MOST IMMEDIATE
SPECIAL MESSENGER

X.11035/32/2012-DFQC
Government of India
Ministry of Health & Family Welfare

Nirman Bhavan, New Delhi
Dated the 12 September, 2012

OFFICE MEMORANDUM

Subject: The 59th report of the Parliamentary Standing Committee on the functioning of Central Drugs Standard Control Organisation (CDSCO)-regarding.

The undersigned is directed to refer to Rajya Sabha Secretariat's O.M. No. R.S.10/2(vi)/2010-Com(H&FW), dated the 29th August, 2012 on the above mentioned subject and to enclose herewith interim Action Taken Note in English & Hindi on the observations/recommendations contained in the aforesaid Report for information and necessary action. The final Action Taken Note will be sent shortly.

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OBSERVATIONS/RECOMMENDATIONS ON THE FUNCTIONING OF THE CENTRAL DRUGS STANDARD CONTROL ORGANISATION (CDSCO)

PARA No.	RECOMMENDATIONS	ACTION TAKEN NOTE / COMMENTS
Para 2.2	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.	2.2: The functions of CDSCO emanate from the provisions of the Drugs and Cosmetics Act, 1940 and Drugs and Cosmetics Rules, 1945. 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. The 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."
Para 2.19	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.	2.19: Recruitments to all the posts in the Government are governed by the respective Recruitment Rules (RRs). These RRs are framed by the concerned administrative Ministry on the basis of the basic criteria and guidelines formulated by the Department of Personnel & Training (DoPT). In respect of Group B and Group A posts, the RRs are framed in mandatory consultation with the DoPT and UPSC. While framing the RRs, though the administrative Ministry initiates the proposal and indicates the basis requirements of the posts, these two agencies have the upper hand in deciding the qualifications and experience required for the posts apart from giving essential directions in respect of other aspects of the RRs, like the method of recruitment, etc. Accordingly, it is decided whether a post is to be

		filled by promotion, direct recruitment or deputation, the three recognized methods of recruitment to any post. After the framing of the RRs, which evidently is a very time consuming process, undertaking the recruitment to the posts is again a time consuming procedure in Government. Given the demands of transparency, the recruiting agency follows the long process and the laid down procedures. Therefore, despite the seriousness of the Ministry, the progress in the various recruitments has been extremely slow. There is no substitute for these procedures. The Ministry has been regularly taking up the matter with the UPSC. In view of the constraints of staff due to delay in regular appointments, the Government has had to resort 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. As regards to employment of medically qualified persons, the Ministry of Health and Family Welfare has taken up various measures to strengthen CDSCO including appointment of medical specialists during the 12th Plan. (Annexure-1)
Para 2.20	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	2.20: The CDSCO is already working with the help of 113 professionally qualified personnel engaged on contract basis and would continue to do so as per its requirements. Requisite care is taken to avoid conflict of interests while appointing these personnel.

	specified period.	
Para 2.21	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.	2.21: In view of its staff constraints, it is the constant effort of the CDSCO to employ the existing man power in a way so as to ensure optimum utilization of resources for discharging the functions prescribed under the rules. Focus of the CDSCO is to ensure that safe and effective drugs are allowed to be manufactured and marketed in the country. For the approval of the new drugs and clinical trials, CDSCO is being assisted by 12 New Drug Advisory Committees (NDAC) consisting of medical experts working in various Government hospitals, medical institutes. Moreover, two Committees of Experts to advise the DCG(I) in matters related to regulatory approval of clinical trials for Investigational New Drugs (IND) and special biological products and 6 Medical Device Advisory Committees (MDAC) have also been formed.
Para 2.22	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.	2.22: The Ministry is continuously engaged in augmenting the infrastructure of the CDSCO and drug testing labs. Presently there are 6 Zones and 3 Sub-Zones of CDSCO in different parts of the country. More Zones and Sub-Zones are being created and Sub-Zones are being upgraded. More and more sophisticated instruments are being provided to the drug testing labs. The 12th Plan document of the Ministry pertaining to the Drugs Quality Control is also an ambitious document aimed at major capacity development of the sector. A copy of the intended interventions during the 12th Plan in drug quality control sector is enclosed at Annexure I.
Para 2.23	In the absence of any reasons for unwillingness on the part of medically qualified persons to join CDSCO, the	2.23: The functions of CDSCO are derived from the Drugs and

