MINUTES OF THE 83RD MEETING OF DRUGS TECHNICAL ADVISORY BOARD HELD ON 11.06.2019 AT DGHS, NIRMAN BHAWAN, NEW DELHI

PRESENT

1. Dr. S. Venkatesh — Chairman
   Director General of Health Services,
   Nirman Bhawan, New Delhi
2. Dr. S. Eswara Reddy — Member Secretary
   Drugs Controller General (India),
   FDA Bhawan, New Delhi
3. Shri C. Hariharan — Member
   Director (I/C),
   Central Drugs Laboratory, Kolkata
4. Dr. A. K. Tahlan — Member
   Director, Central Research Institute,
   Kasauli, Himachal Pradesh
5. Dr. Tapas K. Kundu — Member
   Director, CDRI, Lucknow
6. Shri. Pankaj Patel — Member
   Chairman and Managing Director,
   Zydus Cadila Group, Ahmedabad
7. Dr. Nilima Kshirsagar — Member
   Chair in Clinical Pharmacology,
   ICMR, Mumbai
8. Dr. R.N. Tandon — Member
   Past Honorary Secretary General, IMA, New Delhi
9. Shri. M.S Lokesh Prasad — Member
   Scientific Officer & Govt. Analyst,
   Bengaluru, Karnataka

INVITEES

1. Dr. Mohammad Shaukat
   Advisor, NCD,
   Dte. GHS, MoHFW
2. Dr. L. Swasticharan
   Chief Medical Officer
   Dte. GHS, MoHFW
3. Dr. Arun Bhardwaj
   Director, Central Drugs Laboratory, Kasauli

CDSCO REPRESENTATIVES

1. Dr. Santosh Indraksha
   ADC (I), CDSCO (HQ), New Delhi
2. Shri. Asheesh Kaundal
   Drugs Inspector, CDSCO (HQ), New Delhi
3. Shri. G. Raghuvaran
   Drugs Inspector, CDSCO (HQ), New Delhi
4. Shri. Rajesham Pambala
   Drugs Inspector, CDSCO (HQ), New Delhi

The Director, Indian Veterinary Research Institute, Izatnagar; President, Pharmacy Council of India, New Delhi; Drugs Controller (I/C), Assam; Dr. Pallavi Jain Govil, Commissioner, FDA, Madhya Pradesh; Prof. M. D. Karvekar, Bangalore, Karnataka; Elected member by MCI; Dr. T.V. Narayana, President, IPA, Bengaluru; and Dr. Vaishali N Patel, Govt. Analyst, Food & Drugs Laboratory, Vadodara, Gujarat could not attend the meeting because of their other commitments.

Dr. S. Venkatesh, Director General of Health Services & Chairman DTAB welcomed the Board members and invitees. Thereafter, he requested DCG(I) to initiate the proceedings. DCG(I) initiated the deliberation on DTAB agenda along with Action Taken Reports on previous DTAB recommendations.

AGENDA NO. 1

ACTION TAKEN REPORT (ATR) FOR 82nd DTAB MEETING HELD ON 02.04.2019

The Action Taken Report (ATR) on the recommendations of DTAB in 82nd meeting was approved by the Board.

AGENDA NO. 2

CONSIDERATION OF THE PROPOSAL THAT THE ELECTRONIC NICOTINIC DELIVERY SYSTEMS (ENDS) INCLUDING E-CIGARETTES (EC), HEAT NOT BURN DEVICES, VAPE, E-SHEESHA, E-NICOTINE FLAVOURED HOOKAH AND THE LIKE DEVICES THAT ENABLE NICOTINE DELIVERY ARE COVERED UNDER THE DEFINITION OF 'DRUG' UNDER THE DRUGS AND COSMETICS ACT, 1940

The Board was apprised that, Electronic Nicotine Delivery Systems (ENDS) are devices that heat a solution to create an aerosol, which contains nicotine and frequently many other chemical flavors, dissolved usually in a solvent of Propylene Glycol and/or Glycerin. ENDS come in different glamorous shapes and sizes. ENDS do not burn or use tobacco leaves but instead heat to vaporize a solution, which the user then inhales. ENDS solutions and emissions contain chemicals, many of which are common with traditional tobacco and of known toxicity and several others which are being subjected to studies. Although ENDS is generally talked of as a single product class, these products constitute a diverse group with potentially significant

differences in the production of toxicants and mechanisms for delivery of nicotine. There are various types of ENDS, the most common being what is known as electronic cigarettes or E-cigarettes. Therefore, e-cigarettes can resemble like traditional tobacco products like cigarettes, cigars, pipes or common gadgets like flashlights, flash drives/pen-drives or pens. Currently, there are more than 460 different e-cigarette brands with varied configuration of nicotine delivery (first generation or so-called cigar likes, second- generation tank systems and even larger third-generation or personal vaporizers) available in the market with over 7,700 flavors.

ENDS including e-cigarettes are promoted by the industry body as a smoking cessation aid but their efficacy and safety as a quitting aid has not yet been firmly established. Though, some smokers claim to have cut-down smoking while using ENDS, the total nicotine consumption seems to remain unchanged. Moreover, a considerable number of ex-smokers who have reported stopping cigarette use with the aid of ENDS continue using the latter product, thus, sustaining nicotine dependence. There have been various surveys and studies which reported that ENDS is used as a way to obtain nicotine in smoke-free spaces, indicating that ENDS were being used to satisfy nicotine addiction during periods of temporary or forced abstinence.

