institutional deliveries, and treatment for chronic diseases under NDCP initiatives.

- Promotion of access to improved healthcare at household level through the female health activist (ASHA).
- Preparation and Implementation of an intersectoral District Health Plan prepared by the District Health Mission, including drinking water, sanitation and hygiene, nutrition and school education.
- Mainstreaming AYUSH in collocated and revitalizing local health traditions.
- Grievance redressal mechanism for health care users at district to facilitate improvements in the commutization process and increase in the utilization of public health services in rural areas.
- Various monetary and non - monetary incentives are provided to health personnel serving in remote, underserved and tribal areas. Generalist doctors are given the following incentives towards post graduate degrees:

  (i) 50% reservation in Post Graduate Diploma Courses for Medical Officers in the Government service who have served for at least three years in remote and difficult areas

  (ii) Incentive at the rate of 10% of the marks obtained for each year in service in remote or difficult areas up to the maximum of 30% of the marks obtained in the entrance test for admissions in Post Graduate Medical Courses.

Monitoring system for illegal clinical trials

2429. SHRI B.S. GNANADESIKAN: Will the Minister of HEALTH AND FAMILY WELFARE be pleased to state:

(a) whether Government is concerned about the increasing number of deaths by the illegal clinical trials of untested drugs being conducted by multinational companies in our country;

(b) if so, the details thereof;

(c) whether Government has initiated a strong monitoring system to prevent increasing number of deaths due to illegal clinical trials; and

(d) if so, the details thereof?

THE MINISTER OF HEALTH AND FAMILY WELFARE (SHRI GHULAM NABI AZAD): (a) to (d) Drugs and Cosmetics Rules provide that no clinical trial on new drugs shall be conduced except under and in accordance with the permission in writing from the Licensing Authority *i.e.* DCG (I). The Schedule 'Y' of these Rules provides elaborate requirements and guidelines for regulation of clinical trials in the country including provisions for safeguarding the rights, safety and well being of trial subjects. Trials are conducted by Indian as well as multinational companies.

During the last three years, nine cases of alleged irregularities in the conduct of clinical trial have been reported in the country. A statement giving the details of the cases investigated and action taken there on is given in Statement (*See* below).

The Serious Adverse Events (SAEs) of deaths may occur during clinical trials due to various reasons. These deaths could be due to life-threatening diseases like cancer, cardio-vascular conditions like congestive heart failure/stroke and other serious diseases etc. Thus, all deaths during clinical trials may not be due to clinical trials.

Following steps have been taken to strengthen the approval procedures, monitoring mechanism for clinical trials to ensure that safety, rights and well-being of clinical trial subjects are ensured:

1. 12 New Drug Advisory Committees (NDAC) consisting of leading experts mostly from the Government medical colleges and institutes from all over the country have been constituted to advise the Central Drugs Standard Control Organization (CDSCO) in the matters related to approval of clinical trials and new drugs.

2. Applications of Investigational New Drugs (IND) *i.e.*, New Drug Substances which have never been used on human beings are evaluated by an IND Committee, chaired by the Director General, Indian Council of Medical Research (ICMR).

3. Registration of clinical trial in JCMR's registry at 'www.ctri.in' has been made mandatory.

4. Guidelines for conducting inspection of clinical trial sites and sponsor/ Clinical Research Organizations (GROs) have been prepared.

5. Proposal to amend the toxicity study data requirements for approval of clinical trial/new drugs to make it harmonized with the international guidelines has been approved by Drugs Technical Advisory Board (DTAB)

6. To further strengthen the regulatory provisions and the monitoring mechanism of clinical trials in the country the Drugs and Cosmetics Rules, 1945 have been amended as follows:

   (a) Amendment *vide* Gazette Notification G.S.R. 53(E) dated 30-01-2013 specifying procedures to analyse the reports of Serious Adverse Events occurring during clinical trials and procedures for payment of compensation in case of trial related injury or death as per prescribed timelines.

   (b) Amendment *vide* Gazette Notification G.S.R. 63(E) dated 01-02-2013 specifying various conditions for conduct of clinical trials, authority for conducting clinical trial inspections and actions in case of non-compliance.

   (c) The registration of the Ethics Committees has been made mandatory in the Drugs and Cosmetics Rules *vide* Gazette Notification G.S.R No. 72(E) Dated 08.02.13 specifying requirements and guidelines for registration of Ethics Committee.

