GOVERNMENT OF INDIA
MINISTRY OF HEALTH AND FAMILY WELFARE
DEPARTMENT OF HEALTH AND FAMILY WELFARE

LOK SABHA
UNSTARRED QUESTION NO.1118
TO BE ANSWERED ON 4TH DECEMBER, 2015

CLINICAL TRIALS

1118. SHRIMATI V. SATHYA BAMA:
DR. VIRENDRA KUMAR:
SHRI JYOTIRADITYA M. SCINDIA:

Will the Minister of **HEALTH AND FAMILY WELFARE** be pleased to state:

(a) the number of clinical trial applications received for imported and indigenously developed medicines, separately and granted permission by the Central Drugs Standard Control Organization (CDSCO) during each of the last three years and the current year;

(b) the cases of irregularities and noncompliance of clinical trial governing rules/ guidelines reported and the action taken/ proposed to be taken by the Government thereon during the said period, State/UTwise;

(c) the number of clinical trial related injuries and casualties reported along with the compensation paid in each of these cases during the said period, State/UT-wise;

(d) the number of complaints for nonpayment of compensation received and the action taken/proposed to be taken by the Government thereon during the said period; and

(e) the corrective steps being taken by the Government to strengthen laws to ensure safety and protection of the rights of the human subjects during clinical trial or medical and scientific research?

ANSWER
THE MINISTER OF HEALTH AND FAMILY WELFARE
(SHRI JAGAT PRAKASH NADDA)

(a) : The number of clinical trial for new drug (s) related applications received and number of permissions granted by Central Drugs Standard Control Organization during last three years and current year is as under:

Year	No. of Application Received	No. of Permission Granted*
2012	480	253
2013	207	73
2014	230	198
2015 (as on 27/11/2015)	170	191

*this includes permissions granted for applications received in previous years.

(b): During last three years and the current year, action has been taken by the Government in 13 cases against persons /hospitals /investigators and sponsors (pharmaceutical companies) found involved in irregular trial (Annexure).

(c): The number of Serious Adverse Events (SAEs) of death and Injury (other than death) reported during the clinical trials during last three years and current year are as under:

Year	**Nos. of SAEs where death was reported.**	**Nos. where death established to be related to Clinical Trial.**	**Nos. where SAEs (other than death), i.e., injury was reported.**	**Nos. where injury established to be related to Clinical Trial.**
2012	436	16	2786	184
2013	590*	46	1122	159
2014	443[a]	22	1326[b]	95
2015 (as on 27/11/ 2015)	330	Under Examination	2137[c]	16

***** - out of 590 reports, 534 reports of SAEs of death have been examined and the remaining are under examination.

a - out of 443 reports, 345 reports of SAEs of death have been examined and the remaining are under examination.

b - relatedness has been examined in 1200 out of 1326 cases.

c - relatedness has been examined in 1050 out of 2137 cases.

Compensation has been paid till November, 2015 in following related cases of death and injury:-

Year	Compensation paid in related cases of	
	Death	Injury
2012	16	112
2013	41	127
2014	18	58
2015	Nil	02

(d): No complaint of non-payment of compensation has been received by Drugs Controller General (India). However, as per information available, compensation in three cases of SAEs of death related to Clinical Trial, one each for 2005, 2006 and 2010 has not been paid as the whereabouts of the legal heir could not be located.

(e) : Adequate provisions have been made in rules 122DA, 122DAA, 122DAB, 122DAC, 122DD and 122E of the Drugs and Cosmetics Rules, 1945 to specify the requirements for conducting clinical trials in India. Further, Schedule-Y of the said Rules prescribes the responsibilities of the Sponsor, Investigator and Ethics Committee to protect the rights, safety and well-being of clinical trial subjects. The measures taken in the recent past to strengthen the regulation of clinical trials include evaluation of the clinical trial proposals by the Subject Expert Committees/ Investigational New Drugs Committee, review of their recommendations by the Technical Committee and, thereafter, approval by the Apex Committee. Compensation is required to be paid in case of trial related injury or death within the prescribed timelines. It has been made mandatory for the sponsor or his representatives to furnish details of the contract entered into by the sponsor with the investigator with regard to financial support, fees, honorarium, payments, etc. Further, it has also been decided that with effect from 30.11.2013, in all clinical trials, in addition to the requirement of obtaining written informed consent, audio-visual informed consent will also be recorded in respect of each trial subject.