	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 (DDC), 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 DM) 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.	Cosmetics Act, 1940 and Rules made thereunder. The objective of the Act is to regulate the import, manufacture, distribution and sale of drugs and cosmetics in the country. CDSCO is responsible for multi-disciplinary activities relating to quality control of drugs. Hence, manufacture or testing of drugs or enforcement of the provisions of the Drugs and Cosmetics Act are essential pre-requisites for appointment to the post of DCG(I). As per the Recruitment Rules framed in consultation with the DoPT and UPSC, the post of DCG(I) is required to be filled up as on date by 'deputation'. The RRs provide equal opportunity to the medical professionals to compete. If by virtue of their working and experience in a Government organisation, they have acquired essential experience required for the post as per the notified RRs, they are eligible to participate in the selection process. Rules for recruitment (direct recruitment, deputation and promotion) are framed keeping in view the existing and the future needs of the organization. A medically qualified doctor with requisite qualification would be eligible to participate in the process of recruitment. However, he may have to report to his superior who may be less qualified but may have greater experience and who would have been selected to that post having fulfilled its basic requirement. CDSCO is part of the Directorate General of Health Services headed by the Director General who is a medically qualified doctor. Therefore, for all technical matters, guidance of the DG, Dte. GHS is available to the organization in general and the DCG(I) in particular.

Para 3.6	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 DM and PhD qualifications and vast experience in the practice of medicine and even research.	3.6: The Ministry agrees that equating a B. Pharm with an MBBS with specialization in Clinical Pharmacology or Microbiology is not rational and needs to be corrected. The issue would be addressed by the DTAB. As per the present recruitment rules for the post of DCG(I), the incumbent has to be Post Graduate in Pharmacy or other specialties as mentioned in RRs. Candidate having Graduate Degree in Pharmacy alone is not eligible for the post of DCG (I) as is evident from the following provisions of the notified RRs: "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"
Para 3.7	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	3.7: The recruitment rules notified in 2005 for the post of Drugs Controllers (India) required Post Graduate Degree in Chemistry / Pharmaceutical Chemistry /

	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.	Biochemistry / Pharmacy / Pharmacology as essential qualification. These rules were amended in 2011 and Post Graduate Degree in the field of Microbiology was also included as essential qualification. However, the Ministry will review the recruitment rules (RRs) of the DCG(I) in view of the recommendations of the Hon'ble Committee.
Para 3.8	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.	3.8: The UPSC has already completed the recruitment process for filling the post and has given its recommendation about the selected candidate. The Government is waiting for the stay granted by the Madras High Court to be vacated before appointing the selected person to the post. The selected candidate is an eminent scientific and professionally qualified person. The qualifications and experience held by the selected candidate are as follows: "i) B.Pharm ii) M.Pharm iii) Ph.D in Pharmaceutics iv) MBA (U.K.) v) Experience: (a) 2 years as Secretary-cum-Scientific Director, IPC (b) 6 years 10 months as Director, CIPL, Ghaziabad (c) 13 years in various capacities as Senior Manager (R&D)/ Manaager (R&D) / Dy.Manager (FDRL) / Sr. Executive / Executive in Indian Drugs & Pharmaceuticals Ltd (IIDPL), Gurgaon (d) 1 year as Pool Officer, CSIR (e) Experience includes working as

