMER Pondicherry
- LHMC and RML Hospital, New Delhi
- VMMC and Safdatjung Hospital, New Delhi
- Tata Memorial Hospital, Mumbai
- CMC, Vellore
- MAMC with GB Pant and LNJP Hospital, New Delhi
- UCMS (University College of Medical Sciences) with GTB Hospital, New Delhi
- Seth GS Medical College and KEM Hospital, Mumbai
- Regional Cancer Centre, Trivandrum
- SMS Medical College, Jaipur
- Medical College, Kolkata
- KGMU, Lucknow
- IPGME&R and SSKM Hospital, Kolkata
- Madras Medical College, Chennai
- Institute of Medical Sciences, Banaras Hindu University, Varanasi

- Gawahati Medical College and Hospital, Gawahati
- Government Medical College, Jammu
- Nizam's Institute of Medical Sciences, Hyderabad

1.44 The Committees would be more broad-based. The criteria for selection of experts will be decided by a committee of experts and willing experts from Government, other institutions of high repute and excellence will be invited for preparing a panel of experts to advise CDSCO in various technical matters.

1.45 The DCG(I) has been adequately sensitized in this regard.

Further Recommendation

1.46 **The Committee notes that to begin with the Ministry has formed twelve New Drug Advisory Committees (NDAC) consisting of ten members each. These 120 experts have been drawn from twenty institutions. Given the fact that the country has 135 government medical colleges, the Committee finds this composition of NDACs not at all representative of the vast pool of expertise available countrywide. However, taking the assurance of the Ministry about broad basing of NDACs on face value, the Committee is confident that the Ministry will give due representation to experts from different Government medical colleges when the NDACs are constituted next.**

RECOMMENDATIONS/OBSERVATIONS

1.47 The Committee observed that even, in those cases where the PSURs were submitted, the frequency and/or format was not as per rules. In the case of two drugs of MNCs (dronedarone of Sanofi Aventis and pemetrexid of Eli Lilly), the PSURs were neither India specific nor in the approved format as required by law. Some companies submitted PSURs for the products being marketed in the country but very few PSURs were India-specific. (Para 12.4)

1.48 The Committee is of the firm view that there is a poor follow-up of side effects in Indian patients both by doctors and manufacturers. The objective of PSURs is to collect information about adverse effects on patients in India which would help to determine ethnic differences, if any and result in dosage adjustment, revision of precautions and warnings, if necessary. The Committee takes strong exception to such rampant violation of the mandatory requirements. (Para 12.5)

1.49 The Committee strongly recommends that the Ministry should direct CDSCO to send a stern warning to all manufacturers of new drugs to comply with mandatory rules on PSURs or face suspension of Marketing Approval. PSURs should be submitted in CDSCO-approved format which would help track adverse effects discovered in Indian ethnic groups. (Para 12.6)

Action taken

1.50 The applicants who have been granted approval of new drugs, have been instructed *vide* letter dated 13.9.2012 to submit India specific PSUR in the format as specified in the rules.

1.51 The non-compliance of this provision would attract suspension/cancellation of the marketing approval.

Further Recommendation

1.52 **The Committee notes that in pursuance of its Recommendation, applicants who have been granted approvals of new drugs have been instructed formally on 13 September, 2012**

to submit India specific PSUR in the format specified in the rules or risk suspension/cancellation of the marketing approval. The Committee is happy with this step in the right direction. It, however, cautions the Ministry to merely not rest with the issue of instructions but also monitor and follow up vigorously the compliance of these instructions by the manufacturers so as to ensure that they do not remain restricted merely on paper.

RECOMMENDATIONS/OBSERVATIONS

1.53 It is known that retail chemists also stock and sell items other than drugs including chocolates, cold drinks etc. During summer these items are stored in the refrigerator while due to paucity of space temperature-sensitive medicines may be lying outside. When samples are picked up, tested and found to be sub-standard, the State Drug Authorities blame and prosecute manufacturers. Therefore the Committee recommends that specifically in the case of temperature sensitive products such as insulins, due consideration should be given to the reference samples of the same batch preserved by the manufacturers. (Para 15.7)

Action Taken

1.54 The Ministry has noted the observations of the Committee.

1.55 The State Drugs Controllers have already been directed to take necessary action.

CHAPTER-II

**RECOMMENDATIONS/OBSERVATIONS IN RESPECT OF WHICH THE COMMITTEE
DOES NOT DESIRE TO PURSUE IN VIEW OF THE GOVERNMENT'S REPLIES**

-NIL-

CHAPTER-III

RECOMMENDATIONS/OBSERVATIONS IN RESPECT OF WHICH REPLIES OF THE GOVERNMENT HAVE NOT BEEN ACCEPTED BY THE COMMITTEE

RECOMMENDATIONS/OBSERVATIONS

3.1 At the same time, the optimal utilization of the current staff in the best interest of public is the responsibility of those who run the CDSCO. In a resource constrained country like India, it is extremely difficult to meet the demands, however, genuine, of all the State entities in full. Hence, prioritization is the key. For example, work relating to an application for Marketing Approval of a New Drug that will be used by millions and thus have an impact on the well being of public at large in India for years to come, is far more important and urgent than giving permission to a foreign company to conduct clinical trials on an untested new patented, monopoly drug.
(Para 2.21)

Action Taken

3.2 The Government agrees with the observations of the Hon'ble Committee and has noted them for due compliance.

3.3 The DCG (I) has been adequately sensitized in this regard. However, the requisite policies and Standard Operating Procedures (SOPs) for prioritization in this regard would also be prepared.

Further Recommendation

3.4 The Committee is really dismayed by this casual attitude of the Government as it strongly feels all these actions only involve routine application of mind and could have been completed immediately after the Recommendations of the Committee were conveyed to the Government. The Committee, therefore, feels that enough time has been wasted by the Government in extending assurances in the matter and they should now complete all action required in this context including preparation of policies and standard operating procedures within one month of presentation of this Report to the Parliament.

RECOMMENDATION/OBSERVATION

3.5 The Committee also observes that the strengthening of drugs regulatory mechanisms cannot be achieved by manpower augmentation alone. A host of issues involving capacity-building of CDSCO like upgradation of existing offices, setting up of new offices, creation of new central drugs testing laboratories and equipping them with the state-of-the-art technology to enable them to carry out sophisticated analysis of drugs, upgradation of the existing 6 Central Drugs Testing Laboratories, skill development of the regulatory officials, implementation of an effective result-oriented pharmacovigilance programme drawing on global experience, increased transparency in decision-making of CDSCO etc. will have to be addressed before the desired objectives are realized.
(Para 2.22)

Action Taken

3.6 The Government agrees with the observations of the Hon'ble Committee and has noted them for due compliance.

Further Recommendation

3.7 The Committee finds the instant reply of the Government yet another instance of delaying tactics. If the Government agrees with this Recommendation of the Committee what has stopped it from implementing it during last so many months is the moot point. The Committee, therefore, reiterates its Recommendation for immediate compliance by the Government.

RECOMMENDATIONS/OBSERVATIONS

3.8 In the absence of any reasons for unwillingness on the part of medically qualified persons to join CDSCO, the Committee is of the opinion that emoluments and perquisites may not be the main or only reason. It is noticed that minimum prescribed academic qualifications for the post of DCGI is barely B.Pharm. On the other hand for Deputy Drugs Controller (DOC), the prescribed minimum qualification is post-graduation for medically qualified persons. The stumbling block is the requirement that DCGI should have experience in the “manufacture or testing of drugs or enforcement of the provisions of the Drugs and Cosmetic Act for a minimum period of five years.” This requirement virtually excludes even highly qualified medical doctors from occupying the post of DCGI. Moreover the rule stipulates that doctors with post-graduation should be either in pharmacology or microbiology only, thus excluding post- graduates, even doctorates (like OM) in a clinical subject. Besides, highly qualified medical doctors may be reluctant to work under and report to a higher officer with lesser qualifications in a technology driven regulatory authority set-up. Unless these concerns are addressed, it would be difficult to get the desperately required medically qualified professionals on the rolls of CDSCO. (Para 2.23)

3.9 The Committee fails to understand as to how a graduate in pharmacy or pharmaceutical chemistry (B.Pharm) is being equated with a medical graduate with MD in Pharmacology or Microbiology. Apart from the obvious anomaly, with rapid progress in pharmaceutical and biopharmaceutical fields, there is urgent need to revise the qualifications and experience as minimum eligibility criteria for appointment as DCGI. The Committee is of the view that it is not very rational to give powers to a graduate in pharmacy, who does not have any clinical or research experience to decide the kinds of drugs that can be prescribed by super specialists in clinical medicine such as those holding OM and PhD qualifications and vast experience in the practice of medicine and even research. (Para 3.6)

3.10 On a larger plane, the Committee is disillusioned with the qualifications provided in the age old Rules for the head of a crucial authority like CDSCO. The extant Indian system is nowhere in so far as sheer competence and professional qualifications are concerned when compared with countries like USA and UK. There is, therefore, an urgent need to review the qualifications, procedure of selection and appointment, tenure, emoluments, allowances and powers, both administrative and financial of the DCGI. While doing so, the Government may not only rely on the Mashelkar Committee Report which recommended augmented financial powers to DCGI but also take cue from similar mechanisms functioning in some of the developed countries like USA, UK, Canada, etc in order to ensure that only the best professional occupies this onerous responsibility. The Committee should be kept informed of the steps taken to address this issue. (Para 3.7)

3.11 In the considered opinion of the Committee, there can never be a more opportune time than now, to usher in these changes recommended by it. The post of DCGI is vacant as of now, with an official holding temporary charge. They, therefore, desire that the government should take immediate measures in terms of their instant recommendations to ensure that CDSCO is headed by an eminent and professionally qualified person. (Para 3.8)

Action Taken

3.12 The Government has duly taken care of the observations of the Hon'ble Committee. The Drugs and Cosmetics Rules provide the qualification for the post of licensing and controlling authority as "Graduate in Pharmacy or Pharmaceutical Chemistry or in Medicine with specialization in Clinical Pharmacology or Microbiology". These rules were made long before. As per these existing rules, the DCG(I) being the licensing and controlling authority in CDSCO must have these minimum qualifications.

3.13 The post of DCG(I) is equivalent to Joint Secretary and hence the qualification for the post is required to be of sufficiently higher level to maintain its high level position. Therefore, additional higher qualifications were considered for this post. Accordingly, the present notified RRs for the post of DCG(I) contain the basic qualification prescribed in the Drugs and Cosmetics Rules and additional higher qualifications as under:

“Essential: (i) Graduate degree in Pharmacy or Pharmaceutical Chemistry or in Medicine with specialization in Clinical Pharmacology or Microbiology from a recognized University established in India by law;

(ii) Postgraduate degree in Pharmacy/Pharmaceutical Chemistry/Biochemistry/Chemistry/Microbiology/Pharmacology from a recognized University or equivalent; and

(iii) 15 years' experience in manufacture or testing of drugs in a concern of repute or enforcement of the provisions of the Drugs and Cosmetics Act, 1940 and Rules.

Desirable: (i) Two years' experience in dealing with problems connected with drugs standardization and control and import and export of Drugs, and/or administration of the Drugs and Cosmetics Act and Rules.

(ii) Ph.D in Pharmaceutical Sciences”.

3.14 However, the qualifications and the notified Recruitment Rules for the post of DCG(I) are *sub-judice* in the Madras High Court on the directions of the Hon'ble Supreme Court.

3.15 However, the Ministry would set up an expert committee as also recommended by the three member expert committee to review and lay down the qualifications/experience, job description, powers and responsibilities etc. for the post of DCG(I) in consultation with the Ministry of Law as the matter is *sub-judice*. Additionally, this committee would also review these issues relating to other senior level posts in the organization.

Further Recommendation

3.16 The Committee notes that the modifications carried out previously by the Government in the qualification and recruitment rules for the post of DCG (I) are a matter of litigation. In any case these modified qualifications and rules do not address the concerns of the Committee to any extent whatsoever. The Committee also notes that unfortunately and as in the case of several of its other Recommendations, the Government has merely decided to setup an expert committee which has been recommended by the previously setup three member expert committee, referred to earlier in this Report, to lay down the qualifications, experience, job description, powers and responsibilities for the post of DCG (I) in consultation with the Ministry of Law. The proposed committee would also review these issues relating to other senior level positions in the Organization.

3.17 The Committee derives no solace from this very open-ended response of the Government. Nothing tangible has been done by the Government in the direction of

implementing this Recommendation of the Committee. The Committee understands that the matter is *sub-judice* in the context of the modifications carried out by the Government previously in the qualifications and recruitment rules for the post of DCG(I). The Committee is certain that this situation does not inhibit the Government from carrying out all necessary activities including the formation of an expert committee for and in connection with the implementation of the instant Recommendation of the Committee. It, therefore, considers the delay by the Government in constitution of an expert committee, as also other preparatory action, as unpardonable and desires that the same may be completed within a month of presentation of this Report to the Parliament.

RECOMMENDATIONS/OBSERVATIONS

3.18 As regards lack of databank and accurate information, the Committee would like to observe that given the information technology resources currently available, developing an effective system of coordination amongst State Drug Authorities for providing quality and accurate data could have been accomplished long back had the Ministry taken any initiative towards encouraging the States to establish a system of harmonized and inter-connected databanks. Evidently, no serious efforts seem to have been made in this regard. The Committee, however, expects that the Ministry would, at least now, play a more pro-active role in encouraging the States to employ modern information technology in the implementation of tasks assigned to them. At the same time a centralized databank (*e.g.* licenses issued, cancelled, list of sub-standard drugs, prosecutions etc.) may be created to which all the State Drug Authorities should be linked. (Para 4.8)

Action Taken

3.19 The Ministry agrees with the observations of the Hon'ble Committee.

3.20 The following steps have so far been taken by the CDSCO in this regard:

- (i) The data regarding about 85000 brands of drug formulations approved by the various State licensing authorities as obtained from the State Food and Drug Control Administration (FDCA), Gujarat has been uploaded on the web-site of CDSCO.
- (ii) Information on various approvals/licenses granted by the CDSCO are uploaded on its website from time-to-time.
- (iii) Recommendations of the NDACs in matters related to approval of new drugs and clinical trials are being uploaded on the CDSCO web-site from time-to-time.
- (iv) A file tracking system and posting of queries/approvals etc on the website of CDSCO on daily basis have been introduced.

3.21 The Government would take further necessary action on priority basis on creation of the required infrastructure in this direction. During the 12th Plan, the Ministry envisages to put a proper e-Governance system in place which will include inter-linking of all offices of Zonal/Sub-Zonal/Port offices/Laboratories of CDSCO and offices of State Drugs Controllers for fast communication and effective monitoring of quality of Drugs. The proposed system will include IT enabled services, National Registry, Video Conferencing facilities, archiving of all files etc.

3.22 The WHO assessors during the assessment of the National Regulatory Authority (NRA) in December 2012 have also recommended to have e-governance in the functioning of CDSCO.

Further Recommendation

3.23 **The Committee takes note of the various steps taken by the Government in**

consonance with its instant Recommendation. As a test case they also accessed the CDSCO website with a view to evaluate the data regarding 85,000 brands of drugs that have been uploaded on the website by the Ministry after obtaining the same from Food and Drug Control Administration, Gujarat. To their utter surprise, they could locate only 65,500 odd formulations on the site. They also found several banned drugs on the site; Drugs, which have been discontinued and are generally known to be so to the public at large also featured there. The Committee also noted a great degree of variance in the prices of some of the generally known drugs as reflected on the website and as prevalent in the market. To sum up, the Government has undertaken this measure in extreme hurry and in a very unprofessional manner, without even bothering about the serious consequences it may have in prescription procedures and also in financial terms on the poor hapless patients. The Committee while strongly deprecating this action of the Ministry recommends that the said data be immediately removed from the website of CDSCO so as to prevent any further dissemination of wrong and archaic information about drugs, many of which may have life-saving/threatening implications. It also recommends that since the data base is a critical requirement for information generation, the information received from Gujarat authorities be updated on war footing and put up on the website of CDSCO within a month of the presentation of this Report to the Parliament.

