1	2	3	4	5	6	7	8	9	10
26.	Uttarakhand	0	0	178	0	454	5	110	2
27.	West Bengal	399	0	805	1	510	0	6225	11
28.	Andaman and Nicobar Islands	0	0	25	0	6	0	19	0
29.	Chandigarh	25	0	221	0	73	0	341	0
30.	Delhi	1153	3	6259	8	1131	8	1980	4
31.	Dadra and Nagar Haveli	0	0	46	0	68	0	138	1
32.	Daman and Diu	0	0	0	0	0	0	54	0
33.	Puducherry	66	0	96	0	463	3	1102	3
	TOTAL:	15535	96	28292	110	18860	169	37070	227

Complaints against drug trials

†1150. SHRI RAGHUNANDAN SHARMA: Will the Minister of HEALTH AND FAMILY WELFARE be pleased to state:

(a) the number of cases registered against drug trials conducted in the country and out of that in how many cases complaints were received and punishment was given;

(b) the names of cities in Madhya Pradesh from where such incidents came into notice of the Central or State Governments during the last three years and the details of legal action taken thereon; and

(c) the details thereof?

THE MINISTER OF HEALTH AND FAMILY WELFARE (SHRI GHULAM NABI AZAD): (a) to (c) During the last three years and the current year, nine cases of alleged irregularities in clinical trials were inspected/investigated, out of which, six cases are reported from Indore and Bhopal cities of Madhya Pradesh. A Statement containing the details of the cases and action thereon is given in Statement.

†Original notice of the question was received in Hindi.

Statement

Cases of inspection/investigation in alleged irregularities in clinical trials and action taken in these cases during 2010-11 *and* 2012 *(till date)*

Sl. No.	Year	Name of Firm	Name of Site/State	Drug	Action Taken
1	2	3	4	5	6
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. Khammam District, Andhra 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 (Programme 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 "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.

1	2	3	4	5	6
					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	BioMimeSiro1-imus 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.,	Bhopal Memorial Hospital and Research	Tigecycline	M/s Quintiles Research (I) Pvt. Ltd., Bangalore was permitted to conduct clinical trial entitled "A

Bangalore	Centre, Bhopal, Madhya Pradesh	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 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

1	2	3	4	5	6
					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)". 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.

1	2	3	4	5	6
6.	2011	Axis Clinical Ltd., Andhra Pradesh	Axis Clinical Ltd., (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 25 mg 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 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 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 (West Zone) 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 from DCG(I).

1	2	3	4	5	6
					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., Ahmedabad; M/s Emcure Pharmaceuticals, Pune; M/s Intas Pharmaceuticals, Ahmedabad	MGM Medical College and Hospital, (Department of Psychiatry, Madhya Pradesh	Fixed dose combination capsule of Paraxetine HC1 controlled release and Clonazepam, Dapoxitine, Doxepin	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, 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., Ahmedabad, M/s Emcure Pharmaceuticals, Pune, and M/s Intas Pharmaceuticals, Ahmedabad and the investigators Dr. Abhay Paliwal, Dr. Ujwal 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

1	2	3	4	5	6
					accordance with 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 GCP guidelines and applicable regulations.
9.	2012	Dr. Hemant Jain	Chacha Nehru Hospital, Indore	Clinical trials on children	In view of the reports of alleged irregularities 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 was not as per the requirement 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 on 07.08.2012. Further, the Chairman of the Ethics Committee of the MGM Medical College and MY Hospital, Indore has also been asked on 07.08.2012 to explain the position on the observations made by the inspection team.