		Govt. Analyst for statutory testing of drugs, working in appellate laboratory for condom testing as per Drugs & Cosmetics Act/Rules, Scientific and administrative management of formulation development/ R&D and quality assurance in IDPL, as head of IPC direction and leadership in preparation of monographs for drugs and formulations for inclusion in Indian Pharmacopoeia (IP), etc."
Para 4.5	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.	4.5 & 4.6: The Government has already proposed the strengthening of the States' drug control departments during the 12th Five Year Plan. Considering the importance of making good quality drugs available to the public at large, for the first time, Central Government has proposed to strengthen the drug regulatory mechanism in the State/UTs through a centrally sponsored scheme. This included both the physical and human infrastructure. A new budget line has been opened and an initial token provision of Rs. 2 crores has been made in 2012-13 budget. Kind attention is drawn to the 12th Plan Proposals (Annexure 1).
Para 4.6	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 4.7	It is a matter of grave concern that there are serious shortcomings in Centre- State coordination in the implementation of Drugs & 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.	4.7: The Ministry of Health and Family Welfare has issued directions under section 33P from time to time for uniform administration of the provisions of Drugs and Cosmetics Rules especially in respect of grant of permissions by the State Licensing Authorities for certain formulations considered to be New drugs , whose efficacy and safety has not yet been approved by the Drugs Controller (India). The issue of cancellation of licences 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 licence for new drugs for unapproved FDCs must not be granted by any State Licensing Authorities. The Ministry of Health and Family Welfare is also considering to issue directions to the State Governments on the following issues. 1. To refrain from granting new drugs licensing including FDCs without approval of DCG (I). 2. Issuance of license of drugs in generic names only.
Para 4.8	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.	4.8: The Government is hopeful that creation of data bank will be feasible during 12th Plan (Annexure-1). The government has proposed networking of CDSCO, State Drug Control Departments, airports, seaports, Drug testing labs and also for archiving of important files during the 12th Plan.
Para 5.11	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.	5.11: The Ministry has been consistently working to equip the central drug testing labs with more manpower and sophisticated equipments. The Ministry would take up the matter and the concerns of the Hon'ble Committee with the Department of Expenditure about the necessity of augmenting

	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.	the resources of these labs and accordingly expeditiously granting its approvals for creation of more posts as well as for purchase of equipments. As has been mentioned earlier a new budget line with an initial token provision of Rs. 2 crore has been made in the 2012-13 budget for strengthening the state drug regulatory system.
Para 6.2	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.	6.2: 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.
Para 7.13	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.	7.13: The files pertaining to Pefloxacin, Lomefloxacin and Sparfloxacin have been reconstituted, even though complete details are not available. The continued marketing of these drugs and updating of the product monographs in the light of recent knowledge and regulatory changes overseas in respect of these drugs will be examined in consultation with the Experts.
Para 7.14	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. Ademetionine (Akums), x. Pirfenidone (Cipla), and xi. FDC of Pregabalin, Methylcobolamine, Alpha Lipoic Acid, Pyridoxine & Folic Acid (Theon); • In the case of 2 drugs (Dronedarone of Sanofi and	7.14: The Government has already 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 to examine the issues raised by the Hon'ble Committee

	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	and give its report. The Committee is in its final stages of deliberations and likely to submit its report shortly. Further course of action will be decided on the receipt of its recommendations.

	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 7.15	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.	7.15: Ministry of Health and Family Welfare has in principle no objection to putting on website the final recommendations made by NDACs.
Para 7.16	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.	7.16: As mentioned in response to the recommendation No. 7.14, these issues are under examination by an expert committee and further course of action will be decided on the receipt of its recommendations.
Para 7.27	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.	7.27: The major population of India pertains to Dravidians and Indo Aryan ethnic groups, apart from certain other ethnic groups like Negritos and Mongoloids. Indian population is polygenetic and is an amazing amalgamation of various races and cultures. Normally, trials are conducted at major Metros and other cities in different parts of the country which have developed medical facilities. Thus, the data generated at the centers like Delhi, Mumbai, Chennai, Kolkata and places in central India covers major races of the country. 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.
Para 7.28	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	7.28: While examining the applications for clinical trials by CDSCO, the proposals are examined in consultation with

	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.	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.
Para 7.29	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.	7.29: As per the current requirements specified in Schedule Y, the number of subjects in clinical trials depend on nature and objective of the trial. Schedule Y does not specify minimum number of subjects and number of sites to be included in clinical trials. However, in order to have detailed guidelines in this regard, the matter is required to be deliberated in consultation with subject experts. Ministry and CDSCO would take expeditious steps to formulate detailed guidelines in this regard.
Para 7.31	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. (Annexure 8)	7.31: As mentioned in response to the recommendation No. 7.14, these issues are under examination by an expert committee and further course of action will be decided on the receipt of its recommendations.