RECOMMENDATIONS/OBSERVATIONS

3.24 The CDSCO has eleven airport and seaport offices. During its visit to Chennai-Bangalore-Coonoor from 1 to 5 November, 2011, the Committee interacted with the authorities at Air Cargo Complex, Chennai to understand the systems and procedures followed by Assistant Drugs Controller's Office to facilitate processing of pharmaceutical imports and exports. Subsequently, Airports Authority of India, in a written submission, informed that the freight forwarders/shippers were required to bring the cargo requiring cold storage facility through refrigerated trucks only at Air Cargo complex to avoid spoilage of the contents of such cargo. The custodians at air cargo complexes were required to provide necessary infrastructure for the temperature sensitive cargo, at all stages, and ensure timely and proper handling of such cargo whilst in their custody. It was further stated that the role of the airlines was of paramount importance when the cargo stands released from the custodian and is to be uploaded to the connected flight. It was pointed out that the grey area was on the apron of the Airport where the incoming/outgoing cargo was often under the scorching sun for few hours by the airlines before loading of the same on their planes. It was suggested that the cooled dollies and thermal blankets could be pressed into service on the apron side by the airlines to provide requisite care to pharmaceutical products, thereby avoiding the deterioration/decay of the inside contents or potency of the vaccines/drugs/medicines etc. (Para 6.1)

3.25 The Committee agrees with the above suggestion and recommends that the Ministry of Health and Family Welfare should take initiative towards addressing the shortcomings forthwith in coordination with the Ministry of Civil Aviation at all seaports/airports handling import and exports of pharmaceutical products. The Committee will like to be informed of steps taken to address this problem. (Para 6.2)

Action taken

Interim Reply

3.26 Initiatives have been taken for creation of Pharma zones at various ports in collaboration with the concerned airport authorities, for providing dedicated areas for storage of drugs at the ports. Pharma zone has been created at Hyderabad airport. The creation of Pharma zone at Delhi

airport is at an advanced stage. The Ministry is in communication with the Department of Civil Aviation for creation of such facilities.

Final Reply

3.27 The Ministry would take up the issue with the concerned authorities in the Ministry of Civil Aviation and Ministry of Shipping for necessary action.

Further Recommendation

3.28 The Committee finds it incomprehensible as to why the final reply of the Government fails to mention some of the concrete actions in this regard mentioned in the first action taken reply. The Committee, therefore, desires a detailed explanatory note in the matter from the Ministry bringing out the exact position within one month of presentation of this Report to the Parliament.

RECOMMENDATIONS/OBSERVATIONS

3.29 The Committee is of the view that due to untraceable files on three drugs, it is not possible to determine if all conditions of approval (indications, dosage, safety precautions) are being followed or not. Moreover the product monographs cannot be updated in the light of recent developments and regulatory changes overseas. Therefore all the missing files should be re-constructed, reviewed and monographs updated at the earliest. (Para 7.13)

Action Taken

3.30 The concerned files have since been reconstituted, though the complete details are still not available. The issues relating to continued marketing of these drugs and updating of their product monographs in the light of recent knowledge and regulatory changes overseas will be referred to the NDAC for examination and review.

Further Recommendation

3.31 The Committee finds the action taken reply of the Ministry on this very important aspect highly unsatisfactory. Even after the passage of several months these drugs continue to be marketed with impunity though their exact effect, harmful or otherwise, is yet to be ascertained. The Government without caring a bit about the ramifications is still contemplating referring the issues related to continued marketing of these drugs and updating of their product monographs in the light of recent knowledge and regulatory changes overseas to NDAC for examination and review. The continued inaction of the Government on this vital matter of public health needs to be deprecated in strongest terms. The Committee also recommends that the Ministry should come out of its contemplation mode and take action as recommended by the Committee in the context of these three drugs without any further loss of time.

RECOMMENDATIONS/OBSERVATIONS

3.32 On scrutiny of 39 drugs on which information was available, the Committee found the following shortcomings:

- In the case of 11 drugs (28%) Phase III clinical trials mandated by Rules were not conducted. These drugs are (i) Everolimus (Novartis), (ii) Colistimethate (Cipla), (iii) Exemestane (Pharmacia), (iv) Buclizine (UCB), (v) Pemetrexid (Eli Lilly),

(vi) Aliskiren (Novartis), (vii) Pentosan (West Coast), (viii) Ambrisentan (GlaxoSmithKline), (ix) Ademetonine (Akums), (x) Pirfenidone (Cipla), and (xi) FDC of Pregabalin, Methylcobalamine, Alpha Lipoic Acid, Pyridoxine and Folic Acid (Theon);

- In the case of 2 drugs (Dronedarone of Sanofi and Aliskiran of Novartis), clinical trials were conducted on just 21 and 46 patients respectively as against the statutory requirement of at least 100 patients;
- In one case (Irsogladine of Macleods), trials were conducted at just two hospitals as against legal requirement of 3-4 sites;
- In the case of 4 drugs (10%) (Everolimus of Novartis; Buclizine of UCB; Pemetexid of Eli Lilly and FDC of Pregabalin with other agents), not only mandatory Phase III clinical trials were not conducted but even the opinion of experts was not sought. The decision to approve these drugs was taken solely by the non-medical staff of CDSCO on their own.
- Of the cases scrutinized, there were 13 drugs (33%) which did not have permission for sale in any of the major developed countries (United States, Canada, Britain, European Union nations and Australia). None of these drugs have any special or specific relevance to the medical needs of India. These drugs are: (i) Buclizine for appetite stimulation (UCB); (ii) Nimesulide injection (Panacea); (iii) Doxofylline (Mars) (iv) FDC of Nimesulide with Levocetirizine (Panacea); (v) FDC of Pregabalin with other agents (Theon); (vi) FDC of Tolperisone with Paracetamol (Themis); (vii) FDC of Etodolac with Paracetamol (FDC); (viii) FDC of Aceclofenac with Thiocolchicoside (Ravenbhel); (ix) FDC of Ofloxacin with Ornidazole (Venus), (x) FDC of Aceclofenac with Drotaverine (Themis); (xi) FDC of Glucosamine with Ibuprofen (Centaur); (xii) FDC of Diclofenac with Serratiopeptidase (Emcure) and xiii. FDC of Gemifloxacin with Ambroxol (Hetero).
- In the case of 25 drugs (64%), opinion of medically qualified experts was not obtained before approval.
- In those cases (14 out of 39 drugs), where expert opinion was sought, the number of experts consulted was generally 3 to 4, though in isolated cases the number was more. In a country where some 700,000 doctors of modern medicine are in practice such a miniscule number of opinions are hardly adequate to get diverse views and come to a well considered rational decision apart from the possibility of manipulation by interested parties. As against this, to review just the dose of popular pain-killer paracetamol, the United States Food and Drug Administration (USFDA) constituted a panel of 37 experts drawn from all over the country. After extensive debate 20 members sought ban on the combination of paracetamol with narcotics (17 opposed), 24 members sought reduction of dose from 500mg. to 325mg. (13 opposed) and 26 members advised to make high dose (1000mg.) formulation a prescription only medicine (11 opposed). The voting pattern shows independent application of mind by each member. The opinions and decisions are in public domain (website of USFDA) so that anyone is free to scrutinize, offer comments and give suggestions. In India, every discussion and document is confidential away from public scrutiny. This matter needs to be reviewed to ensure safety of patients, fair play, transparency and accountability. (Para 7.14)

3.33 Unless there is some legal hitch, the Committee is of the view that there is no justification in withholding opinions of experts on matters that affect the safety of patients from public. Consideration should be given to upload all opinions on CDSCO website. (Para 7.15)

Action Taken

3.34 The Ministry agrees with the observations of the Committee regarding review of the approvals to ensure safety of patients, fair play, transparency and accountability.

3.35 The issues relating to continued marketing of these drugs and updating of their product monographs in the light of recent knowledge and regulatory changes overseas will, however, be referred to the NDACs for examination and review.

3.36 The Ministry agrees with putting the recommendations of the experts on the web-site.

3.37 The DCG(I) has been adequately sensitized in this regard.

3.38 The Ministry will also take further measures to bring transparency and accountability in approvals.

Further Recommendation

3.39 The Committee is shocked to note this dilly-dallying by the Ministry on a matter, which could be affecting lives of lakhs of people in the country who are consuming these drugs. The Ministry agrees with Committee's viewpoint about review of approvals to ensure safety of patients, fair play, transparency and accountability, but instead of taking strict and immediate action in all these proven cases of delinquency and omission and commission, it still continues to be in a state of profound procrastination and wants to refer the issues relating to continued marketing of these drugs and updating of their product monographs in the light of recent knowledge and regulatory changes overseas to the NDACs for examination and review. The continued inaction on the part of the Ministry on this serious matter almost borders on collusion with an intention to save the guilty. Committees after committee are being constituted to postpone the day of reckoning of the guilty people. On another plane this inaction which has led to unhindered marketing of these drugs with unknown and unspecified risks to the unsuspecting people who are consuming them amounts to a serious violation of human rights of the hapless patients. While condemning this continued inaction of the Ministry, the Committee recommends immediate and conclusive action on this Recommendation of the Committee without indulging into the charade of having a plethora of committees after committee to stall a decision in the matter.

RECOMMENDATION/OBSERVATION

3.40 According to information provided by the Ministry, a total of 31 new drugs were approved in the period January, 2008 to October, 2010 without conducting clinical trials on Indian patients. The figure is understated because two drugs (ademetionine and FDC of pregabalin with other ingredients) were somehow not included in the list. Thus there is no scientific evidence to show that these 33 drugs are really effective and safe in Indian patients. (Para 7.16)

Action Taken

3.41 The Ministry has noted the observations of the Committee. Accordingly, the 33 drugs will be referred to the NDACs for examination and review. The Ministry will also constitute an expert committee to define policies and lay down SOPs for approval of new drugs.

Further Recommendation

3.42 This is yet another instance where the Ministry inspite of appreciating the serious

problem the continued marketing of these 33 drugs may pose to the Indian patients has chosen to take no action to resolve it. Even after a lapse of more than seven months and with virtually nothing concrete having been suggested by the three-member expert committee on this contentious matter, the Government intends to delay a decision by referring it to yet another committee. These tactics have been, as stated at several places in this Report, resorted to by the Government to delay indefinitely the decisions and consequent actions that would be required to be taken against several officials and non-officials who have indulged in rampant acts of omission and commission while approving these drugs in gross violation of the law of the land. The Committee takes strong objection to these dilatory tactics and recommends immediate decision on all these proven gross violations lest the health of the people is compromised irrevocably.

RECOMMENDATIONS/OBSERVATIONS

3.43 It is obvious that DCGI clears sites of pre-approval trials without application of mind to ensure that major ethnic groups are enrolled in trials to have any meaningful data. Thus such trials do not produce any useful data and merely serve to complete the formality of documentation. (Para 7.27)

3.44 The Committee recommends that while approving Phase III clinical trials, the DCGI should ensure that subject to availability of facilities, such trials are spread across the country so as to cover patients from major ethnic backgrounds and ensure a truly representative sample. Besides, trials should be conducted in well equipped medical colleges and large hospitals with round the clock emergency services to handle unexpected serious side effects and with expertise in research and not in private clinics given the presence of well equipped medical colleges and hospitals in most parts of the country in present times. (Para 7.28)

3.45 The Committee is of the view that taking into account the size of our population and the enormous diversity of ethnic groups there is an urgent need to increase the minimum number of subjects that ought to be included in Phase III pre-approval clinical trials to determine safety and efficacy of New Drugs before marketing permission is granted. In most western countries the required numbers run into thousands. However since the major objective in India is to determine the applicability or otherwise of the data generated overseas to Indian population, the requirement should be re-assessed and revised as per principles of medical statistics so that major ethnic groups are covered. A corresponding increase in the number of sites so as to ensure a truly representative sample spread should also be laid down in black and white. Furthermore, it should be ensured that sites selected for clinical trials are able to enroll diverse ethnic groups. For domestically discovered drugs, the number of subjects should be revised as well. This can be easily achieved by changes in the Good Clinical Practice (GCP) guidelines. (Para 7.29)

Action Taken

3.46 The Ministry has noted the observations of the Committee. While examining the applications for clinical trials by CDSCO, the proposals are examined in consultation with NDACs. The NDACs at the time of approving the trial sites will be advised to take note of the recommendations of the Parliamentary Standing Committee.

3.47 The DCG(I) has been adequately sensitized in this regard.

3.48 The Ministry will also constitute an expert committee to define policies, lay down guidelines and SOPs for approval of clinical trials and new drugs.

3.49 This Committee would also examine the issues relating to the minimum number of subjects, number of sites, their distribution, etc. in clinical trials for the purpose of approval of new drugs in the country.

Further Recommendation

3.50 The Committee notes with trepidation, its instant Recommendation of considerable import for the health sector in the country, also getting lost in the maze of inactivity which is all pervading in the final action taken notes of the Ministry. The systemic improvements suggested by the Committee for pre-approval trials are easily doable, if the Government has a will to carry them out. Unfortunately, however, apparently due to extraneous considerations the Government is still contemplating constitution of committees and other formalities to stall expeditious implementation of these measures for public good. The Committee also feels that half measures like NDACs being advised to take note of the Recommendations of the Parliamentary Committee would not suffice, as it would then not be obligatory upon NDACs to scrupulously adhere to these norms. The Committee, therefore, recommends that the Ministry should immediately codify all these measures in the form of mandatory Rules so that the NDACs and all other agencies/bodies are left with little room for exercising their discretion or their own interpretation of any measure, a malaise that has, hitherto, wreaked havoc on the health care system of the Country.

RECOMMENDATIONS/OBSERVATIONS

3.51 A review of the opinions submitted by the experts on various drugs shows that an overwhelming majority are recommendations based on personal perception without giving any hard scientific evidence or data. Such opinions are of extremely limited value and merely a formality. Still worse, there is adequate documentary evidence to come to the conclusion that many opinions were actually written by the invisible hands of drug manufacturers and experts merely obliged by putting their signatures. Is the Committee mistaken in coming to the conclusion that all these letters were collected by interested party from New Delhi, Mumbai, Chandigarh and Secunderabad and handed over to office of the DCGI on the same day? If so, it is obvious that the interested party was in the loop in the entire process of consultation with experts. (Annexure 6).....It is inconceivable that a letter dated 17-6-2005 from New Delhi will be delivered to the office of DCGI also in New Delhi after more than two months. The conclusion, as in aforementioned cases, is obvious. (Para 7.31)

3.52 If the above cases are not enough to prove the apparent nexus that exists between drug manufacturers and many experts whose opinion matters so much in the decision making process at the CDSCO, nothing can be more outrageous than clinical trial approval given to the Fixed Dose Combination of aceclofenac with drotaverine which is not permitted in any developed country of North America, Europe or Australasia. In this case, *vide* his letter number 12-298/06-DC dated 12.2.2007, an official of CDSCO advised the manufacturer, Themis Medicare Ltd. not only to select experts but get their opinions and deliver them to the office of DCGI! No wonder that many experts gave letters of recommendation in identical language apparently drafted by the interested drug manufacturer. (Para 7.32)

3.53 In the above case, the Ministry should direct DCGI to conduct an enquiry and take appropriate action against the official(s) who gave authority to the interested party to select and obtain expert opinion and finally approved the drug. (Para 7.33)

3.54 Such expert opinions in identical language and/or submitted on the same day raise one question: Are the experts really selected by the staff of CDSCO as mentioned in written submission by the Ministry? If so how can they, situated thousands of miles away from each other, draft identically worded letters of recommendation? Is it not reasonable to conclude the names of experts to be consulted are actually suggested by the relevant drug manufacturers? It has been admitted that CDSCO does not have a data bank on experts, that there are no guidelines on how experts should be identified and approached for opinion. (Para 7.34)

Action Taken

3.55 The Ministry has noted the observations of the Committee.

3.56 The applications for new drugs including FDCs are now examined by the NDACs and decisions on their approval are taken based on the recommendations of these committees.

3.57 The issues relating to the Fixed Dose Combination of aceclofenac with drotaverine would be referred to the NDAC for examination and review.

3.58 As mentioned earlier, the Ministry had constituted a three member expert committee. The expert committee submitted its report to the Ministry on 22.11.2012. The committee has recommended instituting an enquiry into the matter.

3.59 As recommended by the Hon'ble Committee, the DCG(I) will constitute an enquiry committee to investigate into the matter.