Annexure

S.No.	Year	Name of the Firm/Sponsor/CRO/Principal Investigator	State /U-T	Investigational Medicinal Product (IMP)	Action Taken
1	**2012**	Dr. Hemant Jain, Chacha Nehru Hospital, Indore	**Madhya Pradesh**	➢ G-Meningococcal conjugate vaccine ➢ Diphtheria-Tetanus-whole cell Pertussis-Hepatitis B and LBVH0101 Haemophilus influenzae type b tetanus toxoid conjugate vaccine ➢ Diphtheria-Tetanus-whole cell Pertussis-Hepatitis B vaccine ➢ Rabeparazole ➢ Virosomal hepatitis A virus (HAV) vaccine ➢ Monovalent Type 1 Oral Poliomyelitis Vaccine ➢ Bivalent Oral poliovirus vaccine (bOPV) ➢ Haemophilus influenzae b conjugate vaccine ➢ Easyfive TM Vaccine ➢ DTwP Vaccine ➢ Inactivated Polio Vaccine	Based on press reports and the complaint regarding conduct of illegal clinical trials on children, at M/s. Chacha Nehru Hospital, Indoreby Dr. Hemant Jain, a team of officials from CDSCO had carried out inspection (from 16th to 20th April 2012) of clinical trials conducted at this site. It was observed that 26 clinical trials were conducted by Dr. Hemant Jain during the period 2006 to 2010. For the clinical trials conducted by the following sponsors/CROs under the investigator Dr. Hemant Jain, the Office of DCGI issued warning letters to: 1. M/s. Glaxo SmithKline Pharmaceuticals Ltd, Mumbai 2. M/s. Siro Clinpharm Pvt. Ltd. Thane. 3. M/s. LG Life Sciences India Pvt. Ltd.,New Delhi 4. M/s. Quintiles Research (India) Private Limited, Bangalore. 5. M/s. Progenitor Clinical Research Pvt. Ltd., Ahmedabad 6. M/s. PPD Pharmaceutical Development India Pvt. Ltd, Mumbai. Moreover The Office of DCG(I) after issuing show cause notices and obtaining their replies reviewed the matter further and restricted the following from conduct of any new clinical trial for a period of 3

				➢ Monovalent H1N1 Influenza A ➢ Valsartan ➢ Multivalent Human Papillomavirus [HPV] L1 Virus-Like Particle [VLP] Vaccine ➢ Montelukast	months vide orders dated 05.12.2013. 1. Dr. Hemant Jain, M. G. M. Medical College & M. Y. Hospital, Indore, M.P. (Principal Investigator) 2. Ethics Committee, M. G. M. Medical College & M. Y. Hospital, Indore, M.P.. 3. M/s Panacea Biotec Ltd, New Delhi 4. M/s MSD Pharmaceuticals Pvt. Ltd., Gurgaon.
2	**2013**	**Pharmaceutical Companies/Clinical Trial Applicant:** M/s SIRO Clinpharm Pvt. Ltd.,Thane (W) - 400 610, Maharashtra **PI-**Dr. Kim Ramasamy, Arvind Eye Hospital & PG Institute of Ophthalmology, Madurai **EC**- Arvind Eye Hospital & PG Institute of Ophthalmology, Madurai.	**Tamilnadu**	Vitreosolve for ophthalmic interavitreal injection	Debarred from initiating any new clinical trial for 3 months dt. 20.08.2014 Reasons: ▪ Protocol Violation: The antibiotics were administered one and half days before intravitreal injection instead of 3 days as per approved protocol. ▪ The ICF contents were not in conformance with the requirements of GCP.
#During the Year 2013-2014 routine surveillance inspection at clinical trial sites for GCP compliance were conducted by the zonal/sub zonal offices of CDSCO. Explanation/clarification from the sponsors, PI's and Ethics Committees has been called for. The responses are reviewed and suitable action is being initiated as per rule, if the explanation is not satisfactory.					
3	**2013**	**Clinical Trial Applicant:** M/s. CliniRx, Research Pvt. Ltd., New Delhi. **PI-**Dr. Gundugurti Prasad Rao M/s Asha Hospital, Plot No. 298, Road No. 14, Banjara Hills, Hyderabad- 500034	**Telangana**	CYP-1020 compared to Risperidone in patients with schizophrenia.	Debarred for 1 year vide order dt. 06.02.2014 Reasons: ▪ The patients were experiencing an acute exacerbation of schizophrenia at enrolment. However, the informed consent in the presence of legally acceptable representative and or the impartial witness were not obtained. ▪ There were no documentary evidence for the travel expenses reimbursement to the subjects.(Patient's rights have been affected, Totally 33 patients were participated in the trial.)