Para 7.32	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.	7.32: As mentioned in response to the recommendation No. 7.14, these issues are under examination by an expert committee and further course of action will be decided on the receipt of its recommendations.
Para 7.33	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.	7.33: As mentioned in response to the recommendation No. 7.14, these issues are under examination by an expert committee and further course of action will be decided on the receipt of its recommendations.
Para 7.34	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.	7.34: As mentioned in response to the recommendation No. 7.14, these issues are under examination by an expert committee and further course of action will be decided on the receipt of its recommendations.
Para 7.35	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.	7.35: As mentioned in response to the recommendation No. 7.14, these issues are under examination by an expert committee and further course of action will be decided on the receipt of its recommendations.
Para 7.36	There is sufficient evidence on record to conclude that there is collusive nexus between drug manufacturers, some functionaries of CDSCO and some medical experts.	7.36: As mentioned in response to the recommendation No. 7.14, these issues are under examination by an expert committee and further course of action will be decided on the receipt of its recommendations.
Para 7.37	On a more fundamental issue the Committee has come	7.37 & 7.38: Proposals for

	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.	permission of clinical trials and approval of new drugs are at present being examined by CDSCO in consultation with the NDACs for scientific evaluation. Decision for approval on such proposals is taken by CDSCO based on recommendations of the committees. Further, as mentioned in response to the recommendation No. 7.14, these issues are under examination by an expert committee and further course of action will be decided on the receipt of its recommendations.
Para 7.38	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 7.41	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.	7.41: As mentioned in response to the recommendation No. 7.14, these issues are under examination by an expert committee and further course of action will be decided on the receipt of its recommendations.
Para 7.42	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	7.42: As mentioned in response to the recommendation No. 7.14, these issues are under examination by an expert committee and further course of action will be decided on the receipt of its recommendations.

	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 7.43	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.	7.43: As mentioned in response to the recommendation No. 7.14, these issues are under examination by an expert committee and further course of action will be decided on the receipt of its recommendations.
Para 7.45	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.	7.45: As mentioned in response to the recommendation No. 7.14, these issues are under examination by an expert committee and further course of action will be decided on the receipt of its recommendations.
Para 7.46	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	7.46: As mentioned in response to the recommendation No. 7.14, these issues are under examination by an expert committee and further course of action will be decided on the receipt of its recommendations.

	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 7.47	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.	7.47: As mentioned in response to the recommendation No. 7.14, these issues are under examination by an expert committee and further course of action will be decided on the receipt of its recommendations.
Para 7.49	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.	7.49: As mentioned in response to the recommendation No. 7.14, these issues are under examination by an expert committee and further course of action will be decided on the receipt of its recommendations.
Para 7.51	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.	7.51: As mentioned in response to the recommendation No. 7.14, these issues are under examination by an expert committee and further course of action will be decided on the receipt of its recommendations.
Para 7.52	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.	7.52: As mentioned in response to the recommendation No. 7.14, these issues are under examination by an expert committee and further course of action will be decided on the receipt of its recommendations.
Para 8.4	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	8.4: The issue of continued marketing of Analgin is being examined by DTAB in consultation with the expert committee.