Statement

Cases of inspection/investigation in alleged irregularities in clinical trials and action taken in these cases during 2010, 2011 *and* 2012

Sl.No.	Year	Name of Firm	Name of Site/State	Drug	Action Taken
1.	2010	QUINTILES Research (India) Pvt. Ltd., Bangalore	Bhopal Memorial Hospital and Research Centre, Bhopal, Madhya Pradesh	Telavancin Versus Vancomycin	A team of officials from the Central Drugs Standard Control Organization (CDSCO) had carried out an Inspection of one clinical trial conducted at Bhopal Memorial Hospital and Research Centre (BMHRC) during 10th to 12th August, 2010. Findings of the inspection showed some deficiencies like non-payment of compensation to the trial subjects for participation, non-reporting of serious adverse events within the prescribed timelines etc. for which Principal Investigator and M/s. Quintiles Ltd., Bangalore were asked to explain their position *vide* letter dated 28-09-2010. The Principal Investigator and M/s. Quintiles

					Ltd. submitted their clarification to the office of Drugs Controller General (I) [DCG(I)]. The office of DCG (I) issued warning letter to Principal Investigator and M/s. Quintiles Ltd. on 23-12-2010 so as to ensure that such deficiencies/discrepancies are not repeated in future.
2.	2010	Path (in Collaboration with ICMR), A-9, Qutab Institutional Area, USO Road, New Delhi-110067, India	1. Khamamam District, Andhhra Pradesh 2. Vadodara, District Gujarat	Human Papilloma Virus Vaccine (HPV Vaccine)	This was a Phase-IV post licensure clinical trial. The trial was initiated by PATH (Programm for Appropriate Technology in Heath), an NGO. The Indian Council of Medical Research (ICMR) and the State Governments of Andhra Pradesh and Gujarat were the collaborating partners. 14091 girls received the vaccine in Andhra Pradesh whereas 10686 girls received the vaccine in Gujarat. Media reported death of 7 girls during the trial. The trial was suspended by ICMR on 7th April 2010. A Committee appointed to enquire into

Sl.No.	Year	Name of Firm	Name of Site/State	Drug	Action Taken
					"Alleged irregularities in the conduct of studies using Human Papilloma Virus Vaccine by Path in India" reported certain discrepancies in taking informed consent, Ethics Committee's approval, reporting of serious adverse event and monitoring, etc. in the conduct of the trial. Based on the findings of report, a warning letter has been issued to M/s. PATH on 03.07.2012 asking them to be careful while conducting clinical trial so as to ensure that such discrepancies/violation are not repeated in future and also directed them to comply with the corrective action taken to ensure strict compliance of Schedule-Y and GCP guidelines in ongoing study and proposed to be started in future research studies.

3	2010	M/s Meril Life Sciences Ltd., Vapi, Gujarat.	M/s. Escorts Heart Institute and Research Centre, Okhla Road, New Delhi.	BioMimeSirolimus Eluting Coronary Stent System	The trial pertains to a clinical trial of medical device, which was already approved by the DCG(I) for manufacture and marketing in India. The investigations revealed that the site carried out the trial as per the requirements of Drugs and Cosmetics Rules except permission from the office of DCG(I). The Sponsors have been warned not to initiate any trial without approval of the DCG(I) in future.
4	2011	QUINTILES Research (India) Pvt. Ltd, Bangalore	Bhopal Memorial Hospital and Research Centre, Bhopal, Madhya Pradesh	Tigecycline	M/s. Quintiles Research (I) Pvt.Ltd., Bangalore was permitted to conduct clinical trial entitled "A multicenter, open label, randomized, comparative study of tigecycline versus ceftriaxone sodium plus metronidazole for the treatment of hospitalized subjects with complicated intra-abdominal infections" on the basis of

Sl.No.	Year	Name of Firm	Name of Site/State	Drug	Action Taken
					permission granted by the office of DCG(I) on 21.04.2006. The approval of the Ethics Committee of the Bhopal Memorial Hospital and Research Centre, Bhopal was obtained by the investigator on 06.04.2006. In view of the alleged irregularities reported in the conduct of the clinical trials in BMHRC, a team of officials from the Central Drugs Standard Control Organization (CDSCO) carried out an Inspection of this trial at the said Centre during 28th February to 2nd March, 2011. Findings of the inspection showed some deficiencies like non-payment of compensation to the trial subjects for participation, non-reporting of serious adverse events within the prescribed timelines etc. for which Principal Investigator and the company were asked to explain their position *vide* letter dated