4	**2013**	**Manufacturer/Pharmaceutical Companies/Clinical Trial Applicant:** M/s ISSAR Pharmaceutical Pvt. Ltd., Seren Chambers, 3rd Floor, Banjara Hills, Hyderabad-500 034	**Telangana**	GENOPEP 1 (ISSAR 1)	Debarred for 1 year vide order dt. 20.08.2014 Reasons: ▪ The Investigational Medicinal Product was manufactured without following the tenets of GMP and certain QC test on the finished dosage form/investigational medicinal product were not performed. ▪ IP dose calculation for the trial subjects was ambiguous.
5	**2013**	Calcutta School of Tropical Medicine, Govt. of West Bengal	**West Bengal**	Amniotic membrane, amniotic fluid and placental dressing in advanced burn patients.	• The matter has referred to Medical Council of India and is under sub-judice to high Court of Kolkata.
6	**2014**	M/s Apac Biotech, Gurgaon	**Haryana**	Autologous preparation containing mature Dendritic cell (Brand Name: APCEDEN)	▪ The firm did not take clinical trial permission for the conduct of the trial as per Rule 122 DA of Drugs and Cosmetics Rules 1945. ▪ The product falls under the purview of Drugs & Cosmetics Act and Rules there under and the firm provided autologous matured Dendritic Cell product to some patients without new drug permission under Rule 122 B. ▪ An order was issued on 15.07.2014 to stop the collection and sale of Autologous preparation containing mature Dendritic cell (Brand Name: APCEDEN). ▪ An order was issued on 19.08.2015 for revocation of order dated 15.07.2015 for purpose of conducting clinical trial, if any, as permitted & also require the firm to distribute the product for using in particular indication only after it is permitted.
7	**2014**	M/s Denvax Clinic, Institute of Cellular Therapies Pvt. Ltd., Noida	**Haryana**	Autologous Dendritic cell cancer vaccine (Brand Name: DENVAX)	▪ The firm did not take clinical trial permission for the conduct of the trial as per Rule 122 DA of Drugs and Cosmetics Rules 1945. ▪ The product falls under the purview of Drugs

					and Cosmetics Act 1940 and Rules made there under and the firm was administering to the patients without new drug permission under Rule 122 B. ▪ An order was issued on 23.07.2014 to stop collection of blood from any new patients for processing, packaging of product- Dendritic cell preparation. ▪ The matter is under sub-judice to High Court of Delhi.
8	**2014**	M/s Nichi-In Centre for Regenerative Medicine, Chennai	**Tamilnadu**	Natural Killer Cell and T Cells	▪ The product falls under the purview of Drugs and Cosmetics Act 1940 and Rules made there under and the firm was administering to the patients without new drug permission under Rule 122 B. ▪ An order was issued on 25.08.2014 to stop collection of blood from any new patients for processing and administration of Natural Killer Cell and T Cells.
9	**2014**	M/s Wellness Solution, Bangalore	**Karnataka**	Dendritic cell cancer vaccine	▪ The product falls under the purview of Drugs and Cosmetics Act 1940 and Rules made there under and the firm was administering to the patients without new drug permission under Rule 122 B. ▪ An order was issued on 28.08.2014 to stop collection of blood from any new patients for processing, packaging and administration of Dendritic cell vaccine.
10	**2014**	M/s Chaitanaya Hospital, Pune	**Maharashtra**	Bone marrow derived Stem Cell Product	▪ The firm did not take clinical trial permission for the conduct of the trial as per Rule 122 DA of Drugs and Cosmetics Rules 1945. ▪ An order was issued on 11.12.2014 to stop the treatment with stem cell products to the patients in the name of clinical trial.