	manufacturers, the CDSCO should be directed to re-examine the rationality of continued marketing of Analgin.	
Para 8.5	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.	8.5: As per the existing provisions under Drugs and Cosmetics Act, Central Government is empowered to prohibit manufacture, sale of a drug in following situations : • the use of any drug is likely to involve any risk to human beings or animals or • that any drug does not have the therapeutic value claimed or purported to be claimed for it or • contains ingredients and in such quantity for which there is no therapeutic justification As such, there is no provision in the said Act to prohibit a drug when safer, more efficacious drugs are launched. Safety of a drug and its use for specific disease is well established based on the period of time it is available in the market. For a particular disease, even though safer, more efficacious drugs may be available, the treatment with old drugs may be required for certain groups of patients. Therefore, banning of an old drug when safer and more efficacious drugs are available may not always be feasible. However, while examining the issue of continued marketing of a particular drug, various parameters including safety, efficacy as well as the availability of safer and efficacious alternatives are taken into consideration before taking final regulatory decision in the matter.
Para 8.7	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	8.7: As and when serious adverse reaction of a drug is reported from database of the Pharmacovigilance

	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.	programme and or large scale Phase IV trials and the drug is restricted/ prohibited/ withdrawn in other countries with well developed regulatory system, such matter is taken into cognizance and risk benefit profile of the drug is evaluated in consultation with expert committee(s) / DTAB in the context of safety, efficacy and availability of safer cost effective alternatives, disease prevalence in the country. Decision on continued marketing of such drug is taken as per the recommendations of the expert committee(s) in the interest of public. So far, 90 different categories of drugs have been prohibited in the country, most of which are based on reports of adverse drug reactions from database of their Pharmacovigilance programme and or large scale Phase IV trials in other countries. Presently application for approval of new drug in the country are examined in consultation with the NDACs consisting of subject experts from various Govt. institutes and Medical colleges. While recommending for approval of new drug, the Committee recommends conduct of appropriate Phase IV clinical trials in the country wherever considered necessary, so as to capture the safety data of the drugs. The decision to ban or withdraw a drug by the regulatory authority is normally based on the risk assessment process, which is influenced by a number of factors such as disease pattern in a country, indications and dosages of the drug permitted, varying reactions of certain ethnic groups in a given population, availability of safer substitutes and overall safety profile of the drug. These conditions

		are different for different countries. It is for this reason that a drug banned / restricted in one country may continue to be marketed in other countries. In this regard, to develop its own data for the purpose instead of depending upon the steps taken by other countries, the Pharmacovigilance Programme of India (PvPI) was initiated by the Government with the Indian Pharmacopoeia Commission, Ghaziabad, (U.P.) as the National Co-Ordination Centre for monitoring Adverse Drug Reactions (ADR) in the country for safe-guarding Public Health. 60 ADR Monitoring Centres (ADRMCs) including AIIMS, New Delhi have been set up in different parts of the country. These centres need to be strengthened. The number of these ADRMCs is proposed to be increased substantially so as to cover all medical colleges, hospitals, etc so that larger data base could be generated . The PvPI Programme aims to generate broad based ADR (Adverse Drug Reactions) data on the Indian population and share the information with global health care community through WHO-UMC (World Health Organization – Upsaala Monitoring Centre) based at Sweden.
Para 8.8	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.	8.8: CDSCO would continue to give due attention to the regulatory developments on safety issues of drugs reported in countries with well developed regulatory systems. As and when such development on a drug is reported, the matter is examined in consultation with expert committee(s) / DTAB and decision is taken on continued marketing of the drug in the interest of the patients considering the disease pattern, indications, dosage, availability of safer

		substitutes and overall safety profile of the drug.
Para 8.10	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.	8.10: The experts are invited on the basis of their experience and availability. In order to have expert consultation in an efficient and timely manner earlier most of the experts were invited from Delhi, as there are many government medical colleges and institutes in Delhi and it was considered to be difficult for experts from other cities to attend such meetings because of their busy schedule in academic activities. As regards to 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 & Head, Department of Pharmacology, AIIMS, New Delhi. Dr. Gupta has wide experience and expertise in the relevant field. Therefore, he was invited for attending most of those meetings. However, henceforth, such committees for examination of safety issues of marketed drugs will be constituted with experts from across the country in light of the observation of the Hon'ble Committee. It is pertinent to mention that, New Drug Advisory Committees constituted for evaluation of applications of new drugs and clinical trials already comprise of experts from medical colleges and institutes across the country.
Para 8.11	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	8.11: As and when safety issues of marketed drugs are reported in other countries, the matter is examined in consultation with Drug Technical Advisory Board / Expert Committee. As mentioned above, henceforth, such expert committees for examination of safety issues of marketed drugs as and when required, will be constituted