Further Recommendation

3.60 The Committee is aghast to note the paralytic inertia gripping the Ministry which is preventing it from taking action against guilty official(s) of CDSCO and others involved in proven cases of delinquency and illegality six months should have been more than enough to not only inquire into the misdeeds of those who had so want only indulged in the above cited gross irregularity but also sufficed to take exemplary action against them so as to deter others. The Ministry by still dithering over issuing instructions to NDACs and DCGI has abundantly proved that it has neither the intention to clean the augean stables of CDSCO nor any concern for probity and rule of law. Hoping against hope, the Committee expects the Ministry to atleast even at this late stage take immediate action on these proven cases of delinquency and irregularities so that a stern message is sent to all concerned that the drug regulatory mechanism is not up for grabs for perpetuation of unethical and illegal practices.

RECOMMENDATIONS/OBSERVATIONS

3.61 The Committee is of the view that many actions by experts listed above are clearly unethical and may be in violation of the Code of Ethics of the Medical Council of India applicable to doctors. Hence the matter should be referred to MCI for necessary follow up and action. In addition, in the case of Government employed doctors, the matter must also be taken up with medical colleges/hospital authorities for suitable action. (Para 7.35)

Action Taken

3.62 The Ministry has noted the observations of the Committee.

3.63 As mentioned earlier, the Ministry had constituted a three member expert committee. The expert committee submitted its report to the Ministry on 22.11.2012. The committee has recommended instituting an enquiry into the matter. The committee has also recommended laying down a code of conduct for the members participating in these bodies as also Ethics Committees.

3.64 An expert committee would be constituted to define policies and SOPs for identification of experts and their participation in these bodies.

3.65 However, as recommended by the Hon'ble Committee, the Ministry would also refer the issue to the Medical Council of India for necessary action. For Government employed doctors, the matter will be brought to the notice of the concerned medical colleges/hospital authorities for appropriate action.

Further Recommendation

3.66 The response of the Ministry is clearly indicative of the fact that it wants to drag its feet when it comes to punishing the people who have compromised the system over the years through their sheer illegal activities, which are totally against public interest. It is incomprehensible as to what is stopping the Ministry from forwarding these proven cases of gross illegality and proven collusion of the Medical Council of India and the medical colleges/hospital authorities concerned for appropriate action though more than six months have elapsed since the Committee brought these cases to the knowledge of the Parliament and the Government. The Committee, therefore, while expressing its strong displeasure with the Ministry recommends that these cases be referred to MCI and medical colleges/hospital authorities concerned within seven days of presentation of this Report to the Parliament. With a view to expedite action against these errant experts who have indulged in unethical and illegal practices without any concern for the health and well being of common people the Committee further desire the Ministry to impress upon MCI and all other authorities concerned to act against these experts in a highly time bound manner and report back to the Ministry at the earliest so that the Ministry is able to furnish the feedback on all these cases to the Parliament within one month of presentation of this Report to the Parliament.

RECOMMENDATIONS/OBSERVATIONS

3.67 There is sufficient evidence on record to conclude that there is collusive nexus between drug manufacturers, some functionaries of CDSCO and some medical experts. (Para 7.36)

3.68 On a more fundamental issue the Committee has come to the conclusion that when it comes to approving new drugs, too much is left to the absolute discretion of the CDSCO officials. There are no well laid down guidelines for determining whether consultation with experts is required. Thus the decision to seek or not to seek expert opinion on new drugs lies exclusively with the nonmedical functionaries of CDSCO leaving the doors wide open to the risk of irrational and incorrect decisions with potential to harm public health apart from the possibility of abuse of arbitrary discretionary powers. (Para 7.37)

3.69 The Committee, therefore, strongly recommends that there should be nondiscretionary, well laid down, written guidelines on the selection process of outside experts with emphasis on expertise including published research, in the specific therapeutic area or drug or class of drugs. Currently, the experts are arbitrarily chosen mainly based on their hierarchical position which does not necessarily correspond to the area or level of expertise. All experts must be made to file the Conflict of Interest declaration outlining all past and present pecuniary relationships with entities that may benefit from the recommendations given by such experts. The consulted experts should be requested to give hard evidence in support of their recommendations. (Para 7.38)

Action Taken

3.70 The Ministry has noted the observations of the Committee.

3.71 Now, the applications for new drugs including FDCs are examined by the NDACs and decisions on their approval are taken based on the recommendations of these committees.

3.72 All members of the NDACs are required to sign a declaration of conflict of interest before being involved with NDACs.

3.73 The Ministry will also constitute an expert committee to define policies, lay down guidelines and SOPs for approval of clinical trials and new drugs.

- 3.74 The policies and SOPs for identification of experts would also be formulated.
- 3.75 The recommendations of the NDACs are being put on the web-site for ensuring transparency and accountability.
- 3.76 The DCG(I) has been adequately sensitized in this regard.

Further Recommendation

3.77 **The Committee appreciates that in pursuance of its Recommendation, the applications for new drugs including FDCs are now being examined by NDACs and decision on their approvals are taken based on the recommendation of NDACs. Moreover, all members of NDACs are required to sign a declaration of conflict of interest before being involved with NDACs. They also appreciate the fact that recommendations of NDACs are being put on the website to ensure transparency and accountability. The Committee, however feels that the Ministry has already inordinately delayed constitution of the expert committee to define policies, lay down guidelines and SOPs for approval of Clinical Trials and New Drugs. It also feels that the Ministry has equally badly delayed the formulation of policies and SOPs for identification of experts, as it has not moved beyond mere intent, in their context during more than six odd months. Since a lot of time has already been wasted in these two crucial matters the Committee desires the Ministry to constitute the two committees and recommends the said committees be directed to complete their work in highly time bound manner and submit their respective reports within a period of one month of presentation of this Report to the Parliament.**

RECOMMENDATIONS/OBSERVATIONS

3.78 The Committee is of the view that responsibility needs to be fixed for unlawfully approving Buclizine, a drug of hardly any consequence to public health in India, more so since it is being administered to babies/children. At the same time the approval granted should be reviewed in the light of latest scientific evidence, regulatory status in developed countries, particularly in Belgium, the country of its origin. (Para 7.41)

Action Taken

- 3.79 The issues relating to the drug Buclizine would be referred to the NDAC for examination and review.
- 3.80 As mentioned earlier, the Ministry had constituted a three member expert committee. The expert committee submitted its report to the Ministry on 22.11.2012. The committee has recommended instituting an enquiry into the matter.
- 3.81 As recommended, the DCG(I) will constitute an enquiry committee to investigate into the issue.

Further Recommendation

3.82 **This is yet another instance where the Ministry has failed to act on a proven case of gross illegality. Instead after whiling away more than six months, it has still chosen to take recourse to its favorite ploy of referring the matter for examination and review to NDAC. As far as culpability part is concerned that has also been staggered indefinitely as the Ministry has till now only conveyed that DCG (I) will constitute an inquiry committee to investigate into the issue. The Committee takes serious umbrage over these more than apparent dilatory tactics being adopted by the Ministry to somehow delay action against the**

wrongdoers. The Committee, therefore, reiterates its Recommendation that responsibility be fixed in this case without any further loss of time and the approvals granted be reviewed in the light of latest scientific evidence regulatory states in developed countries, particularly in Belgium, the country of its origin, equally quickly.

RECOMMENDATIONS/OBSERVATIONS

3.83 Letrozole discovered by Novartis, is an anti-cancer drug for use only in postmenopausal women and is contraindicated (not permitted) to be used in women of reproductive age. If it is to be used for any other indication except breast cancer, then the drug is categorized as a New Drug under Indian laws. On 10-04-2007, DCGI approved the use of letrozole for improving female fertility. The Drugs and Cosmetic Rules require that while approving a drug for use in females of reproductive age, animal studies are to be done in this specific group. No such studies were done in India. The innovator also did not conduct such studies abroad because there was no plan to use letrozole in women of reproductive age. Under Indian rules, Phase II studies should have been conducted before Phase III since such studies were not conducted anywhere. Permission to conduct Phase III studies was given without prior Phase II studies. Phase III clinical trial was conducted on just 55 women by three doctors in private practice while the minimum requirement as per mandatory Good Clinical Practice (GCP) rules is at least 100. After approval, the sponsor, Sun Pharmaceuticals did not submit periodic PSURs due every six months as required by law. No action was taken against the Company in such a sensitive case since India is the only country where the drug is permitted to be used for female infertility. Post-marketing data is crucial and critical in detecting adverse effects both in women and babies born to them if they use letrozole before the onset of pregnancy. Clearly there was a serious lapse on the part of CDSCO. In the wake of media outcry, in a diversionary move, the DCGI instead of investigating the allegations of regulatory lapse and taking corrective measures referred the matter to clinical experts, DTAB etc. on the restricted issue of safety and efficacy. DCGI is expected to take action against those CDSCO functionaries who colluded with private interests and got the drug approved in violation of laws. The drug has since been banned by the Ministry for use in female infertility. (Para 7.42)

3.84 The Committee takes special note of this case of gross violation of the laws of the land by the CDSCO. First, in approving the drug for use in case of female infertility and thereafter, in exhibiting overt resistance in taking timely corrective steps despite very strong reasons favouring immediate suspension of use of letrozole for the said indication. Belatedly, the drug has been banned for use in female infertility. (Para 7.43)

Action Taken

3.85 As mentioned earlier, the Ministry had constituted a three member expert committee. The expert committee submitted its report to the Ministry on 22.11.2012. The committee has recommended instituting an enquiry into the matter.

3.86 As recommended the DCG(I) will constitute an enquiry committee to investigate into the issue.

Further Recommendation

3.87 **The Committee find it deeply perturbing as to why the Ministry has failed to take action in this very open and shut case of impropriety and criminal lapse though more than six months have elapsed the Committee strongly feel that if perpetrators of such illegalities and collusive acts which are detrimental to public health are allowed to go scot-free then the total collapse of an ethical health care system is inevitable. The Committee, therefore,**

reiterates their Recommendation with all force at their command and desire immediate and exemplary action against officials of CDSCO who colluded with private interest and got the drug approved in violation of laws at once and without the delaying instrument of another inquiry Committee.

RECOMMENDATIONS/OBSERVATIONS

3.88 The Committee is of the opinion that there must be some very good reasons for Danish Medicine Agency (Denmark) not to approve a domestically developed drug where an anti-depressant drug would perhaps be in greater demand as compared to India. Curiously, Deanxit is allowed to be produced and exported but not allowed to be used in Denmark. (Para 7.45)

3.89 The Committee feels that the DCGI should have gone into the reasons for not marketing the drug in major developed countries such as United States, Britain, Ireland, Canada, Japan, Australia just to mention a few. United States alone accounts for half of the global drug market. It is strange that the manufacturer is concentrating on tiny markets in unregulated or poorly regulated developing countries like Aruba, Bangladesh, Cyprus, Jordan, Kenya, Myanmar, Pakistan, and Trinidad instead of countries with far more patients and profits. Many of these developing countries are handicapped due to lack of competent drug regulatory authorities. Instead of examining and reversing regulatory lapses, DCGI has referred the matter to an Expert Committee to look at the isolated and restricted issue of "safety and efficacy" instead of unlawful approval in the first place. (Para 7.46)

3.90 The Committee recommends that in view of the unlawful approval granted to Deanxit, the matter should be re-visited and re-examined keeping in mind the regulatory status in well developed countries like Denmark, the country of origin; the United States, Britain, Canada, European Union and Japan etc. It is important to keep in mind that in Europe, there are two types of marketing approvals: Community-wide (cleared by European Medicine Agency) and individual regulators of member nations. EMEA is known to clear drugs after great deal of scrutiny while the competence and expertise of drug regulatory authorities of individual nations is not uniform and varies greatly from country to country. (Para 7.47)

Action Taken

3.91 The Ministry has noted the observations of the Committee. 3.82 Now, the applications for new drugs including FDCs are examined by the NDACs and decisions on their approval are taken based on the recommendations of these committees.

3.92 The drug FDC of Flupenthixol and Melitracen, of which the Deanxit is also a brand, is already under examination in consultation with an expert committee. The expert committee recommended for conducting Phase *N* Clinical trial after getting the protocol approved. The protocol for the trial submitted by the firm is under examination by that expert committee.

3.93 The drug was approved in the country in 1998 and since then it is in the market. It is also marketed in other countries.

3.94 Since the Hon'ble Committee has raised concern over the manner of approval of the drug and has recommended that the same needs to be revisited, it has been decided that the manufacturer of the drug shall be instructed to establish the safety and efficacy of the FDC within 6 months, failing which the drug would be considered for being prohibited for manufacture and marketing in the country.

Further Recommendation

3.95 **In its Fifty-ninth Report in another case study had noted that a drug Deanxit which**

is marketed in India is allowed to be produced and exported by DMA but not allowed to be used in Denmark. Opining that there must be some very good reasons for Danish Medicine Agency (Denmark) not to approve a domestically developed drug where an anti-depressant drug would perhaps be in greater demand as compared to India.

3.96 The Committee had felt that the DCGI should have gone into the reasons for not marketing the drug in major developed countries such as United States, Britain, Ireland, Canada, Japan, Australia just to mention a few. Noting further that instead of examining and reversing regulatory lapses, DCGI has referred the matter to an Expert Committee to look at the isolated and restricted issue of “safety and efficacy” instead of unlawful approval in the first place the Committee had recommended that in view of the unlawful approval granted to Deanxit, the matter should be revisited and re-examined keeping in mind the regulatory status in well developed countries like Denmark, the country of origin; the United States, Britain, Canada, European Union and Japan etc.

3.97 In its final ATNs the Government has stated that now, the applications for new drugs including FDCs are examined by the NDACs and decisions on their approval are taken based on the recommendations of these committees.

3.98 The drug FDC of Flupenthixol and Melitracen, of which the Deanxit is also a brand, is already under examination in consultation with an expert committee. The expert committee recommended for conducting Phase IV Clinical trial after getting the protocol approved. The protocol for the trial submitted by the firm is under examination by that expert committee.

3.99 The drug was approved in the country in 1998 and since then it is in the market. It is also marketed in other countries. Since the Hon’ble Committee has raised concern over the manner of approval of the drug and has recommended that the same needs to be revisited, it has been decided that the manufacturer of the drug shall be instructed to establish the safety and efficacy of the FDC within 6 months, failing which the drug would be considered for being prohibited for manufacture and marketing in the country.

3.100 The case of Deanxit conveys a strong whiff of collusion and cover up, briefly put, in its initial ATN, the Ministry informed the Committee that the matter had been referred to the 3-member expert committee and hence action would be taken when the recommendation is received. Surprisingly in its final ATN, there is no mention of any recommendation from the 3-member expert committee. In order to investigate the matter, the Committee went into the records of the 3-member expert committee and found a major intriguing omission. In its report to the Ministry, the 3-member expert committee had grouped various cases of wrong doing under heading (a) on pages 4, 13 and 49. However either by design or default, the case of Deanxit (FDC of flupenthixol and melitracen) identified by the Committee as a blatant example of unlawful approval was omitted under the group while other cases were listed. The Committee finds it more intriguing that such an omission was not noticed by the Ministry.

3.101 The marketing approval granted to Deanxit (the first formulation of the Fixed-Dose Combination of Flupenthixol and Melitracen) was patently unlawful as stated in Para 7.44 of the Committee’s Fifty-ninth Report on the following counts:

3.102 Deanxit, though permitted to be manufactured and exported, is not allowed to be prescribed to patients in Denmark, the country of innovation/origin. Hence permission to import and manufacture granted by CDSCO was in violation of Rule 30-B of the Drugs and Cosmetics Rules.

3.103 One of the ingredients, Melitracen, was not approved earlier; hence as per Appendix VI (a) of the Drugs and Cosmetics Rules the clinical trials should have been conducted as per Rule 122 (E) (a). In effect it means clinical trials on each indication on at least 100 patients at 3-4 sites. It was approved for four distinct and different indications. Such trials were not conducted.

3.104 In its submission to the Committee, the Ministry referred to a vague letter dated 10.08.1998 written by a psychiatrist employed by Lady Hardinge Medical College, New Delhi directly to the DCGI alluding to some unspecified trial with no details (such as number of patients enrolled, protocol, results etc.). Mandatory pre-approval clinical trials are sponsored and conducted by applicant companies and then results submitted to DCGI for marketing approval. This was a strange case where the purported letter was written by a self-appointed investigator to the DCGI. The Ministry failed to give an authenticated copy of the letter and results of the trial. Even if this vague, unsubstantiated letter is accepted as a substitute for a clinical trial at one site, the same cannot account for trials at 3-4 centres for each indication. It is clear that marketing approval was given without mandatory trials.