11	**2015**	**Clinical Trial Sponsor:** M/s MSD Pharmaceuticals Pvt. Ltd. Gurgaon-122 002. **Investigator-** **a)** Dr. A. Sharda, Endocrinology Diabetes Centre, Indira Nagar, Bangalore-560 038 **b)** Dr. S. S. Srikanta Jnana Sanjeevini Medical Centre, Marenahalli, J.P. Nagar, 2nd Phase, Bangalore-560 078 **c)** Dr. S. R. Aravind**,** Diacon Hospital Rajajinagar, Bangalore-560010.	**Haryana & Karnataka**	Sitagliptin	• Sponsor debarred for 4 months and two Investigators (a & b) for 6 months and Investigator (c) for 3 months from initiating any new clinical trial vide order dated 07/09/2015. **Reasons:** **Sponsor-** (i) No oversight over the clinical trial (Protocol no. MK-0431-082], like SAE reporting, management & due analysis etc. (ii) This is subsequent non-compliance(s) by M/s MSD. **Investigator [for (a) & (b)]:** • No Investigational Medicinal Product (IMP) dose titration as per protocol in spite of the fact that the subject had low eGFR (violation of standard care and protocol). Investigator (a) changed the CRF & subject's medical record after receiving query from O/o DCGI. • Neither SAE reported nor SAE due analysis reported to O/o DCGI. • No in-house labs for testing of CT samples of trial subjects but printed the tests result of another lab (M/s Clumax Diagnostics) on CT site(s) letter head, no data/record for the authenticity of test results (data integrity issues). • No legal/formal contract entered between CRO & PI/site since 26/09/2014, however confidential patient data & information is shared with CRO without any legal contract/agreement. **Investigator [for (c)]:** • No Investigational Medicinal Product (IMP) dose titration as per protocol in spite of the fact that the subject had low eGFR (violation of standard care and protocol).

12	**2015**	**Clinical Trial site:** Karnataka Cancer Hospital & Research Centre, Department of Clinical Research Karnataka Cancer Hospital & Research Centre, J.B. Karal Nandhini Layout Krishnanandannagar, Bangalore-560096	**Karnataka**	Not applicable	• O/o DCGI received a complaint vide letter dated 20/07/2015 from a Social Scientist. Wherein on the basis of a local newspaper report it was alleged that the hospital had no 'histopathology Dept.' but all report issue in Karnataka Cancer Hospital only and they manipulate the reports. • Vide letter dated 30/07/2015 order issued to inspect the site and ascertain the allegations. Inspection was carried out and further is under process.
13	**2015**	**Ethics Committee:** Hippocrates Independent Ethics Committee (HIEC), Street No. 7, New T Block, Phase II, Nanhe Park, Uttam Nagar, New Delhi- 110 059	**Delhi**	Not applicable	• A number of complaints received in July & Aug. 2015 by O/o DCGI via email(s) from Investigator(s) about the irregular functioning and misconduct of said HIEC in approving the clinical trials & BA/BE studies. • A team constituted by CDSCO conducted an inspection of the said EC on 06/08/2015 & 07/08/2015. Thereafter based on non-compliances reported, a Show Cause Notice (SCN) was issued to HIEC on 04/09/2015. HIEC reply to SCN was received on 30/10/2015 and the matter is under process for final action as per rules.

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