	evidence in support of their recommendation.	incorporating adequate number of experts with experience to take broad based decision on continued marketing of the drug.
Para 9.2	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.	9.2, 9.3, 9.4, 9.5, 9.6 & 9.7: The issue of cancellation of licences 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 licence for new drugs for unapproved FDCs must not be granted by any State Licensing Authorities. The Ministry is also considering issuing such directions to the State Governments under Section 33P of the Drugs & Cosmetics Act. Earlier, directions under 33P were issued in 2003, 2007 to the State Government directing them to ask the State Licensing Authority to refrain from granting license of fixed dose combinations considered as new drugs without the approval of DCG(I). In 2007, direction was also issued by the then DCG(I) 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 Central Govt. has filed the reply along with application for vacation of stay. The Hon'ble Madras High court has admitted the petition for hearing.
Para 9.3	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 9.4	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 9.5	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 9.6	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 9.7	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 9.8	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.	9.8: 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, Ministry is considering issuing directions to the State Governments under Section 33P of the Drugs & Cosmetics Act to ensure that state licensing authorities refrain from granting license for such unapproved FDCs.
Para 10.2	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.	10.2: The 12 New Drug Advisory Committees have been constituted. Each of the committee comprises ten members including two clinical pharmacologists and eight medical specialists from Government medical colleges and reputed institutes across the country which are as under: • AIIMS, New Delhi • PGIMER, Chandigarh • JIPMER Pondicherry • LHMC & RML Hospital, New Delhi • VMMC &Safdarjung Hospital, New Delhi • Tata Memorial Hospital, Mumbai • CMC, Vellore • MAMC with GB Pant & LNJP Hospital, New Delhi • UCMS (University College of Medical Sciences) with GTB Hospital, New Delhi • Seth GS Medical College & 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 • Gauhati Medical College and Hospital, Guwahati • Govt. Medical College, Jammu • Nizam's Institute of Medical Sciences, Hyderabad
Para 11.2	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.	11.2: The matter was discussed at length in 44th DCC on 20.7.2012 and it was agreed to make necessary amendment in the rule in this regard. It was agreed in the meeting that the applicant shall apply for grant of manufacturing licence, in proper / generic name only. The data bank would certainly help the matters and the CDSCO would take action in this regard in consultation with the State Drug Controllers.
Para 12.2	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.	12.2: The requisite documents had been submitted to the Hon'ble Committee. However, they are being furnished again in respect of 23 drugs(Annexure-2). The other 16 drugs were not launched in the market. Hence, PSURs for these drugs could not be furnished
Para 12.3	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.	12.3: 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 so far.
Para 12.4	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.	12.4 & 12.5: The applicants who have been granted approval of new drugs, are now being instructed to submit India specific PSUR in the format specified in the rules. In case of non-adherence to the requirements, stringent action including suspension/ cancellation of new drug permission would be taken against the defaulter.
Para 12.5	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 12.6	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.	12.6: The manufacturers which have not submitted PSURs as provided under Drugs and Cosmetics rules have been asked to comply with the mandatory requirements of submission of PSURs. The non-compliance of this provision would attract suspension/ cancellation of the marketing approval.
Para 13.3	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.	13.3: 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.

