DCG (I)/Misc./2013-(18)
Directorate General of Health Services
Central Drugs Standard Control Organisation
O/o Drugs Controller General (I)

FDA Bhawan,
Kotla Road, New Delhi

Dated: 26/03/2013

ORDER

SUB: Constitution of Committee to review the procedure and practices followed by CDSCO for granting marketing approval and clinical trials on certain drugs - reg.

The Ministry of Health & Family Welfare has submitted Action Taken Report (ATR) on the 59th Report of the Department related Parliamentary Standing Committee (PSC) on Health & Family Welfare regarding functioning of the Central Drugs Standard Control Organization (CDSCO). In the Action Taken Report, the Ministry of Health has mentioned in certain cases of approval of new drug including Fixed Dose Combination (FDC) and clinical trial, as recommended by the Hon'ble Parliamentary Standing Committee that DCG (I) will constitute a Committee to investigate such cases.

Accordingly, a committee comprising of following expert is hereby constituted:

1. Prof T.M. Mahapatra, Former Director, Institute of Medical Sciences, Banaras Hindu University, Varanasi - **Chairman**

2. Prof. Satyawan Singh, Former Scientist, Central Drug Research Institute, Lucknow, UP-**Member**

3. Mr. VenkatKrishnan, Former Drug Controller, Kerala, 12/548, Dhanya Sree, Vrindavanam Gardens, Kodunganoor, Thiruvananthpuram-695013-**Member**

4. Representative of Chief Vigilance Officer, Ministry of Health & Family Welfare, Nirman Bhawan, New Delhi-**Member**

Terms of Reference:

To review the procedure and practices followed by CDSCO for granting marketing approval and clinical trials on new drugs including FDC and to see that the scientific requirements and the regulatory compliance have been adhered with respect to the following four cases, as recommended by the Department related Parliamentary Standing Committee on Health & Family Welfare in its 59th report:-

1. The Fixed Dose Combination of Aceclofenac with Drotaverine which is not permitted in any developed country of North America, Europe or Australia. In this case, vide this office 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. Many experts gave letters of recommendation in identical language apparently drafted by the interested drug manufacturer and finally drug was approved.

In this case, the Hon'ble Parliamentary Standing Committee recommended that the Ministry should direct DCGI to conduct an enquiry and take appropriate action against the official(s) who gave authority to the interested party to select and obtain expert opinion and finally approved the drug. **(Para 7.32, 7.33 of the 59th Department related Parliamentary Standing Committee on Health & Family Welfare report)**

2. Buclizine (applicant: UCB, Belgium) was approved on 28-6-2006 for appetite stimulation without clinical trials and without consulting experts for use in children. Under the law of the land if an old drug approved for a disorder (such as allergy) is to be used for another indication (such as appetite stimulation), then it is deemed to be a New Drug and must undergo the entire procedure applicable to New Drugs and meet all regulatory requirements. The Company's own Core Data Sheet issued from its headquarters in Belgium says: "Because of lack of approved clinical studies and scientific data, the benefit/risk is negative for the indication of buclizine for appetite stimulation." Thus, buclizine is not currently approved in Belgium, the innovator country, for appetite stimulation. Buclizine is just one of the many drugs that have been approved in violation of the Indian laws.

   The Hon'ble Parliamentary Standing Committee is of the view that responsibility needs to be fixed for unlawfully approving Buclizine, a drug of hardly any consequence to public health in India, more so since it is being administered to babies/children. At the same time the approval granted should be reviewed in the light of latest scientific evidence, regulatory status in developed countries, particularly in Belgium, the country of its origin. **(Para 7.39 to 7.41of the Department related Parliamentary Standing Committee on Health & Family Welfare report)**

3. Letrozole, is an anti-cancer drug for use only in post- menopausal women and is contraindicated to be used in women of reproductive age. On 10-04-2007, DCGI approved the use of letrozole for improving female fertility. The Drugs and Cosmetic Rules require that while approving a drug for use in females of reproductive age, animal studies are to be done in this specific group. No such studies were done in India. The innovator also did not conduct such studies abroad because there was no plan to use letrozole in women of reproductive age. Under Indian rules, Phase II studies should have been conducted before Phase III since such studies were not conducted anywhere. Permission to conduct Phase III studies was given without prior Phase II studies. *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.

   The Hon'ble Parliamentary Standing Committee recommended that DCGI is expected to take action against those CDSCO functionaries who colluded with private interests

and got the drug approved in violation of laws. **(Para 7.42 to 7.43 of the Department related Parliamentary Standing Committee on Health & Family Welfare report)**

4. Placenta Extract: As per Drugs and Cosmetics Rules, whenever there is either an additional formulation or proposal to use in additional indications, the drug is deemed to be a 'New Drug'. In violation of this clear rule, vide its letter number 4-97/89-DC dated 11th February, 2000, an official of the office of the Drugs Controller General (India) wrote a letter to the manufacturer that Placenta Extract was "not a New Drug' and gave permission to promote placenta extract gel in additional indications (Burns and Wounds, Non-Healing Indolent Ulcers, Bed Sores, Mucositis etc.). By including the term "etc.", loopholes were left wide open to add other indications. Thus CDSCO went out of the way to unlawfully and wrongly certify, in black and white, that the drug was "not a New Drug" thus helping the manufacturer to market an additional formulation for additional indications.

   The Hon'ble Parliamentary Standing Committee recommended for an enquiry into the said letter. The responsibility should be fixed and appropriate action taken against the guilty. **(Para 7.48 to 7.49 of the Department related Parliamentary Standing Committee on Health & Family Welfare Report)**

Honorarium and TA/DA will be paid to the experts as per the Central Govt. Rules from the budgetary allocation of CDSCO.

(Dr. G. N. Singh)
Drugs Controller General (I)

To:

1. To Prof T.M. Mahapatra, Former Director, Institute of Medical Sciences, Banaras Hindu University, Varanasi
2. Prof. Satyawan Singh, Former Scientist, Central Drug Research Institute, Lucknow, UP
3. Mr. Venkat Krishnan, Former Drug Controller, Kerala, 12/548, Dhanya Sree, Vrindavanam Gardens, Kodunganoor, Thiruvananthpuram-695013
4. Representative of Chief Vigilance Officer, Ministry of Health & Family Welfare, Nirman Bhawan, New Delhi

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PPS to Secretary (H & FW)/PPS to DG/PPS to AS & DG/PS to JS (AKP)