					08-12-2011. The Principal Investigator and M/s. Quintiles Ltd submitted their clarifications to the office of DCG (I) on 26.12.2011. After considering the clarifications, the office of DCG(I) issued warning letters to the Principal Investigator and M/s. Quintiles Ltd. on 20-03-2012 to be careful while conducting clinical trials so as to ensure that such deficiencies/ discrepancies are not repeated in future.
5.	2011	M/s. Organon India	Bhopal Memorial Hospital and Research Centre, Bhopal, Madhya Pradesh	Fondaparinux	M/s. Organon India was permitted on 09.07.2004 to conduct, clinical trial entitled "An international randomized study evaluating the efficacy and safety of (a) Fondaparinux sodium *vs.* control therapy and b) glucose insulin potassium infusion versus control in a broad range of patients with ST segment elevation acute Myocardial infarction (Low molecular weight Heparin)".

Sl.No.	Year	Name of Firm	Name of Site/State	Drug	Action Taken
					The permission was later transferred to M/s Sanofi-Synthelabo (India) Ltd, Mumbai. The inspection was carried out from 03-03-2011 to 04-03-2011. The team of officials from the Central Drugs Standard Control Organization (CDSCO) carried out an Inspection of this trial at the said Centre during 3rd and 4th March, 2011. Findings of the inspection showed some deficiencies like non-payment of compensation to the trial subjects for participation, non-reporting of serious adverse events within the prescribed timelines etc. for which Principal Investigator and the company were asked to explain their position vide letter dated 08-12-2011. The Principal Investigator and M/s Sanofi-Synthelabo (India) Ltd, Mumbai

					submitted their clarifications to the office of DCG (I) on 13.01.2012. After considering the clarifications, the office of DCG (I) issued warning letters to the Principal Investigator and M/s Sanofi-Synthelabo (India) Ltd, Mumbai on 20-03-2012 to be careful while conducting clinical trials so as to ensure that such deficiencies/discrepancies are not repeated in future.
6.	2011	Axis Clinical Limited, Andhra Pradesh	Axis Clinical Limited, (Unit No. 1) 1st, 2nd, 3rd 5th, and 6th Floor, H.No. 1-121/1, Sy. No. 66 (Part) and 67 (Part), Miyapur, Hyderabad-500050 and (Unit No. 2) Plot No. 33 to 35, Mirra Hospital, 1st Floor, Alluri Seetaramraju Colony, Opp. JPN Colony, Miyapur, Hyderabad.	Bio-availability and Bio-equivalent studies of Anti-Cancer Drugs (Exemistane 25mg Tablets)	M/s. Axis Clinical Research, Hyderabad was reported to have conducted clinical trial of an anti-cancer drug on poor people without proper informed consent. The investigations revealed that the firm conducted bio-equivalence study on an already approved anti-cancer drug and there were certain irregularities with respect to informed consent process and review and decision making process of Ethics Committee. The permission granted

Sl.No.	Year	Name of Firm	Name of Site/State	Drug	Action Taken
					to the firm for conducting bio-equivalence and bio-availability study was suspended on 22.06.2011. Consequent to this, the firm, on 04.07.2011, submitted corrective actions being taken by them including revised Standard Operative Procedures (SOPs) for subject recruitment process, informed consent process and review and decision making process of the Ethics Committee. Based on further investigations and verifications, M/s. Axis Clinical Research, Hyderabad was granted 'NOC' to conduct bio-equivalence study subject to fulfillment of various conditions regarding informed consent process including documentation of the Informed consent process through audio-video means and functioning of Ethics Committee and investigators.