Para 14.3	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.	14.3: The Indian Pharmacopoeia Commission updates the Indian Pharmacopoeia (IP) every year and makes available reference standards. The sixth edition of Indian Pharmacopoeia, IP 2010 was released on 01.12.2010. It contains 287 new monographs out of which 18 monographs are included on antiretroviral drugs which are not available in any Pharmacopoeia of the World. The Addendum, 2012 to IP, 2010 was released on 27.12.2011. The Indian Pharmacopeia Commission has also published the 4th edition of 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., after a gap of 40 years. The NFI has been put on the official website of CDSCO so that relevant information reaches the user at the click of the mouse.
Para 15.4	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.	15.4 & 15.5: Although the Drugs and Cosmetics Rules specify the detailed requirements for manufacturer to ensure in-house quality checks at the time of manufacture and also to the distributors/ retailers for storage/ distribution, monitoring by the regulatory authorities is not upto the expected level mainly due to constraints of infrastructure and manpower in the States as well as Centre. Further the present capacity to test drug samples by State as well as Central testing laboratories is inadequate. In order to address above issues, a comprehensive proposal for strengthening regulatory infrastructure in terms of both physical and manpower in state as well as centre has been proposed
Para 15.5	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.	

		for the 12th plan. The proposal includes enhancing the testing capacities of existing laboratories as well as setting up of new laboratories so as to ensure timely testing of drugs. Once the laboratories are strengthened, quantum of sampling can be increased which will ensure greater quality assurance. As regards imports, the requirements for grant of import and registration license allowing import of raw material to ensure that quality drugs are imported into the country are already specified in the Drugs and Cosmetics Rules. Further, to check the GMP facilities of foreign manufacturing sites, overseas inspections of such sites have started. CDSCO is considering to put into place a system of alerting the state licensing authorities and public in general as and when any drug is declared sub-standard by any competent authority.
Para 15.6	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.	15.6: The Drugs and Cosmetics Act, 1940 was amended in 2008 enhancing the punishment to imprisonment for not less than ten years but which may extend to imprisonment for life and also fine which shall not be less than ten lacs or three times value of the drugs confiscated. It can thus be seen that punishment for selling any not-of-standard quality drug which may cause death or grievous hurt is same as that applicable for spurious drug causing death or grievous hurt.
Para 15.7	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	15.7: As per the provisions of Drugs and Cosmetics Rules, the chemists and druggists must store the medicines as per the storage conditions mentioned on the label.

	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.	As and when a sample of drug declared not of standard quality by the Govt. Analyst, necessary investigations are required to be conducted by the concerned State Drugs Inspector at the place where the sample was drawn and at the manufacturer's end. The investigation at manufacturer's level should include verification of manufacturing and testing records, reference samples, distribution records etc.
Para 15.9	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.	15.9: As per Drugs and Cosmetic Rules any firm having valid sale license is eligible for import of drugs into the country under valid import license issued by DCG (I). Further, there are provisions to take care of quality of drugs marketed in the country, whether imported or manufactured in India. Ministry, would write to Department of Revenue to look into the matter of disallowing sales promotion expenses of the pharma MNCs if the revenue arising out of the sale of the same drugs (for which sales promotional expenses have been claimed and debited to the expense account) are not credited to their sales account.
Para 15.11	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.	15.11: Under the Drugs and Cosmetic Act, State Licensing Authorities are responsible for grant of license for manufacture and sale of license to ensure quality of drugs marketed in the country and is empowered to take action in respect of drugs declared as not of standard quality. They are, therefore, expected to take initiative to ensure that this information is made available to the chemists as well as consumers in the State. CDSCO is also considering to put into place a system of alerting the state licensing authorities and public in general as and when any

		drug is declared sub-standard by any competent authority.
Para 16.2	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.	16.2: CDSCO has already initiated the steps to make necessary provisions under Drugs and Cosmetic Rules to prohibit advertisement of Schedule H drugs. Proposed amendment in this regard has been deliberated in DCC on 20.7.12 as well as in DTAB on 24.7.12.
Para 17.3	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.	17.3: The Indian Pharmacopoeia Commission updates the Indian Pharmacopoeia (IP) every year and makes available reference standards. The sixth edition of Indian Pharmacopoeia, IP 2010 was released on 01.12.2010. It contains 287 new monographs out of which 18 monographs are included on antiretroviral drugs which are not available in any Pharmacopoeia of the World. The Addendum, 2012 to IP, 2010 was released on 27.12.2011. The Indian Pharmacopeia Commission has also published the 4th edition of 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., after a gap of 40 years. The NFI has been put on the official website of CDSCO so that relevant information reaches the user at the click of the mouse.
Para 18.2	Due to the sensitive nature of clinical trials in which foreign companies are involved in a big way and a wide spectrum of ethical issues and legal angles, different aspects of Clinical trials need a thorough and in-depth review. This Committee has, accordingly, taken it up as a subject for detailed examination separately under the heading 'Clinical Trials of Drugs'.	18.2: No comments