3.105 Deanxit is not allowed for marketing in any of the other advanced countries such as United States, Britain, EU Community, Canada, Australia and Japan where depression is more common than India. In the United States the two ingredients, Flupenthixol and Melitracen are not even individually allowed to be marketed.

3.106 In the ATNs, the Ministry has gone out of the way to inform the Committee that the drug "is also marketed in other countries," as if it is a good defence for permitting the use of the drug in India. The Ministry is advised to read Para 7.44 carefully of the Committee's Report where in the Committee has acknowledge that Deanxit is indeed marketed in countries like Aruba, Cyprus, Jordan, Kenya, Pakistan, Trinidad etc and some other developing countries which are handicapped by lack of competent drug regulatory system.

3.107 Neither Flupenthixol nor Melitracen is listed in the National List of Essential Medicines (NLEM) published by the Government of India.

3.108 Notwithstanding this lapse, the 3-member expert committee has indeed stated, "Fixed Dose Combinations have become a malaise. The rationality of the combinations is not critically examined. Even where multiple drugs are required for treatment, the FDCs jeopardize dose adjustment of individual medicines. Convenience and profit seem to have overtaken service. The requirements for clearance of FDCs should be more stringent – requiring empirical clinical trial to show advantage of FDC- before their approval."

3.109 The Committee is amazed that such a crucial recommendation of the 3-member Expert Committee is not being applied to the instant case.

3.110 If any drug is promoted for unapproved indications, DCGI has the statutory duty to take action and even cancel marketing approval. The Committee is aghast that no action was taken against the Danish manufacturer, Lundbeck even when it was openly flouting Indian laws. Compare the lack of action in India with the United States where for a similar offence Pfizer had to shell out Rs. 2,300 crores for promoting gabapentin for unapproved indication.

3.111 Attempt by the Ministry to club Deanxit brand with other subsequent formulations is also diversionary and misleading. Under Drugs and Cosmetic Rules, a New Drug is deemed to be a new drug for four years after initial approval. As per records submitted to the Committee the initial approval was granted to manufacturer of Deanxit. No other approval was given by CDSCO to any other applicant in the first four years. Other

manufacturers launched the drug after four years not by seeking approval from CDSCO but by obtaining manufacturing licenses from the State Drug Authorities which is perfectly legal. Hence if initial approval by CDSCO is irregular or unlawful then nothing can stop other manufacturers from marketing the product. Therefore the focus needs to be squarely on the first approval.

3.112 The Committee, therefore, reiterate that concrete and exemplary action by the Ministry on (a) unlawful approval against functionaries of CDSCO (b) reversal of unlawful approval, (c) unlawful promotion by Lundbeck.

3.113 In the opinion of the Committee it is an open and shut case that needs immediate action, not promise of prolonged fruitless deliberation designed to delay action. Why should the people of India consume a questionable drug approved in a questionable manner even for a day longer, more so when the drug regulator of the innovator country Denmark is not allowing its use within its jurisdiction but allowing its export to developing countries with weak or non-existent drug regulation?

RECOMMENDATIONS/OBSERVATIONS

3.114 The Committee recommends an enquiry into the said letter. The responsibility should be fixed and appropriate action taken against the guilty. The Committee should be kept informed on this case. (Para 7.49)

Action Taken

3.115 As mentioned earlier, the Ministry had constituted a three member expert committee. The expert committee submitted its report to the Ministry on 22.11.2012. The committee has recommended instituting an enquiry into the matter.

3.116 As recommended the DCG(I) will constitute an enquiry committee to investigate into the issue. The Hon'ble Standing Committee would be kept informed on this issue.

RECOMMENDATIONS/OBSERVATIONS

3.117 The Committee takes special notice of this case of persistent insolence on the part of CDSCO and hopes that never again shall the DCGI approve drugs in violation of laws, that too for use in neonates and young children. (Para 7.51)

3.118 The Committee expresses its deep concern, extreme displeasure and disappointment at the state of affairs as outlined above. The Ministry should ensure that the staff at CDSCO does not indulge in irregularities in approval process of new drugs that can potentially have adverse effect on the lives of people. It is difficult to believe that these irregularities on the part of CDSCO were merely due to oversight or unintentional. Hence all the cases listed above and cases similar to these should be investigated and responsibility fixed and action taken against erring officials whether currently in service or retired. (Para 7.52)

Action Taken

3.119 The Ministry has noted the observations of the Committee and action will be taken as mentioned in previous recommendations.

3.120 As mentioned earlier, the Ministry had constituted a three member expert committee. The expert committee submitted its report to the Ministry on 22.11.2012. The committee has recommended instituting an enquiry into the matter.

3.121 The enquiry committee would be constituted by the DCG(I) to investigate into the matters.

3.122 As regard similar other cases, as and when they are brought to the notice, appropriate action will be taken.

Further Recommendation

3.123 The Committee in its Fifty-ninth Report in another fully documented irregularity of the Organisation had noted that though as per the Drugs and Cosmetics Rules, whenever there is either an additional formulation (*viz.* tablets, solutions, suspensions, injections, controlled-release, gels, etc.) or proposal to use in additional indications, the drug is deemed to be a New Drug. But, in a clear case of extreme collusion and breach of this rule an official of CDSCO though a letter dated February 11, 2000, inspite of additional indications (burns and wounds, non-healing indolent ulcers, bedsores, mucositis, etc.), conveyed to the manufacturer that Placenta Extract was not a New Drug and gave permission to promote the Placenta Extract gel. By including the term 'etc.' loopholes were left wide open to add other indications, which is an unprecedented irregularity and illegality. The collusive element was so overpowering that the letter of the manufacturer dated February 7, 2000, not only reached Delhi from Kolkata at breakneck speed, the permission, albeit wrong, was also granted within four days on February 11, 2000.

3.124 The Committee had therefore, considering the serious dimensions of this violation recommended an enquiry into the said letter so that responsibility is fixed and appropriate action is taken against the guilty so that never again did the DCG(I) approve drugs in violation of laws, that too for use in neonates and young children. Expressing its deep concern, extreme displeasure and disappointment at the state of affairs the Committee had asked the Ministry is to ensure that the staff at CDSCO does not indulge in irregularities in approval process of new drugs that can potentially have adverse effect on the lives of people and that all the cases listed and cases similar to these should be investigated and responsibility fixed and action taken against erring officials whether currently in service or retired.

3.125 In its final ATNs the Government has stated that as mentioned earlier, the Ministry had constituted a three member expert committee. The expert committee submitted its report to the Ministry on 22.11.2012. The committee has recommended instituting an enquiry into the matter. As recommended the DCG(I) will constitute an enquiry committee to investigate into the issue. The Hon'ble Standing Committee would be kept informed on this issue.

3.126 The Committee finds the instant response of the Government clear stonewalling to protect the guilty. The matter of inquiring into and taking action against CDSCO functionary who violated the rules to favour the manufacturer by treating a new drug (Placenta extract) as old drug and permitting the use for additional indications, with potential risk to patients, is a very simple open and shut case. In any case the 3-member expert committee instead of straightaway suggesting concrete action has recommended an enquiry, which the Ministry to its great comfort and convenience has interpreted to mean forming an "inquiry committee". Such repetitive references from the Ministry to the 3-member Expert Committee to another "inquiry committee" would mean further delay in taking action, if not placing the issue in cold storage. In the opinion of the Committee, this is one case where no extraordinary investigative skills or legal acumen is required to fix responsibility and punish the guilty official(s). A rule has been violated, all evidence is on board and the extraordinary interest of the perpetrator(s) is also clearly visible. What purposes, other than delaying the judgment day, would a series of inquiries serve is the

central message. The Government's response that the Committee would be kept informed on this issue is a clear indicator that quick action in this case of blatant violation is not at all on Government's mind. The Committee, therefore, reiterates immediate and conclusive action in this instant case without any further dilly-dallying.

RECOMMENDATIONS/OBSERVATIONS

3.127 The Committee has noted that there are a very large number of alternative analgesics, antipyretics in the Indian market. With so many countries banning Analgin, not to mention unlawful over-promotion by manufacturers, the CDSCO should be directed to re-examine the rationality of continued marketing of Analgin. (Para 8.4)

Action Taken

3.128 The issue of rationality and continued marketing of Analgin in the country was examined by DTAB in its 61st meeting held on 24th July, 2012. The board after deliberations recommended that the continued marketing of the drug may be examined by expert committee in the context of present day knowledge while the manufacturers of Analgin may be directed to market the product giving the full indications approved earlier by DTAB as under:

“Severe pain or pain due to tumor and also for bringing down the temperature in refractory cases when other antipyretics fail to do so.”

3.129 The board further recommended that the use of all analgesics with special reference to Analgin should be placed under focused Pharmacovigilance under Pharmacovigilance Programme of India (PvPI). The safety data so collected should be properly analyzed to take further suitable action on use of such drugs.

3.130 Based on recommendations of the board, the DCG(I) has issued letters to all State Drug Controllers on 13.09.2012 requesting them to direct the manufacturers of analgin formulations to market the drug mentioning the above indications in the package insert *I* promotional literature of Analgin formulation.

3.131 Further, as per the recommendations, all analgesic with special reference to analgin have been placed under focused PvPI.

3.132 The continued marketing of analgin will also be referred to NDAC for examination.

3.133 The DCG(I) has been adequately sensitized in this regard.

Further Recommendation

3.134 The continued marketing of Analgin, discarded the world over, is a matter of grave concern for the Committee. Analgin is not listed in the National List of Essential Medicines (NLEM). Bureaucratic delays, repetitive references from one committee to another can do nothing but hurt patients.

3.135 The Committee also feels that merely requesting State Drug Authorities to direct manufacturers to label the drug Analgin as approved by CDSCO without exemplary, penal action for documented violations is itself an act of negligence. The indications are approved by CDSCO, not State Drug Authorities. Hence CDSCO should itself take immediate action for violations.

3.136 Given the near non-existence pharmacovigilance in the country putting Analgin under so called “focussed pharmacovigilance” is nothing but a dilatory and diversionary

move to let the drug be sold in the country to benefit the manufacturer. The Committee, therefore, desires that a decision be taken on this open and shut case without taking refuge behind committees after committees within one month of presentation of this Report.

RECOMMENDATION/OBSERVATION

3.137 It is to be kept in mind that a drug becomes a candidate for withdrawal not only due to serious side effects but also when safer, more efficacious drugs are launched. Unfortunately, no attention is being paid to this issue. This principle should apply to all cases and all drugs need to be evaluated periodically. (Para 8.5)

Action Taken

3.138 As mentioned earlier, the Ministry had constituted a three member expert committee. The expert committee submitted its report to the Ministry on 22.11.2012. The committee is also of the view that there should be an adequate system for withdrawal of drugs – with appropriate guidelines and SOPs, so that unsafe drugs are weeded out in a timely fashion.

3.139 It would be pertinent to mention that most newer drugs are generally found to be more expensive, while the previous drugs may be less expensive and relatively affordable. Thus, this would require examination on case-to-case basis.

3.140 The matter would be referred to an expert committee to formulate guidelines, policies and procedures in this regard.

Further Recommendation

3.141 **The Committee is astounded to note the almost U-turn made by the Ministry on this vital issue. In its initial ATN, the Ministry had taken the stand that; a drug could not be banned when safer, more efficacious drugs for the same disorder are launched since there is no such provision in the Drugs and Cosmetics Rules. There was incidentally no mention of the matter having been referred to 3-member expert committee.**

3.142 **In any case the Committee finds no merit in the reason given by the Ministry. Under current rules, any drug found to be unsafe can be banned under Rule 26-A irrespective of whether safer substitutes are launched in the market or not. If there is no safer substitute and the drug is essential or life saving, then obviously it is not possible to ban the drug. Once a safer substitute is available then nothing stops the Central Government from invoking Rule 26-A.**

3.143 **In its final ATN, the Ministry in spite of their own expert committee opining that there should be an adequate system for withdrawal of drugs has found one more reason not to ban risky remedies by stating that “most newer drugs are generally found to be more expensive” The Committee has been given to understand that there is no provision under Drugs and Cosmetics Rule to take the cost of drugs into consideration while approving or banning drugs. It does not require a great deal of intelligence to conclude that it is better to consume a safer drug, even if it is more expensive, than consume a risky drug that ultimately will be far more costly due to adverse effects.**

RECOMMENDATIONS/OBSERVATIONS

3.144 The Committee is of the view that Section 26A is adequate to deal with the problem of irrational and/or FDCs not cleared by CDSCO. There is a need to make the process of approving and banning FDCs more transparent and fair. In general, if an FDC is not approved anywhere in

the world, it may not be cleared for use in India unless there is a specific disease or disorder prevalent in India, or a very specific reason backed by scientific evidence and irrefutable data applicable specifically to India that justifies the approval of a particular FDC. The Committee strongly recommends that a clear, transparent policy may be framed for approving FDCs based on scientific principles. (Para 9.8)

Action Taken

3.145 The Ministry agrees with the observations of the Committee.

3.146 Requirements for approval of FDCs are specified in Appendix VI of schedule Y. At present, all proposals of new fixed dose combinations are examined in consultation with the NDACs. Decision to approve any FDCs in the country is taken based on the recommendations of these committees. Further, the Ministry of Health and Family Welfare has recently issued statutory direction under section 33P to the State Governments on 1.10.2012 to refrain from granting new drugs licensing including FDCs without approval of DCG (1).

3.147 The CDSCO would constitute a Committee of experts to lay down policies, guidelines and procedures to be adopted for approval of FDCs.

3.148 The DCG(I) has been adequately sensitized in this regard.

Further Recommendation

3.149 The Committee has already expressed its views on the directions issued by the Union Government under Section 33 P to State Governments, previously in this Report. As regards the intention of the Ministry to constitute another committee of experts to lay down policies, guidelines and procedures to be adopted for approval of FDCs, the committee considers it like many other replies of the Government to its other Recommendations contained in the Fifty-ninth Report, a ploy to waste time and avoid an expedition decision to curb this rampant and harmful practice. With piles of evidence available locally as well as in the form of global best practices, the Ministry can do the needful *suo motu* and without resorting to this time tested, time consuming device of an expert Committee. The Committee expects the Ministry to take decisions in the matter accordingly at the soonest so that the approval of FDCs is regulated by well laid out policies, guidelines and procedures expeditiously.

RECOMMENDATIONS/OBSERVATIONS

3.150 The Committee strongly recommends that all such cases should be thoroughly reviewed in close coordination with State Drug Authorities. Specific procedures may be framed for approval of brand names. The procedure adopted by the Registrar of Newspapers to avoid duplication may be worth emulating. As a beginning, a data bank of all branded pharmaceutical products along with their ingredients should be uploaded on the CDSCO website and regularly updated. (Para 11.2)

Action Taken

3.151 The Ministry of Health and Family Welfare has recently issued statutory direction under section 33P to the State Governments on 01.10.2012 for Issuance of manufacturing license of drugs in generic names only.

3.152 The Ministry will take initiative to set up data bank with networking with all state drug controllers.

3.153 The DCG(I) has also been adequately sensitized in this regard.

3.154 The CDSCO has already uploaded in its web-site about 85000 brands of drug formulations as obtained from the State Food and Drug Control Administration (FDCA), Gujarat.

3.155 The State Governments have been advised to initiate immediate action to have data base of all drugs licensed by them, manufacturers, etc.

Further Recommendation

3.156 The mess created by the uploading of the totally outdated data bank obtained by CDSCO from its Gujarat counterpart has already been commented upon along with remedial measures suggested previously in this report and thus requires no reiteration. The Committee, however, expects from the Ministry to pursue the matter proactively with the State Governments as also itself work towards setting-up a reliable, effective and real time database on branded pharmaceutical products without any further loss of time.