7.	2011	Dr. Anil Bharani and Dr. Ashish Patel,	Maharaja Yashwant Rao Hospital and Mahatma Gandhi Memorial College, Indore-452001, Madhya Pradesh	Tadalafil in Pulmonary Arterial Hypertension (PAH)	There was a news report in respect of alleged flouting of clinical trial norms at Maharaja Yashwant Rao Hospital and Mahatma Gandhi Memorial College, Indore. The news item quoted one specific issue of of use of drug Tadalafil in Pulmonary Arterial Hypertension (PAH) in clinical trial. The office of DCG(I) directed CDSCO (West Zone) on 12-07-11 to carry out an investigation to ascertain the facts. Accordingly, an investigation was carried out by the office of CDSCO(WZ) and State Drugs Control Authority on 10-08-11 in respect of clinical trials conducted at M.G.M. Medical college and associated M.Y. Hospital in Indore. As per the investigation report, a trial was conducted by Dr. Anil Bharani and Dr. Ashish Patel with tadalafil in patients with group-1 pulmonary hypertension without permission

Sl.No.	Year	Name of Firm	Name of Site/State	Drug	Action Taken
					from DCG(I). The study with tadalafil in Pulmonary Arterial Hypertension (PAH) was initiated on 18-09-05 when the drug was not approved for the said indication in the country. However, the drug was approved in the country for another indication - male erectile dysfunction on 10.06.2003. In view of above, the CDSCO *vide* their letter dated 2.11.2011 stopped the clinical trial forthwith and debarred Dr. Anil Bharani and Dr.Ashish Patel from conducting any clinical trial for a period of six months.
8	2011	M/s. Cadila Healthcare Ltd., Ahemadabad; M/s. Emcure Pharmaceuticals, Pune; M/s. Intas Pharmaceuticals, Ahemadabad	MGM Medical College and Hospital, Department of Psychiatry, Madhya Pradesh	Fixeddose combination capsule of Paraxetine HCI controlled release and Clonazepam,	An inspection was conducted by the CDSCO with expert to investigate the reports of irregularities in the conduct of clinical trials at Indore in mentally ill patients during 22nd to 25th December,

Dapoxitine, Doxepin	2011. Investigating team observed some discrepancies like non-maintenance of original Informed Consent Form/Case Record Form, irregularities in transcribing data from original source documents etc. with respect to Schedule Y and Good Clinical Practices (GCP) guidelines. CDSCO(HQ) issued show cause notices on 04.01.2012 to the firms M/s. Emcure, M/s. Intas and M/s. Cadila and to Investigators - Dr. Abhay Paliwal, Dr. Ujwal Sardesai, Dr. Ramghulam Razdan and Dr. Pali Rastogi asking to show cause and explain their position on the observations made by the Inspection team. Consequently, the firms M/s. Cadila Healthcare Ltd., Ahemadabad, M/s. Emcure Pharmaceuticals, Pune, and M/s. Intas Pharmaceuticals, Ahemadabad and the investigators Dr. Abhay Paliwal, Dr. Ujwal

Sl.No.	Year	Name of Firm	Name of Site/State	Drug	Action Taken
					Sardesai, Dr. Ramghulam Razdan and Dr. Pali Rastogi submitted their clarifications in response to the show cause notices. Considering the findings of the inspections and clarifications submitted by the firm and the investigators, it has been observed that there have been certain irregularities as mentioned above in conduct of clinical trials which are not in accordance to the Good Clinical Practices (GCP) guidelines for clinical research in India. In view of above, the said firms and the investigators have been issued warning letters to be careful while conducting clinical trials so as to ensure strict compliance of GCP guidelines and applicable regulations.
9.	2012	Dr. Hemant Jain	Chacha Nehru hospital,	Clinical trials on	In view of the reports of alleged irregula-

Indore	children	rities in clinical trials conducted by Dr. Hemant Jain on 1883 children at Chacha Nehru Hospital in Indore, Madhya Pradesh from 2006 to 2010, a team was constituted to carry out detailed inspection of clinical trials conducted by Dr. Hemant Jain at above mentioned site to verify the compliance to Drugs and Cosmetic Rules and other applicable guidelines. The team carried out inspection from 15.04.2012 to 20.04.2012. As per the inspection report, out of 26 clinical trials, there were some irregularities in 23 trials. In remaining 3 clinical trials, there were no irregularities. The main findings in all the 23 trials were that the quorum of the Ethics Committee of MGM Medical College and MY Hospital that reviewed and accorded approvals of the trial protocols were not as per requirement

Sl.No.	Year	Name of Firm	Name of Site/State	Drug	Action Taken
					of Schedule Y to Drugs and Cosmetics Rules as no lay person/legal expert was present in the meetings of the Ethics Committee. Based on findings of the inspection, the concerned Sponsor/companies and Dr. Hemant Jain (Investigator), have been issued show cause notice. Further, the Chairman of the Ethics Committee of the MGM Medical College and MY Hospital, Indore has also been asked to explain the position on the observations made by the inspection team.