ANNEXURE - I

TOTAL FINANCIAL OUTLAY FOR 12TH FIVE YEAR PLAN FOR DRUGS SECTOR:

S. No	Item	Cost (Crore)
A	For CDSCO	
1	Manpower	Rs 630
2	New offices	Rs 35
3	Up gradation of existing offices	Rs 60
4	Mini labs at Port offices	Rs 160
5	New CDTL labs	Rs 320
6	Up gradation of existing labs	Rs 90
7	Running/Maintenance of labs	Rs 92
8	National Training Academy	Rs 50
9	Mobile labs	Rs 250
10	Pharma Research lab	Rs 50
11	CDSCO Overseas Country offices	Rs 175
12	E-governance/Archiving	Rs 250
13	Pharmacovigillance	Rs 250
14	IEC	Rs 150
15	Overseas Inspections	Rs 25
16	Man power for S.no 4, 5,6,8,9,10,12, 17,18 and Medical devices lab. (4300 personnel)	Rs 964
17	Training to Regulators	Rs 50
18	Travel Expenditure	Rs 20
19	Cosmetics labs	Rs 200
20	Diagnostic labs/Blood testing labs	Rs 60
21	Spurious drug survey and Samples cost for testing of Drugs, Cosmetics, Medical Devices etc	Rs 20
	Total of A	3901
B	For Strengthening of State Drug Regulatory System	
1	Central Govt Share(60%) for Strengthening States Drugs Regulatory Systems	Rs 1920
	Total of A & B	5821
C	Medical Devices	
1	National Labs	Rs 200
2	Funds for International Travel	Rs 25
	Total of A, B & C	Rs. 6046
	IPC	
1	Manpower/other expenses	Rs 100
	NIB	
1	Manpower/other expenses	Rs 100
	CDL Kasauli	
1	Manpower, Infrastructure, Training etc	RS 10
	Grand Total	Rs 6256 cr

Annexure-2

List of the Periodic Safety Update Report (PSUR)*

Sr.No.	Drug	Annexure Number
1.	Cinacalcet	Annexure 'A'
2.	Rasagiline	Annexure 'B'
3.	Everolimus	Annexure 'C'
4.	Trospium	Annexure 'D'
5.	Colistimethate	Annexure 'E'
6.	Exemestane	Annexure 'F'
7.	Fabuxostat	Annexure 'G'
8.	FDC of Diclofenac with serratiopeptidase	Annexure 'H'
9.	Camostate	Annexure 'I'
10.	FDC of Nimesulide with Levocetirizine	Annexure 'J'
11.	Paliperidone	Annexure 'K'
12.	Doxophylline	Annexure 'L'
13.	Buclizine (appetite stimulant)	Annexure 'M'
14.	Pemetrexid (initial approval)	Annexure 'N'
15.	Aliskiren	Annexure 'O'
16.	Rivaroxaban	Annexure 'P'
17.	Cinitapride	Annexure 'Q'
18.	Dronedarone	Annexure 'R' (CD)
19.	Ramosetron	Annexure 'S'
20.	Nimesulide Injection	Annexure 'T'
21.	FDC of Aceclofenac with Thiocolchicoside	Annexure 'U'
22.	FDC of Ofloxacin with Ornidazole	Annexure 'V'
23.	FDC of Aceclofenac with Drotaverine	Annexure 'W'

* In separate boxes and folders.