RECOMMENDATIONS/OBSERVATIONS

3.157 In order to scrutinize the compliance of this rule, the Ministry was asked to furnish PSURs in respect of 42 randomly selected new drugs. Since files in respect of three drugs were reportedly missing, PSURs should have been supplied for the balance 39 drugs. The Committee is, however, constrained to note that PSURs in respect of only 8 drugs were submitted by the Ministry. The Committee was informed that 14 drugs though approved were not being marketed or were launched lately and hence PSURs would be expected later. There was no explanation for not submitting PSURs in respect of rest of 17 drugs. (Para 12.2)

3.158 Out of 14 drugs that were reported to be either not yet launched or lately launched, the Committee discovered that, at least, two products (FDC of glucosamine with ibuprofen; and moxonidine) were indeed in the market for some time and concerned manufacturers should have submitted PSURs. But the Committee has not been given any explanation for non-submission of PSURs for these two drugs. (Para 12.3)

Action Taken

3.159 Out of 42 new drugs, the files in respect of 3 drugs were missing. Out of the remaining 39 drugs, the requisite documents have already been furnished to the Rajya Sabha Secretariat in respect of 23 drugs. The other 16 drugs were reportedly not launched in the market.

3.160 The FDC of glucosamine with ibuprofen was approved in favour of M/s Centaur Pharma Ltd. on 21.10.2009. As per the letter of the firm dated 22.2.2011, the firm informed that they propose to launch this FDC In the year 2012 (first quarter) and would comply with the requirement of submitting the PSUR. In other case, Moxonidine drug was approved in favour of M/s Solvay Pharma (I) Ltd. On 27.2.2007. The firm *vide* their letter dated 21.2.2011 informed the office of DCG(I) that they had not launched the product for marketing in the country.

3.161 It has been decided that the DCG(I) will issue general directions addressed to all the State Licensing Authorities and the manufacturers stating that in case an applicant/manufacturer fails to launch their product for marketing in the country within a period of six months from obtaining the permission/license from CDSCO, the permission /license will be treated as cancelled.

3.162 Further to ensure that the PSURs are submitted by the companies as per the regulatory requirement, the system is being streamlined and a new cell in CDSCO under the overall charge of a Deputy Drugs Controller has been set up.

Further Recommendation

3.163 The Committee is not at all convinced by the reply of the Government as it hides more than what it reveals. The letters of the two manufacturers whose cases were pointed out by the Committee have datelines of 21 and 22 February, 2011 respectively that is more than a year before the examination of the Committee concluded. The proposal of one of the manufacturers conveyed through its letter dated 22 February, 2011 schedules the launch of the FDC in first quarter of 2012, a date which again preceded the culmination of the examination of the Committee. Thus, the action of the Government on the observation made by the Committee cannot be termed as irrefutable under any circumstances. The least the Ministry could have done was to obtain updated information on these two cases not only from the two manufacturers in question but also through market intelligence. The Committee expects the Ministry to do so at least now and take further necessary action, accordingly. The Committee also desires the Ministry to instruct the DGCI to issue the general directive to state authorities as well as manufacturers about the failure to launch the product within six months of obtaining permission entailing cancellation of permission/ license forthwith.

RECOMMENDATIONS/OBSERVATIONS

3.164 The Committee feels that the conventional system of locating side effects through spontaneous reporting by doctors to either drug companies or drug regulators has been found to be unsatisfactory. The most effective system is by controlled post-marketing Phase IV studies on a very large number of patients. In the past decade, all the major adverse effects that led to banning of drugs were identified in large scale Phase IV trials. The Ministry may wish to consider the possibility of using this format in the country. (Para 13.3)

Action Taken

3.165 The Ministry has noted the observations of the Committee.

3.166 At present, proposals for approval of new drugs are examined in consultation with NDACs. At the time of approval of new drugs, the applicants are instructed to conduct appropriate Phase-IV clinical trial as per the recommendation of the committees wherever considered necessary by the committee. This is in addition to the mandatory requirements of submitting PSURs six monthly for initial 2 years and annually for another 2 years.

3.167 As mentioned earlier, the Ministry had constituted a three member expert committee. The expert committee submitted its report to the Ministry on 22.11.2012. The committee has felt the need for an adequate system for withdrawal of drugs – with appropriate guidelines and SOPs and the need for carrying out Phase IV studies to be made mandatory for special situations.

3.168 The issue raised by the Hon'ble Committee will, however, be addressed by an expert committee while defining the policies, guidelines, procedures etc. for approval of new drugs.

Further Recommendation

3.169 The Committee is disappointed with the non-committal and evasive reply of the Ministry to the Recommendation. Even after spending more than six months, the Ministry is almost directionless on several vital aspects of drug regulation in the country and has, therefore, chosen to prolong decisions by the mechanism of establishing committees even on matters where decision making is not only within its competence but can be arrived at right away. While decrying this escapist tendency of the Ministry in strong terms the Committee desires a categorical response to the adoption of this simple and effective global best practice within fifteen days of presentation of this Report to the Parliament.

RECOMMENDATIONS/OBSERVATIONS

3.170 The Committee feels that unless information on marketed drugs is continuously updated, there is risk of irrational or inappropriate use of medicines putting patients at risk. The Committee, therefore, recommends that immediate steps need to be taken to address this issue. The CDSCO should be directed to continuously update monographs based on information from regulatory authorities the world over. (Para 14.3)

Action Taken

3.171 The Indian Pharmacopoeia Commission has published the National Formulary of India (NFI) 2011, the book of reference for the use of clinicians, pharmacists and nurses containing detailed information about medicines, their dosage, contraindications, etc. The NFI has been put on the official website of CDSCO so that relevant information reaches the user easily.

3.172 A cell has been created in CDSCO to update the information for appropriate and rational use of the marketed drugs.

RECOMMENDATIONS/OBSERVATIONS

3.173 The Committee is of the firm opinion that accurate information on drugs for patients is absolutely essential to prevent inappropriate use more particularly in children, elderly, during pregnancy and lactation. The Committee recommends that the matter may be looked into to ensure that consumers have the required information to use medicines safely. Given the widespread internet connectivity, it is advisable to devise a system where patients can get unbiased information on drugs at the click of the mouse in any language. (Para 17.3)

Action Taken

3.174 The Ministry has noted the observations of the Committee.

3.175 The Indian Pharmacopoeia Commission has published the National Formulary of India (NFI) 2011, the book of reference for the use of clinicians, pharmacists and nurses containing detailed information about medicines, their dosage, contraindications, etc. The NFI has been put on the official website of CDSCO so that relevant information reaches the user easily.

Further Recommendation (Paras 14.3 and 17.3)

3.176 **The Committee is perturbed to note that its concerns and Recommendations have neither been appreciated nor addressed. CDSCO is supposed to approve monographs/labels on all formulations and amend/update them periodically as new information becomes available. The Committee found that changes pertaining to approved drugs are not being incorporated and hence monographs remain outdated had recommended that changes in monographs should be made from time to time. At the same time manufacturers need to be penalized for not keeping CDSCO informed on changes taking place globally as the manufacturers are generally the first to get information on products in their portfolio. Besides they are legally obliged to keep CDSCO informed on all changes. Instead of responding to the Committee's concern the Ministry has given evasive and irrelevant information. The Indian Pharmacopoeia is a book of standards and is meant for use by the pharmaceutical industry and drug testing laboratories. Moreover Indian Pharmacopoeia does not list all drugs marketed in India because molecules appearing in other Pharmacopoeia are also sold in the country, not to mention new, recent additions, which do not appear in any Pharmacopoeia. By the time a new edition appears, lots of changes have already taken**

place. The Committee had found out during the course of examination of the subject that so far only 4 editions have appeared in the last 65 years. Similarly, the Committee had found that the much-touted National Formulary of India (NFI) too has only appeared four times: 1960, 1966, 1979 and 2011. Such an irregular publication cannot serve the purpose of keeping prescribers informed of the latest developments. Moreover it lists just about 350 of 900 basic drugs sold in India. Doctors are interested in prescribing information such as indications, dose, contraindications, precautions, side effects, drug interactions etc. and not in the standards of testing of drugs. The Committee, therefore, reiterates its instant Recommendation for implementation with utmost promptitude.

RECOMMENDATIONS/OBSERVATIONS

3.177 A drug can be categorized 'Not of Standard Quality' for a variety of both major and minor technical reasons such as not stating the name of the pharmacopoeia correctly, problem with quality of bonding agent, colouring agent, dissolution time, etc. However, there are other more serious cases, where the active ingredient is significantly less in quantity that can harm patients. Therefore, this problem needs to be addressed with all the seriousness that it deserves both by more rigorous checks in procuring bulk drugs (particularly from developing countries with not so stringent quality checks and export controls) and by in-house quality control by manufacturers or solving the problem in transportation and/or storage at distribution/retail levels. (Para 15.4)

3.178 By the time a sample is tested, a large number of packs get sold out with undeterminable injury to patients. There is no effective method of recalling unsold stocks lying in the distribution network. This cannot be allowed to go on. (Para 15.5)

Action Taken

3.179 The Ministry has noted the observations of the Committee.

3.180 Recently, guidelines have been issued on good distribution practices for ensuring the quality of biological products during all aspects of distribution process.

3.181 Further, to check the GMP facilities of foreign manufacturing sites, overseas inspections of such sites have started. Six bulk drug manufacturing units in China were inspected in May, 2011. Registration Certificate and Import License of one unit so inspected, was cancelled.

3.182 Further, in March, 2012, four manufacturing units in China were inspected. In one case, Registration certificate was cancelled.

3.183 In another case the inspection of the manufacturing facility showed some non-compliance with the requirements of Schedule M of Drugs and Cosmetics Rules. The firm was issued show cause notice. In reply to the notice, the firm submitted satisfactory compliance report along with documentary evidences. As the firm initially did not comply with the regulatory requirements, the Registration Certificate and Import License of the firm was suspended for 15 days to ensure that the firm will be cautious in future.

3.184 CDSCO has also formulated guidelines on recall and rapid alert system for drugs including biologicals and vaccines. The same has been uploaded on its web-site.

3.185 CDSCO has started the drug alert system in respect of drugs found to be of not-of-standard quality, spurious, adulterated etc by central drug testing laboratories.

Further Recommendation

3.186 The Committee is of the firm view that physical inspection of overseas

manufacturers of bulk drugs, apart from being cumbersome (serious language problem in countries like China, Korea, Cuba, Hungary, Poland, documentation, etc.) and expensive (due to sheer numbers of locations around the globe from Argentina to Turkey and multiple sites within one country) may not be the best option. A sole inspector cannot undertake physical inspection during a short visit, lasting a few days. In order to be effective, the procedure would require a multi-disciplinary team which should have access to the manufacturing premises and documentation (in English) on GMP without advance notice to prevent manipulation; A possibility which, given the serious manpower and infrastructure constraints of CDSCO is next to impossible. It may, therefore, be more practical, cost effective and beneficial to collect samples of all imported APIs at the port of entry and get them tested within the country. CDSCO can also insist on certification of good quality from the Drug Regulatory Authority of the country concerned for each batch of each API being imported into India. If such drugs are found to be of poor quality, the CDSCO will be in a better position to take appropriate action including, but not limited to, blacklisting the overseas manufacturers and taking up the case with the concerned DRA.

In its Fifty-ninth Report, the Committee had stated that the hype on spurious and counterfeit drugs being produced in India was the handiwork of MNC drug producers aided and abetted by so-called anti-counterfeit commercial “solution providers.” Spurious and sub-standard drugs are two entirely different issues and cannot be clubbed. The 3-member expert committee too has taken the bait by wrongly adding “spurious” to the problem of sub-standard drugs. The Committee has serious apprehensions that such a factually incorrect statement from a committee appointed by the Ministry of Health and Family Welfare can and will be used to validate the false propaganda unleashed by MNC drug producers to defame Indian drugs all over the world and hence needs to be rectified at once.

RECOMMENDATIONS/OBSERVATIONS

3.187 The Committee feels that there should be severe punishment for manufacturing and for allowing sub-standard drugs to enter the distribution chain. Products with severe deficiencies should be penalized the same way as producers of spurious drugs by amending rules. There is also a case to incorporate penal provisions for manufacturing misbranded and adulterated drugs. (Para 15.6)

Action Taken

3.188 Dealing in spurious drugs has an element of intent whereas the same in respect of substandard drugs may be for a variety of reasons and may not be intentional.

3.189 However, as per the Drugs and Cosmetics Act, 1940, punishment for selling any not-of-standard quality drug which may cause death or grievous hurt is same as that applicable for spurious or adulterated drugs causing death or grievous hurt which is imprisonment for a term which shall not be less than 10 years but which may extend to imprisonment for life and with fine which shall not be less than ten lac rupees or three times the value of the drug confiscated whichever is more.

3.190 The penal provision for manufacture and sale of misbranded drugs is covered under section 27(d) of the Act.

Further Recommendation

3.191 The Committee is aware of the amendments to Drugs and Cosmetic Rules. The core issue is implementation. Continuous Government inaction inspite of legal provisions have

rendered the entire exercise redundant and useless. Consequently, the market is flooded with misbranded drugs, which exact a great cost on public health and economy. The Committee, therefore, not only expects the Ministry to implement the relevant rules more proactively and with honesty of purpose but also reiterates its Recommendation on incorporating penal provisions for manufacturing misbranded and adulterated drugs with alacrity that matter deserves.

RECOMMENDATIONS/OBSERVATIONS

3.192 The Committee recommends that once a batch of a drug is found to be substandard and reported to CDSCO, it should issue a press release forthwith and even insert paid advertisements in the newspapers apart from uploading the information on the CDSCO website. Retail chemists should be advised to stop selling unsold stocks and return the same to local Drugs Inspectors as per rules. The Committee understands that at least two State Drug Authorities that of Maharashtra and Kerala, have taken the initiative to upload information on spurious and sub-standard drugs on their websites on a monthly basis. These are welcome measures worth emulating by other states and the Centre. (Para 15.11)

Action Taken

3.193 CDSCO has started the drug alert system in respect of drugs found to be of not-of-standard quality, spurious, adulterated etc by central drug testing laboratories.

3.194 The Ministry will, however, consider the feasibility of placing advertisements of such cases regularly in the newspapers.

Further Recommendation

3.195 The Committee notes that to begin with CDSCO has started the drug alert system in respect of drugs found to be not of standard quality, spurious, adulterated, etc. by central drug testing laboratories. Furthermore, the Ministry is considering the feasibility of placing advertisements of such cases regularly in the newspapers. The Committee is convinced that this is a herculean task, which can be achieved only when the efforts of the Centre and State Governments are fully synergized. Drug alerts of evaluations by central drug laboratories though welcome would not take care of this acute problem in entirety as the state drug laboratories handle major volumes of such evaluations. The Committee, therefore, desires the Ministry to take up this matter with State Governments on a highly proactive basis to ensure its early fructification. It also desires early decision by the Ministry on utilizing newspapers in this task.

RECOMMENDATIONS/OBSERVATIONS

3.196 The Committee would like the Ministry to take appropriate action against the companies that have advertised the above Schedule H drugs in the lay press. The provisions in the Drugs and Magic Remedies Act are not stringent enough with the result that manufacturers violate them at will. It also recommends that apart from giving sharper teeth to the Drugs and Magic Remedies Act, a provision should also be incorporated in the Drugs and Cosmetics Rules to ban such practices and penalize offenders. The Committee would like to be informed of the action taken to implement these recommendations. (Para 16.2)

Action Taken

3.197 The Ministry has noted the observations of the Committee.

3.198 The proposed amendment to prohibit advertisement of Schedule H drugs has been deliberated and approved in Drugs Consultative Committee (DCC) on 20.7.12 as well as in DTAB on 24.7.12. The matter is under process.

Further Recommendation

3.199 The Committee notes that the Ministry has proposed an amendment to prohibit advertisement of Schedule H drugs. The said amendment has been deliberated and approved by the Drugs Consultative Committee on 20 July, 2012 and by the DTAB four days later on 24 July, 2012. The Committee is, however, pained to note that the matter instead of being brought to its logical conclusion at the earliest is still under process. Deprecating this laissez-faire attitude of the Ministry, the Committee desires that all necessary formalities to formalize the proposed amendment be completed forthwith so that its proper implementation starts in right earnest without any further delay.

CONCLUSION

3.200 Having said as much about the semblance of action taken by the Government on the Recommendations contained in its Fifty-ninth Report, the Committee would like to dwell upon a larger and more fundamental question, the response of the Government or lack of it in the case of the Fifty-ninth Report has posed before the Parliament and its various entities. In our present constitutional arrangement the Parliament is mandated with the sacrosanct responsibility of oversight over the Executive. The Parliamentary Committees taking a leaf out from this mandate carry out their responsibility of oversight through their Reports presented to the Parliament from time to time. Their advice in the form of Recommendations though not mandatory, is invaluable in the sense that they guide the Government to take remedial measures, for course correction in their various endeavors so that public good and development proceed on an even keel without being impeded by lack of professionalism, incompetence, corruption or injustice. The Government, therefore, is morally bound to heed to the advice of the Parliamentary Committees in national interest or else justify in a well-reasoned manner, their inaction or reluctance to take action on any particular Recommendation of the Committee. In the instant case, it is clearly apparent from the analysis of the action taken by the Government on the Recommendations of Committee that out of 69 Recommendations that were actionable only 19 have been implemented by the Government in varying degrees. In case of 46 Recommendations the action taken by Government is only with the intent to delay, obfuscate, stagger implementation or not implement at all with a view to delay/negate action in proven cases of wrongdoing. This inspite of the fact that the Government took not the stipulated three months to take action on Recommendations of Committee but more than six months and they were afforded not one but an unprecedented two opportunities by the Committee to implement the Recommendations contained in the Fifty-ninth Report. All this has been done when CDSCO, which is mandated with the onerous task of directly ensuring health safety of more than one-sixth of the population of the world has, most unfortunately, not acquitted itself well, both, at professional and ethical planes. The Committee considers this highly regrettable and with extreme pain and anguish is constrained to bring these facts on record.

CHAPTER-IV

RECOMMENDATIONS/OBSERVATIONS IN RESPECT OF WHICH REPLIES OF THE GOVERNMENT ARE STILL AWAITED

RECOMMENDATIONS/OBSERVATIONS

4.1 From an analysis of the above facts, the Committee concludes that shortcomings witnessed in respect of coordination with and between the States as also in implementation of applicable legislations in the States are primarily an offshoot of inadequacies in manpower and infrastructure in the States. Strengthening the regulatory mechanism in the States will remain a far cry unless these infirmities are taken care of. (Para 4.5)

4.2 Given the lack of adequate resources in the States it would be unrealistic to expect them to improve the infrastructure and increase manpower without Central Assistance for strengthening drug control system. The Committee, therefore, recommends that the Ministry of Health and Family Welfare should work out a fully centrally sponsored scheme for the purpose so that the State Drug Regulatory Authorities do not continue to suffer from lack of infrastructure and manpower anymore. The Committee desires to be kept apprised of the initiatives taken by the Ministry in this regard. (Para 4.6)

Action Taken

4.3 The Ministry agrees with the observations of the Hon'ble Committee and envisages strengthening of the States' drug regulatory system during the Twelfth Five Year Plan through a suitable scheme.

Further Recommendation

4.4 The Committee notes that the Ministry has accepted this Recommendation of the Committee and in pursuance, thereof, intends to strengthen the States drug regulatory system during the Twelfth Five Year Plan through a suitable scheme. With one year of the Twelfth Plan almost gone by and the plan yet to be finalized, the Committee feels greatly concerned by the continued delay in the requisite assistance reaching the State drug regulation mechanisms. It, therefore, desires the Ministry to make expeditious efforts to sew up the proposed Scheme and start its implementation proper at least from the Second Fiscal of the Twelfth Plan. The Committee would also like to be apprised of the exact contours of the proposed Scheme as soon as the necessary permissions/approvals in this regard, are obtained by the Ministry.

RECOMMENDATION/OBSERVATION

4.5 The Committee agrees that the capacity-building of the Central Drugs Testing Laboratories is the need of the hour. In this era of newer innovations coming up at rapid pace, equipping the Drug Testing Laboratories with the high-end sophisticated equipments is very essential. However, the Committee is aware that monitoring the quality of drugs is primarily the responsibility of the State Drugs Authorities, supplemented by CDSCO, which play a major role in collection of samples and testing them. Without manpower augmentation and upgradation of State Drugs Testing Laboratories, the objective of ensuring availability of quality drugs to the public cannot be realized.

The Committee, therefore, recommends strengthening of both Central and State Drug Testing Laboratories. (Para 5.11)

Action Taken

4.6 The Ministry agrees with the observations of the Committee. The Ministry would take up the matter with the Department of Expenditure about the necessity of augmenting the resources of the central jobs and consider creation of more posts. The strengthening of the States' drugs regulatory systems, including the upgradation of the State Labs would also be facilitated during the Twelfth Plan period.

Further Recommendation

4.7 **The Committee notes that the Ministry intends to take up the matter of augmentation of resources of the Central Labs and creation of more posts with the Department of Expenditure. The upgradation of States Laboratories would also be facilitated during the of Twelfth Plan period. The Committee is of the view that in the present state of availability of resources it is easier said than done to secure the finances required for the aforementioned purposes. Keeping in view the fact that the upgradation of Central and State Drug Labs would help immensely in ensuring quality drugs for the general public the Committee exhort the Ministry of Health and Family Welfare to make all efforts to secure the requisite funds for the purpose in the Demand for Grants (2013-14) so that this much delayed action is not staggered any further. The Committee would like to be apprised of the results of the efforts of the Ministry at the soonest.**

RECOMMENDATION/OBSERVATION

4.8 The Committee is extremely anxious on both counts: such hugely costly imported drugs losing their potency before use and the possibility of fakes entering the chain. It is strange that multinational drug companies that have well-staffed marketing offices in India, instead of importing drugs from their overseas affiliates and selling them are using traders to handle this activity. Apart from risk to patients, there is leakage of revenue to income tax. While the promotional expenses on imported formulations are being paid by the Indian branch of MNCs thus reducing income tax liability, there is no corresponding income since traders are paying directly to overseas offices of MNCs. The Committee would like the Ministry to ensure that in cases where MNCs have offices in India, traders are not permitted to import formulations of such companies. The Committee would like to be kept informed of the steps taken on this issue. (Para 15.9)

Action Taken

4.9 The Ministry has noted the observations of the Committee.

4.10 Ministry has referred the matter to Department of Revenue to look into the issues raised by the Hon'ble Committee and give its advice.

Further Recommendation

4.11 **The Committee feels that the Ministry has very rightly referred this vexed issue to the Department of Revenue in the Ministry of Finance for its advice. Since the continued operations of such kind are a huge drain on the country's resources in the form of Income Tax avoidance apart from the risk to the quality of these drugs and possibility of fakes entering the market due to these operations, the Committee desires the Ministry to follow-up the matter with the Department of Revenue proactively and take further necessary corrective action with utmost urgency.**

OBSERVATIONS/RECOMMENDATIONS — AT A GLANCE

The Committee takes note of various steps initiated by the Government and action suggested on the Recommendations contained in its Fifty-ninth Report. It is, however, hugely disappointed to observe that inspite of the Government being afforded another opportunity to furnish conclusive responses on the various Recommendations of the Committee, has once again chosen to come up with half measures, vague and dilatory responses to say the least. As the subsequent analysis of the Committee will bear out that general agreement of the Government with the Recommendations of the Committee is mere platitude. The Government has done nothing concrete or conclusive even for the Recommendations and findings of the Committee, which directly concern the safety, and health of crores of our countrymen. The Preliminary Submissions, as is evident from its plain reading only, confirms the intent of the Government in staggering decisions and action on vital matters either by way of referring matters to committees after committees or evolving time-consuming policies. The Committee deprecates this tendency of the Government in strongest terms. (Para 6)

The Committee notes with satisfaction that the Government has at last formulated a Mission Statement, which is in consonance with the mandate of CDSCO. The Committee expects the Government to move beyond the formulation stage and formally implement this Mission Statement in letter and in spirit. (Para 1.5)

The Committee notes that the Government, albeit belatedly, has now started invoking Rule 33P to issue directions to the State Governments in connection with the implementation of the Drugs & Cosmetics Act and Rules. It has in pursuance of the Recommendation of the Committee issued statutory directions to State Governments on October 1, 2012 under Rule 33P on two issues. The Committee while appreciating the action taken by the Government on its Recommendation feels that had the Government shown similar alacrity in resorting to Rule 33P in the past, things would not have come to such a sorry pass. It, therefore, considers the continued inaction of the Government and reluctance to resort to Rule 33 P in the past as inexplicable. (Para 1.16)

The Committee is happy to note that finally pragmatism and concern for public good has prevailed and the Ministry has decided to suspend marketing approval of all drugs prohibited for sale in the US, UK, EU, Australia, Japan and Canada for safety reasons. The Committee is of the firm conviction that drugs not approved for use or approved for extremely restricted use in countries with robust regulation should also be brought under the purview as has been done by the World Health Organisation. It is a well-known fact that drug manufacturers simply do not submit applications for the approval of new drugs to robust regulators to avoid rejection by other agencies/countries. It is precisely for this reason that several manufacturers, in spite of the huge potential of marketing drugs in the US, avoid entering the US market. As once a drug is rejected in the US, it becomes highly impossible to get approval even in countries with poor drug regulation. The Committee is also confident that now when the Ministry has adopted, albeit, belatedly this global best practice in drug regulation, it would immediately apply it on two burning cases *viz.* Analgin and Buclizine. (Para 1.21)

Furthermore as this salutary mechanism has been put in place in India, the Committee going a step further would also like the CDSCO to mandatorily go into the

regulatory status of drugs in countries with robust regulation. And any drug which is relevant to the needs of the countries like the US, Canada, UK, EU, Australia and Japan, if not cleared there should be subjected to intense scrutiny both when it is being considered for approval as also when their continued marketing is being reviewed. The Committee would appreciate a decision in the matter within fifteen days of presentation of this Report to the Parliament. (Parat 1.22)

The Committee notes with satisfaction that the Ministry has finally veered towards the idea of constituting committees with experts from across the country. The Recommendation of the Committee was basically to highlight that the Delhi centric composition of these committees was depriving them of the sage advice and expertise of the immense talent present in government medical colleges spread across the country. In this age of specialization and super specialization in various disciplines and sub disciplines of medical science it is, in any case, not very sensible to confuse expertise with hierarchy. (Para 1.27)

The Committee is happy to note that the Ministry has appreciated the nuances of this recommendation of far reaching import and decided to implement it. It would, however, like the Ministry to take immediate steps to commence the implementation proper of this measure to derive its maximum benefit for the general public without any further loss of time. (Para 1.30)

The Committee derives satisfaction from the fact that at last in pursuance of its Recommendation the issue of manufacturing licenses to unauthorized FDCs has been centre staged after more than eleven years and discussed in the Drugs Consultative Committee meeting held on 20 July, 2012. It further notes with satisfaction that the Ministry has issued statutory direction under Section 33P to State Governments on 1 October, 2012 to refrain from granting drug licenses including FDCs without the approval of DCG (I). The Ministry has also indicated its intention to take action against the 294 FDCs which are a subject of litigation in Madras High Court based on the outcome of the case. Furthermore, in regard to FDCs licensed by the State Authorities before 1 October, 2012, the State Authorities have been asked to direct the manufacturer concerned to prove safety and efficacy of such FDCs before the CDSCO within a period of 18 months or invite prohibition for manufacture and marketing. The Committee feels that 18 months is too long a period for the purpose of proving efficacy and safety of these products. As in the eventuality of these being harmful or less advantageous to health and well being of public can cause incalculable damage in this long interregnum. The Committee therefore strongly recommends that this period should be curtailed to nine month *i.e.* up to 30 June, 2013 without fail. (Para 1.41)

The Committee notes that to begin with the Ministry has formed twelve New Drug Advisory Committees (NDAC) consisting of ten members each. These 120 experts have been drawn from twenty institutions. Given the fact that the country has 135 government medical colleges, the Committee finds this composition of NDACs not at all representative of the vast pool of expertise available countrywide. However, taking the assurance of the Ministry about broad basing of NDACs on face value, the Committee is confident that the Ministry will give due representation to experts from different Government medical colleges when the NDACs are constituted next. (Para 1.46)

The Committee notes that in pursuance of its Recommendation, applicants who have been granted approvals of new drugs have been instructed formally on 13 September, 2012 to submit India specific PSUR in the format specified in the rules or risk suspension/cancellation of the marketing approval. The Committee is happy with this step in the right

direction. It, however, cautions the Ministry to merely not rest with the issue of instructions but also monitor and follow up vigorously the compliance of these instructions by the manufacturers so as to ensure that they do not remain restricted merely on paper. (Para 1.52)

The Committee is really dismayed by this casual attitude of the Government as it strongly feels all these actions only involve routine application of mind and could have been completed immediately after the Recommendations of the Committee were conveyed to the Government. The Committee, therefore, feels that enough time has been wasted by the Government in extending assurances in the matter and they should now complete all action required in this context including preparation of policies and standard operating procedures within one month of presentation of this Report to the Parliament. (Para 3.4)

The Committee finds the instant reply of the Government yet another instance of delaying tactics. If the Government agrees with this Recommendation of the Committee what has stopped it from implementing it during last so many months is the moot point. The Committee, therefore, reiterates its Recommendation for immediate compliance by the Government. (Para 3.7)

The Committee notes that the modifications carried out previously by the Government in the qualification and recruitment rules for the post of DCG (I) are a matter of litigation. In any case these modified qualifications and rules do not address the concerns of the Committee to any extent whatsoever. The Committee also notes that unfortunately and as in the case of several of its other Recommendations, the Government has merely decided to setup an expert committee which has been recommended by the previously setup three member expert committee, referred to earlier in this Report, to lay down the qualifications, experience, job description, powers and responsibilities for the post of DCG (I) in consultation with the Ministry of Law. The proposed committee would also review these issues relating to other senior level positions in the Organization. (Para 3.16)

The Committee derives no solace from this very open-ended response of the Government. Nothing tangible has been done by the Government in the direction of implementing this Recommendation of the Committee. The Committee understands that the matter is sub-judice in the context of the modifications carried out by the Government previously in the qualifications and recruitment rules for the post of DCG(I). The Committee is certain that this situation does not inhibit the Government from carrying out all necessary activities including the formation of an expert committee for and in connection with the implementation of the instant Recommendation of the Committee. It, therefore, considers the delay by the Government in constitution of an expert committee, as also other preparatory action, as unpardonable and desires that the same may be completed within a month of presentation of this Report to the Parliament. (Para 3.17)

The Committee takes note of the various steps taken by the Government in consonance with its instant Recommendation. As a test case they also accessed the CDSCO website with a view to evaluate the data regarding 85,000 brands of drugs that have been uploaded on the website by the Ministry after obtaining the same from Food and Drug Control Administration, Gujarat. To their utter surprise, they could locate only 65,500 odd formulations on the site. They also found several banned drugs on the site; Drugs, which have been discontinued and are generally known to be so to the public at large also featured there. The Committee also noted a great degree of variance in the prices of some of the generally known drugs as reflected on the website and as prevalent in the market. To sum up, the Government has undertaken this measure in extreme hurry and in a very unprofessional manner, without even bothering about the serious consequences it may have

in prescription procedures and also in financial terms on the poor hapless patients. The Committee while strongly deprecating this action of the Ministry recommends that the said data be immediately removed from the website of CDSCO so as to prevent any further dissemination of wrong and archaic information about drugs, many of which may have life-saving/threatening implications. It also recommends that since the data base is a critical requirement for information generation, the information received from Gujarat authorities be updated on war footing and put up on the website of CDSCO within a month of the presentation of this Report to the Parliament. (Para 3.23)

The Committee finds it incomprehensible as to why the final reply of the Government fails to mention some of the concrete actions in this regard mentioned in the first action taken reply. The Committee, therefore, desires a detailed explanatory note in the matter from the Ministry bringing out the exact position within one month of presentation of this Report to the Parliament. (Para 3.28)

The Committee finds the action taken reply of the Ministry on this very important aspect highly unsatisfactory. Even after the passage of several months these drugs continue to be marketed with impunity though their exact effect, harmful or otherwise, is yet to be ascertained. The Government without caring a bit about the ramifications is still contemplating referring the issues related to continued marketing of these drugs and updating of their product monographs in the light of recent knowledge and regulatory changes overseas to NDAC for examination and review. The continued inaction of the Government on this vital matter of public health needs to be deprecated in strongest terms. The Committee also recommends that the Ministry should come out of its contemplation mode and take action as recommended by the Committee in the context of these three drugs without any further loss of time. (Para 3.31)

The Committee is shocked to note this dilly-dallying by the Ministry on a matter, which could be affecting lives of lakhs of people in the country who are consuming these drugs. The Ministry agrees with Committee's viewpoint about review of approvals to ensure safety of patients, fair play, transparency and accountability, but instead of taking strict and immediate action in all these proven cases of delinquency and omission and commission, it still continues to be in a state of profound procrastination and wants to refer the issues relating to continued marketing of these drugs and updating of their product monographs in the light of recent knowledge and regulatory changes overseas to the NDACs for examination and review. The continued inaction on the part of the Ministry on this serious matter almost borders on collusion with an intention to save the guilty. Committees after committee are being constituted to postpone the day of reckoning of the guilty people. On another plane this inaction which has led to unhindered marketing of these drugs with unknown and unspecified risks to the unsuspecting people who are consuming them amounts to a serious violation of human rights of the hapless patients. While condemning this continued inaction of the Ministry, the Committee recommends immediate and conclusive action on this Recommendation of the Committee without indulging into the charade of having a plethora of committees after committee to stall a decision in the matter. (Para 3.39)

This is yet another instance where the Ministry inspite of appreciating the serious problem the continued marketing of these 33 drugs may pose to the Indian patients has chosen to take no action to resolve it. Even after a lapse of more than seven months and with virtually nothing concrete having been suggested by the three-member expert committee on this contentious matter, the Government intends to delay a decision by referring it to yet another committee. These tactics have been, as stated at several places in this Report, resorted to by the Government to delay indefinitely the decisions and

consequent actions that would be required to be taken against several officials and non-officials who have indulged in rampant acts of omission and commission while approving these drugs in gross violation of the law of the land. The Committee takes strong objection to these dilatory tactics and recommends immediate decision on all these proven gross violations lest the health of the people is compromised irrevocably. (Para 3.42)

The Committee notes with trepidation, its instant Recommendation of considerable import for the health sector in the country, also getting lost in the maze of inactivity which is all pervading in the final action taken notes of the Ministry. The systemic improvements suggested by the Committee for pre-approval trials are easily doable, if the government has a will to carry them out. Unfortunately, however, apparently due to extraneous considerations the Government is still contemplating constitution of committees and other formalities to stall expeditious implementation of these measures for public good. The Committee also feels that half measures like NDACs being advised to take note of the Recommendations of the Parliamentary Committee would not suffice, as it would then not be obligatory upon NDACs to scrupulously adhere to these norms. The Committee, therefore, recommends that the Ministry should immediately codify all these measures in the form of mandatory Rules so that the NDACs and all other agencies/bodies are left with little room for exercising their discretion or their own interpretation of any measure, a malaise that has, hitherto, wreaked havoc on the health care system of the Country. (Para 3.50)

The Committee is aghast to note the paralytic inertia gripping the Ministry which is preventing it from taking action against guilty official(s) of CDSCO and others involved in proven cases of delinquency and illegality six months should have been more than enough to not only inquire into the misdeeds of those who had so wantonly indulged in the above cited gross irregularity but also sufficed to take exemplary action against them so as to deter others. The Ministry by still dithering over issuing instructions to NDACs and DCGI has abundantly proved that it has neither the intention to clean the Augean stables of CDSCO nor any concern for probity and rule of law. Hoping against hope, the Committee expects the Ministry to atleast even at this late stage take immediate action on these proven cases of delinquency and irregularities so that a stern message is sent to all concerned that the drug regulatory mechanism is not up for grabs for perpetuation of unethical and illegal practices. (Para 3.60)

The response of the Ministry is clearly indicative of the fact that it wants to drag its feet when it comes to punishing the people who have compromised the system over the years through their sheer illegal activities, which are totally against public interest. It is incomprehensible as to what is stopping the Ministry from forwarding these proven cases of gross illegality and proven collusion of the Medical Council of India and the medical colleges/hospital authorities concerned for appropriate action though more than six months have elapsed since the Committee brought these cases to the knowledge of the Parliament and the Government. The Committee, therefore, while expressing its strong displeasure with the Ministry recommends that these cases be referred to MCI and medical colleges/hospital authorities concerned within seven days of presentation of this Report to the Parliament. With a view to expedite action against these errant experts who have indulged in unethical and illegal practices without any concern for the health and well being of common people the Committee further desire the Ministry to impress upon MCI and all other authorities concerned to act against these experts in a highly time bound manner and report back to the Ministry at the earliest so that the Ministry is able to furnish the feedback on all these cases to the Parliament within one month of presentation of this Report to the Parliament. (Para 3.66)

The Committee appreciates that in pursuance of its Recommendation, the applications for new drugs including FDCs are now being examined by NDACs and decision on their approvals are taken based on the recommendation of NDACs. Moreover, all members of NDACs are required to sign a declaration of conflict of interest before being involved with NDACs. They also appreciate the fact that recommendations of NDACs are being put on the website to ensure transparency and accountability. The Committee, however feels that the Ministry has already inordinately delayed constitution of the expert committee to define policies, lay down guidelines and SOPs for approval of Clinical Trials and New Drugs. It also feels that the Ministry has equally badly delayed the formulation of policies and SOPs for identification of experts, as it has not moved beyond mere intent, in their context during more than six odd months. Since a lot of time has already been wasted in these two crucial matters the Committee desires the Ministry to constitute the two committees and recommends the said committees be directed to complete their work in highly time bound manner and submit their respective reports within a period of one month of presentation of this Report to the Parliament. (Para 3.77)

This is yet another instance where the Ministry has failed to act on a proven case of gross illegality. Instead after whiling away more than six months, it has still chosen to take recourse to its favorite ploy of referring the matter for examination and review to NDAC. As far as culpability part is concerned that has also been staggered indefinitely as the Ministry has till now only conveyed that DCG (I) will constitute an inquiry committee to investigate into the issue. The Committee takes serious umbrage over these more than apparent dilatory tactics being adopted by the Ministry to somehow delay action against the wrongdoers. The Committee, therefore, reiterates its Recommendation that responsibility be fixed in this case without any further loss of time and the approvals granted be reviewed in the light of latest scientific evidence regulatory states in developed countries, particularly in Belgium, the country of its origin, equally quickly. (Para 3.82)

The Committee find it deeply perturbing as to why the Ministry has failed to take action in this very open and shut case of impropriety and criminal lapse though more than six months have elapsed the Committee strongly feel that if perpetrators of such illegalities and collusive acts which are detrimental to public health are allowed to go scot-free then the total collapse of an ethical health care system is inevitable. The Committee, therefore, reiterates their Recommendation with all force at their command and desire immediate and exemplary action against officials of CDSCO who colluded with private interest and got the drug approved in violation of laws at once and without the delaying instrument of another inquiry committee. (Para 3.87)

In its Fifty-ninth Report in another case study had noted that a drug Deanxit which is marketed in India is allowed to be produced and exported by DMA but not allowed to be used in Denmark. Opining that there must be some very good reasons for Danish Medicine Agency (Denmark) not to approve a domestically developed drug where an anti-depressant drug would perhaps be in greater demand as compared to India. (Para 3.95)

The Committee had felt that the DCGI should have gone into the reasons for not marketing the drug in major developed countries such as United States, Britain, Ireland, Canada, Japan, Australia just to mention a few. Noting further that instead of examining and reversing regulatory lapses, DCGI has referred the matter to an Expert Committee to look at the isolated and restricted issue of “safety and efficacy” instead of unlawful approval in the first place the Committee had recommended that in view of the unlawful approval granted to Deanxit, the matter should be re-visited and re-examined keeping in mind the regulatory status in well developed countries like Denmark, the country of origin; the United States, Britain, Canada, European Union and Japan etc. (Para 3.96)

In its final ATNs the Government has stated that now, the applications for new drugs including FDCs are examined by the NDACs and decisions on their approval are taken based on the recommendations of these committees. (Para 3.97)

The drug FDC of Flupenthixol and Melitracen, of which the Deanxit is also a brand, is already under examination in consultation with an expert committee. The expert committee recommended for conducting Phase IV Clinical trial after getting the protocol approved. The protocol for the trial submitted by the firm is under examination by that expert committee. (Para 3.98)

The drug was approved in the country in 1998 and since then it is in the market. It is also marketed in other countries. Since the Hon'ble Committee has raised concern over the manner of approval of the drug and has recommended that the same needs to be revisited, it has been decided that the manufacturer of the drug shall be instructed to establish the safety and efficacy of the FDC within 6 months, failing which the drug would be considered for being prohibited for manufacture and marketing in the country. (Para 3.99)

The case of Deanxit conveys a strong whiff of collusion and cover up, briefly put, in its initial ATN, the Ministry informed the Committee that the matter had been referred to the 3-member expert committee and hence action would be taken when the recommendation is received. Surprisingly in its final ATN, there is no mention of any recommendation from the 3-member expert committee. In order to investigate the matter, the Committee went into the records of the 3-member expert committee and found a major intriguing omission. In its report to the Ministry, the 3-member expert committee had grouped various cases of wrong doing under heading (a) on pages 4, 13 and 49. However either by design or default, the case of Deanxit (FDC of flupenthixol and melitracen) identified by the Committee as a blatant example of unlawful approval was omitted under the group while other cases were listed. The Committee finds it more intriguing that such an omission was not noticed by the Ministry. (Para 3.100)

The marketing approval granted to Deanxit (the first formulation of the Fixed-Dose Combination of Flupenthixol and Melitracen) was patently unlawful as stated in Para 7.44 of the Committee's Fifty-ninth Report on the following counts. (Para 3.101)

Deanxit, though permitted to be manufactured and exported, is not allowed to be prescribed to patients in Denmark, the country of innovation/origin. Hence permission to import and manufacture granted by CDSCO was in violation of Rule 30-B of the Drugs and Cosmetics Rules. (Para 3.102)

One of the ingredients, Melitracen, was not approved earlier; hence as per Appendix VI (a) of the Drugs and Cosmetics Rules the clinical trials should have been conducted as per Rule 122 (E) (a). In effect it means clinical trials on each indication on at least 100 patients at 3-4 sites. It was approved for four distinct and different indications. Such trials were not conducted. (Para 3.103)

In its submission to the Committee, the Ministry referred to a vague letter dated 10.08.1998 written by a psychiatrist employed by Lady Hardinge Medical College, New Delhi directly to the DCGI alluding to some unspecified trial with no details (such as number of patients enrolled, protocol, results etc.). Mandatory pre-approval clinical trials are sponsored and conducted by applicant companies and then results submitted to DCGI for marketing approval. This was a strange case where the purported letter was written by a self-appointed investigator to the DCGI. The Ministry failed to give an authenticated copy of the letter and results of the trial. Even if this vague, unsubstantiated letter is accepted as a substitute for a clinical trial at one site, the same cannot account for trials

at 3-4 centres for each indication. It is clear that marketing approval was given without mandatory trials. (Para 3.104)

Deanxit is not allowed for marketing in any of the other advanced countries such as United States, Britain, EU Community, Canada, Australia and Japan where depression is more common than India. In the United States the two ingredients, Flupenthixol and Melitracen are not even individually allowed to be marketed. (Para 3.105)

In the ATNs, the Ministry has gone out of the way to inform the Committee that the drug "is also marketed in other countries," as if it is a good defence for permitting the use of the drug in India. The Ministry is advised to read Para 7.44 carefully of the Committee's Report where in the Committee has acknowledge that Deanxit is indeed marketed in countries like Aruba, Cyprus, Jordan, Kenya, Pakistan, Trinidad etc. and some other developing countries which are handicapped by lack of competent drug regulatory system. (Para 3.106)

Neither Flupenthixol nor Melitracen is listed in the National List of Essential Medicines (NLEM) published by the Government of India. (Para 3.107)

Notwithstanding this lapse, the 3-member expert committee has indeed stated, "Fixed Dose Combinations have become a malaise. The rationality of the combinations is not critically examined. Even where multiple drugs are required for treatment, the FDCs jeopardize dose adjustment of individual medicines. Convenience and profit seem to have overtaken service. The requirements for clearance of FDCs should be more stringent - requiring empirical clinical trial to show advantage of FDC- before their approval." (Para 3.108)

The Committee is amazed that such a crucial recommendation of the 3-member Expert Committee is not being applied to the instant case. (Para 3.109)

If any drug is promoted for unapproved indications, DCGI has the statutory duty to take action and even cancel marketing approval. The Committee is aghast that no action was taken against the Danish manufacturer, Lundbeck even when it was openly flouting Indian laws. Compare the lack of action in India with the United States where for a similar offence PfiZer had to shell out Rs. 2,300 crores for promoting gabapentin for unapproved indication. (Para 3.110)

Attempt by the Ministry to club Deanxit brand with other subsequent formulations is also diversionary and misleading. Under Drugs and Cosmetic Rules, a New Drug is deemed to be a new drug for four years after initial approval. As per records submitted to the Committee the initial approval was granted to manufacturer of Deanxit. No other approval was given by CDSCO to any other applicant in the first four years. Other manufacturers launched the drug after four years not by seeking approval from CDSCO but by obtaining manufacturing licenses from the State Drug Authorities which is perfectly legal. Hence if initial approval by CDSCO is irregular or unlawful then nothing can stop other manufacturers from marketing the product. Therefore the focus needs to be squarely on the first approval. (Para 3.111)

The Committee, therefore, reiterate that concrete and exemplary action by the Ministry on (a) unlawful approval against functionaries of CDSCO (b) reversal of unlawful approval, (c) unlawful promotion by Lundbeck. (Para 3.112)

In the opinion of the Committee it is an open and shut case that needs immediate action, not promise of prolonged fruitless deliberation designed to delay action. Why should the people of India consume a questionable drug approved in a questionable manner even for a day longer, more so when the drug regulator of the innovator country Denmark is not

allowing its use within its jurisdiction but allowing its export to developing countries with weak or non-existent drug regulation? (Para 3.113)

The Committee in its Fifty-ninth Report in another fully documented irregularity of the Organisation had noted that though as per the Drugs & Cosmetics Rules, whenever there is either an additional formulation (*viz.* tablets, solutions, suspensions, injections, controlled-release, gels, etc.) or proposal to use in additional indications, the drug is deemed to be a New Drug. But, in a clear case of extreme collusion and breach of this rule an official of CDSCO though a letter dated February 11, 2000, inspite of additional indications (burns and wounds, non-healing indolent ulcers, bedsores, mucositis, etc.), conveyed to the manufacturer that Placenta Extract was not a New Drug and gave permission to promote the Placenta Extract gel. By including the term 'etc.' loopholes were left wide open to add other indications, which is an unprecedented irregularity and illegality. The collusive element was so overpowering that the letter of the manufacturer dated February 7, 2000, not only reached Delhi from Kolkata at breakneck speed, the permission, albeit wrong, was also granted within four days on February 11, 2000. (Para 3.123)

The Committee had therefore, considering the serious dimensions of this violation recommended an enquiry into the said letter so that responsibility is fixed and appropriate action is taken against the guilty so that never again did the DCG(I) approve drugs in violation of laws, that too for use in neonates and young children. Expressing its deep concern, extreme displeasure and disappointment at the state of affairs the Committee had asked the Ministry is to ensure that the staff at CDSCO does not indulge in irregularities in approval process of new drugs that can potentially have adverse effect on the lives of people and that all the cases listed and cases similar to these should be investigated and responsibility fixed and action taken against erring officials whether currently in service or retired. (Para 3.124)

In its final ATNs the Government has stated that as mentioned earlier, the Ministry had constituted a three member expert committee. The expert committee submitted its report to the Ministry on 22.11.2012. The committee has recommended instituting an enquiry into the matter. As recommended the DCG(I) will constitute an enquiry committee to investigate into the issue. The Hon'ble Standing Committee would be kept informed on this issue. (Para 3.125)

The Committee finds the instant response of the Government clear stonewalling to protect the guilty. The matter of inquiring into and taking action against CDSCO functionary who violated the rules to favour the manufacturer by treating a new drug (Placenta extract) as old drug and permitting the use for additional indications, with potential risk to patients, is a very simple open and shut case. In any case the 3-member expert committee instead of straightaway suggesting concrete action has recommended an enquiry, which the Ministry to its great comfort and convenience has interpreted to mean forming an "inquiry committee". Such repetitive references from the Ministry to the 3-member Expert Committee to another "inquiry committee" would mean further delay in taking action, if not placing the issue in cold storage. In the opinion of the Committee, this is one case where no extraordinary investigative skills or legal acumen is required to fix responsibility and punish the guilty official(s). A rule has been violated, all evidence is on board and the extraordinary interest of the perpetrator(s) is also clearly visible. What purposes, other than delaying the judgment day, would a series of inquiries serve is the central message. The Government's response that the Committee would be kept informed on this issue is a clear indicator that quick action in this case of blatant violation is not at all on Government's mind. The Committee, therefore, reiterates immediate and conclusive action in this instant case without any further dilly-dallying. (Para 3.126)

The continued marketing of Analgin, discarded the world over, is a matter of grave concern for the Committee. Analgin is not listed in the National List of Essential Medicines (NLEM). Bureaucratic delays, repetitive references from one committee to another can do nothing but hurt patients. (Para 3.134)

The Committee also feels that merely requesting State Drug Authorities to direct manufacturers to label the drug Analgin as approved by CDSCO without exemplary, penal action for documented violations is itself an act of negligence. The indications are approved by CDSCO, not State Drug Authorities. Hence CDSCO should itself take immediate action for violations. (Para 3.135)

Given the near non-existence pharmacovigilance in the country putting Analgin under so called “focussed pharmacovigilance” is nothing but a dilatory and diversionary move to let the drug be sold in the country to benefit the manufacturer. The Committee, therefore, desires that a decision be taken on this open and shut case without taking refuge behind committees after committees within one month of presentation of this Report. (Para 3.136)

The Committee is astounded to note the almost U-turn made by the Ministry on this vital issue. In its initial ATN, the Ministry had taken the stand that; a drug could not be banned when safer, more efficacious drugs for the same disorder are launched since there is no such provision in the Drugs and Cosmetics Rules. There was incidentally no mention of the matter having been referred to 3-member expert committee. (Para 3.141)

In any case the Committee finds no merit in the reason given by the Ministry. Under current rules, any drug found to be unsafe can be banned under Rule 26-A irrespective of whether safer substitutes are launched in the market or not. If there is no safer substitute and the drug is essential or life saving, then obviously it is not possible to ban the drug. Once a safer substitute is available then nothing stops the Central Government from invoking Rule 26-A. (Para 3.142)

In its final ATN, the Ministry in spite of their own expert committee opining that there should be an adequate system for withdrawal of drugs has found one more reason not to ban risky remedies by stating that “most newer drugs are generally found to be more expensive” The Committee has been given to understand that there is no provision under Drugs and Cosmetics Rule to take the cost of drugs into consideration while approving or banning drugs. It does not require a great deal of intelligence to conclude that it is better to consume a safer drug, even if it is more expensive, than consume a risky drug that ultimately will be far more costly due to adverse effects. (Para 3.143)

The Committee has already expressed its views on the directions issued by the Union Government under Section 33P to State Governments, previously in this Report. As regards the intention of the Ministry to constitute another committee of experts to lay down policies, guidelines and procedures to be adopted for approval of FDCs, the committee considers it like many other replies of the Government to its other Recommendations contained in the Fifty-ninth Report, a ploy to waste time and avoid an expedition decision to curb this rampant and harmful practice. With piles of evidence available locally as well as in the form of global best practices, the Ministry can do the needful *suo motu* and without resorting to this time tested, time consuming device of an expert Committee. The Committee expects the Ministry to take decisions in the matter accordingly at the soonest so that the approval of FDCs is regulated by well laid out policies, guidelines and procedures expeditiously. (Para 3.149)

The mess created by the uploading of the totally outdated data bank obtained by CDSCO from its Gujarat counterpart has already been commented upon along with remedial

measures suggested previously in this report and thus requires no reiteration. The Committee, however, expects from the Ministry to pursue the matter proactively with the State Governments as also itself work towards setting-up a reliable, effective and real time database on branded pharmaceutical products without any further loss of time. (Para 3.156)

The Committee is not at all convinced by the reply of the Government as it hides more than what it reveals. The letters of the two manufacturers whose cases were pointed out by the Committee have datelines of 21 and 22 February, 2011 respectively that is more than a year before the examination of the Committee concluded. The proposal of one of the manufacturers conveyed through its letter dated 22 February, 2011 schedules the launch of the FDC in first quarter of 2012, a date which again preceded the culmination of the examination of the Committee. Thus, the action of the Government on the observation made by the Committee cannot be termed as irrefutable under any circumstances. The least the Ministry could have done was to obtain updated information on these two cases not only from the two manufacturers in question but also through market intelligence. The Committee expects the Ministry to do so at least now and take further necessary action, accordingly. The Committee also desires the Ministry to instruct the DGCI to issue the general directive to state authorities as well as manufacturers about the failure to launch the product within six months of obtaining permission entailing cancellation of permission/license forthwith. (Para 3.163)

The Committee is disappointed with the non-committal and evasive reply of the Ministry to the Recommendation. Even after spending more than six months, the Ministry is almost directionless on several vital aspects of drug regulation in the country and has, therefore, chosen to prolong decisions by the mechanism of establishing committees even on matters where decision making is not only within its competence but can be arrived at right away. While decrying this escapist tendency of the Ministry in strong terms the Committee desires a categorical response to the adoption of this simple and effective global best practice within fifteen days of presentation of this Report to the Parliament. (Para 3.169)

The Committee is perturbed to note that its concerns and Recommendations have neither been appreciated nor addressed. CDSCO is supposed to approve monographs/labels on all formulations and amend/update them periodically as new information becomes available. The Committee found that changes pertaining to approved drugs are not being incorporated and hence monographs remain outdated had recommended that changes in monographs should be made from time to time. At the same time manufacturers need to be penalized for not keeping CDSCO informed on changes taking place globally as the manufacturers are generally the first to get information on products in their portfolio. Besides they are legally obliged to keep CDSCO informed on all changes. Instead of responding to the Committee's concern the Ministry has given evasive and irrelevant information. The Indian Pharmacopoeia is a book of standards and is meant for use by the pharmaceutical industry and drug testing laboratories. Moreover Indian Pharmacopoeia does not list all drugs marketed in India because molecules appearing in other Pharmacopoeia are also sold in the country, not to mention new, recent additions, which do not appear in any Pharmacopoeia. By the time a new edition appears, lots of changes have already taken place. The Committee had found out during the course of examination of the subject that so far only 4 editions have appeared in the last 65 years. Similarly, the Committee had found that the much-touted National Formulary of India (NFI) too has only appeared four times: 1960, 1966, 1979 and 2011. Such an irregular publication cannot serve the purpose of keeping prescribers informed of the latest developments. Moreover it lists just about 350 of 900 basic drugs sold in India. Doctors are interested in prescribing information such as indications, dose, contraindications, precautions, side effects, drug interactions etc. and not

in the standards of testing of drugs. The Committee, therefore, reiterates its instant Recommendation for implementation with utmost promptitude. (Para 3.176)

The Committee is of the firm view that physical inspection of overseas manufacturers of bulk drugs, apart from being cumbersome (serious language problem in countries like China, Korea, Cuba, Hungary, Poland, documentation, etc.) and expensive (due to sheer numbers of locations around the globe from Argentina to Turkey and multiple sites within one country) may not be the best option. A sole inspector cannot undertake physical inspection during a short visit, lasting a few days. In order to be effective, the procedure would require a multi-disciplinary team which should have access to the manufacturing premises and documentation (in English) on GMP without advance notice to prevent manipulation; A possibility which, given the serious manpower and infrastructure constraints of CDSCO is next to impossible. It may, therefore, be more practical, cost effective and beneficial to collect samples of all imported APIs at the port of entry and get them tested within the country. CDSCO can also insist on certification of good quality from the Drug Regulatory Authority of the country concerned for each batch of each API being imported into India. If such drugs are found to be of poor quality, the CDSCO will be in a better position to take appropriate action including, but not limited to, blacklisting the overseas manufacturers and taking up the case with the concerned DRA.

In its Fifty-ninth Report, the Committee had stated that the hype on spurious and counterfeit drugs being produced in India was the handiwork of MNC drug producers aided and abetted by so-called anti-counterfeit commercial "solution providers." Spurious and sub-standard drugs are two entirely different issues and cannot be clubbed. The 3-member expert committee too has taken the bait by wrongly adding "spurious" to the problem of sub-standard drugs. The Committee has serious apprehensions that such a factually incorrect statement from a committee appointed by the Ministry of Health & Family Welfare can and will be used to validate the false propaganda unleashed by MNC drug producers to defame Indian drugs all over the world and hence needs to be rectified at once. (Para 3.186)

The Committee is aware of the amendments to Drugs and Cosmetic Rules. The core issue is implementation. Continuous Government inaction inspite of legal provisions have rendered the entire exercise redundant and useless. Consequently, the market is flooded with misbranded drugs, which exact a great cost on public health and economy. The Committee, therefore, not only expects the Ministry to implement the relevant rules more proactively and with honesty of purpose but also reiterates its Recommendation on incorporating penal provisions for manufacturing misbranded and adulterated drugs with alacrity that matter deserves. (Para 3.191)

The Committee notes that to begin with CDSCO has started the drug alert system in respect of drugs found to be not of standard quality, spurious, adulterated, etc. by central drug testing laboratories. Furthermore, the Ministry is considering the feasibility of placing advertisements of such cases regularly in the newspapers. The Committee is convinced that this is a herculean task, which can be achieved only when the efforts of the Centre and State Governments are fully synergized. Drug alerts of evaluations by central drug laboratories though welcome would not take care of this acute problem in entirety as the state drug laboratories handle major volumes of such evaluations. The Committee, therefore, desires the Ministry to take up this matter with State Governments on a highly proactive basis to ensure its early fructification. It also desires early decision by the Ministry on utilizing newspapers in this task. (Para 3.195)

The Committee notes that the Ministry has proposed an amendment to prohibit advertisement of Schedule H drugs. The said amendment has been deliberated and approved

by the Drugs Consultative Committee on 20 July, 2012 and by the DTAB four days later on 24 July, 2012. The Committee is, however, pained to note that the matter instead of being brought to its logical conclusion at the earliest is still under process. Deprecating this laissez-faire attitude of the Ministry, the Committee desires that all necessary formalities to formalize the proposed amendment be completed forthwith so that its proper implementation starts in right earnest without any further delay. (Para 3.199)

CONCLUSION

Having said as much about the semblance of action taken by the Government on the Recommendations contained in its Fifty-ninth Report, the Committee would like to dwell upon a larger and more fundamental question, the response of the Government or lack of it in the case of the Fifty-ninth Report has posed before the Parliament and its various entities. In our present constitutional arrangement the Parliament is mandated with the sacrosanct responsibility of oversight over the Executive. The Parliamentary Committees taking a leaf out from this mandate carry out their responsibility of oversight through their Reports presented to the Parliament from time to time. Their advice in the form of Recommendations though not mandatory, is invaluable in the sense that they guide the Government to take remedial measures, for course correction in their various endeavors so that public good and development proceed on an even keel without being impeded by lack of professionalism, incompetence, corruption or injustice. The Government, therefore, is morally bound to heed to the advice of the Parliamentary Committees in national interest or else justify in a well-reasoned manner, their inaction or reluctance to take action on any particular Recommendation of the Committee. In the instant case, it is clearly apparent from the analysis of the action taken by the Government on the Recommendations of Committee that out of 69 Recommendations that were actionable only 19 have been implemented by the Government in varying degrees. In case of 46 Recommendations the action taken by Government is only with the intent to delay, obfuscate, stagger implementation or not implement at all with a view to delay/negate action in proven cases of wrongdoing. This inspite of the fact that the Government took not the stipulated three months to take action on Recommendations of Committee but more than six months and they were afforded not one but an unprecedented two opportunities by the Committee to implement the Recommendations contained in the Fifty-ninth Report. All this has been done when CDSCO, which is mandated with the onerous task of directly ensuring health safety of more than one-sixth of the population of the world has, most unfortunately, not acquitted itself well, both, at professional and ethical planes. The Committee considers this highly regrettable and with extreme pain and anguish is constrained to bring these facts on record. (Para 3.200)

The Committee notes that the Ministry has accepted this Recommendation of the Committee and in pursuance, thereof, intends to strengthen the States drug regulatory system during the Twelfth Five Year Plan through a suitable scheme. With one year of the Twelfth Plan almost gone by and the plan yet to be finalized, the Committee feels greatly concerned by the continued delay in the requisite assistance reaching the State drug regulation mechanisms. It, therefore, desires the Ministry to make expeditious efforts to sew up the proposed Scheme and start its implementation proper at least from the Second Fiscal of the Twelfth Plan. The Committee would also like to be apprised of the exact contours of the proposed Scheme as soon as the necessary permissions/approvals in this regard, are obtained by the Ministry. (Para 4.4)

The Committee notes that the Ministry intends to take up the matter of augmentation of resources of the Central Labs and creation of more posts with the

Department of Expenditure. The upgradation of States Laboratories would also be facilitated during the of Twelfth Plan period. The Committee is of the view that in the present state of availability of resources it is easier said than done to secure the finances required for the aforementioned purposes. Keeping in view the fact that the upgradation of Central and State Drug Labs would help immensely in ensuring quality drugs for the general public the Committee exhort the Ministry of Health and Family Welfare to make all efforts to secure the requisite funds for the purpose in the Demand for Grants (2013-14) so that this much delayed action is not staggered any further. The Committee would like to be apprised of the results of the efforts of the Ministry at the soonest. (Para 4.7)

The Committee feels that the Ministry has very rightly referred this vexed issue to the Department of Revenue in the Ministry of Finance for its advice. Since the continued operations of such kind are a huge drain on the country's resources in the form of Income Tax avoidance apart from the risk to the quality of these drugs and possibility of fakes entering the market due to these operations, the Committee desires the Ministry to follow-up the matter with the Department of Revenue proactively and take further necessary corrective action with utmost urgency. (Para 4.11)

MINUTES

XI
ELEVENTH MEETING
(2012-13)

The Committee met at 3.00 P.M. on Tuesday, the 23rd April, 2013 in Room No. '67', First Floor, Parliament House, New Delhi.

MEMBERS PRESENT

1. Shri Brajesh Pathak — *In the Chair*

RAJYA SABHA

2. Shri Jagat Prakash Nadda
3. Shri Arvind Kumar Singh
4. Shri D. Raja

LOK SABHA

5. Shri Kirti Azad
6. Shri Kuvarjibhai M. Bavalia
7. Dr. Sucharu Ranjan Halder
8. Dr. Sanjay Jaiswal
9. Shrimati Jayshreeben Patel
10. Dr. Anup Kumar Saha
11. Dr. Raghuvansh Prasad Singh

SECRETARIAT

Shri P.P.K. Ramacharyulu, *Joint Secretary*

Shri R.B. Gupta, *Director*

Shrimati Arpana Mendiratta, *Joint Director*

Shri Dinesh Singh, *Deputy Director*

Shri Pratap Shenoy, *Committee Officer*

I. Opening Remarks

2. At the outset, the Chairman welcomed Members of the Committee and apprised them of the agenda of the meeting, *i.e.* consideration and adoption of draft 66th Report on the action taken by the Government on recommendations/observations contained in the 59th Report of the Committee on the Functioning of Central Drugs Standard Control Organisation and * * *. He invited Members to share their specific suggestions for improvements and incorporation in the Draft Reports.

II. Adoption of the Draft Reports

3. The Committee then considered and discussed the five draft Reports mentioned above. A

*** Relate to other matters.

few changes were suggested by Members for incorporation in the Reports. After some discussion, the Committee adopted all the five Reports with some modifications. The Committee, thereafter, decided that the Reports may be presented to the Rajya Sabha and laid on the Table of the Lok Sabha on Friday, the 26th April, 2013. The Committee authorized its Chairman and in his absence, Shri D. Raja and Dr. Vijaylaxmi Sadho to present the Reports in Rajya Sabha, and Dr. Sanjay Jaiswal, and in his absence, Shrimati Jayshreeben Patel to lay the Reports on the Table of the Lok Sabha.

III. Study visit

4. * * *
5. The Committee adjourned at 3.35 P.M.