However, Electronic Nicotine Delivery System (ENDS) including e-Cigarettes, Heat-Not Burn devices, Vape, e-Sheesha, e-Nicotine Flavoured Hookah and the like devices that enable nicotine delivery have neither been tested and assessed for Safety and Efficacy in Indian population nor have been approved under the provision of the Drugs and Cosmetics Act, 1940 and rules thereunder. But availability of these products is widespread in the country posing serious health risks to the users and non-users.

The state Government of Punjab, Haryana and Union Territory of Chandigarh have declared/notified ENDS or e-cigarettes as an unapproved drug under the Drugs and Cosmetics Act,1940 and Rules, 1945 and have commenced prosecutions of sellers of ENDS under the Drugs and Cosmetics Act, 1940. The Food & Drugs Administration, Haryana has taken action after conducting raids and collected samples of above mentioned products considering these products as un-approved drugs manufactured without licence and launched 37 prosecutions in the competent Courts of Hon'ble Chief Judicial Magistrates of various districts. These actions taken reports were submitted by the Department of Food & Drug Administration, Haryana, in the matter of Public Interest Litigation of Burning Brain Society Vs. Union of India CWP No. 14597 of 2007 and Hon'ble High Court never objected to this action taken by the Department. Rather, recently, the Hon'ble Punjab and Haryana High Court in CRM-M-39328-2015 + 16 other connected cases vide its order dated 06.03.2019 has dismissed the petitions which were filed to quash the order of summoning the traders/ manufacturers of ENDS from different districts of Haryana. The petitioners had contended that they were dealing with the product Hookah, Molasses and it can't be treated as drug and can't fall under the purview of the Drugs & Cosmetics Act. The petitioners also contended that they had a valid licence for Tobacco and they are not required to have a manufacturing licence for drugs. The Hon'ble High

Court after going through the issue in detail did not agree with their contention and dismissed the case.

Also, some cases are underway on this issue before the Delhi High Court and the Hon'ble Court had passed various orders in this regard.

In another case, State through DCO, Gurugram Vs Sh. Parkash Chandi Verma Manager & Sh. Rahul Yadav owner of M/s Kasba pool Snooler Snaks point, M-28, Basement, Opposite of Bank of India, Old DLF Colony, Gurgaon, Chief Judicial Magistrate, Gurugram vide order dated 20.01.2017 convicted the accused persons and sentenced the convict for Rigorous Imprisonment (RI) for a period of three years and a fine of Rs. One Lakh.

The Government of India had issued an advisory dated 28.08.2018 on Electronic Nicotine Delivery System (ENDS) including E-cigarette, Heat-Not burn devices, Vape, e-Sheesha, e-Nicotine, Flavoured Hookah and the like products. This advisory had inter alia advised that in the larger public interest and in order to prevent the initiation of ENDS by non-smokers and youth with special attention to vulnerable groups, to ensure that any ENDS including e-cigarette, Heat-Not burn devices, Vape, e-Sheesha, e-Nicotine, Flavoured Hookah and the like devices that enable nicotine delivery are not sold (including on line sale), manufactured, distributed, traded, imported and advertised in their jurisdiction, except for the purpose and in the manner and to the extent, as may be approved under the Drugs and Cosmetics Act 1940 and Rules made thereunder.

Subsequent to this advisory, CDSCO on 22.02.2019 had issued letters to all State/ UT Drugs Controllers that, Electronic Nicotine Delivery Systems (ENDS) including e-cigarette, Heat-Not burn devices, Vape, e-Sheesha, e-Nicotine, Flavoured Hookah and the like products has not yet been approved under the Drugs and Cosmetics Act 1940 and Rules made thereunder and requested them to ensure that any of aforementioned products are not sold (including on line sale), manufactured, distributed, traded, imported and advertised in their jurisdictions.

Also, the State Governments of Karnataka, Kerala, Mizoram, Maharashtra, Jammu & Kashmir, Uttar Pradesh and Bihar have issued necessary orders banning the manufacture, distribution and sale of e-cigarettes as unapproved drug, under the Drugs and Cosmetics Act, 1940.

The Indian Council of Medical Research (ICMR) has recommended a complete ban on e-cigarettes and other electronic nicotine delivery systems (ENDS) based on currently available scientific evidence. In a white paper released on 29.05.2019, ICMR concluded that ENDS or e-cigarettes and other such devices contains nicotine solution, which is highly addictive as well as harmful ingredients such as certain flavoring agents and vaporizers. The council also emphasized that, use of ENDS has documented adverse effects on humans, which include DNA damage; carcinogenic, cellular, molecular and immunological toxicity; respiratory, cardiovascular and neurological disorders; and adverse impact on foetal development and pregnancy.

DCC in its 56th meeting deliberated the issue considering above facts and revisited the previous recommendation of 48th DCC to finally recommend that

Electronic Nicotinic Delivery Systems (ENDS) including e-cigarette, Heat-Not burn devices, Vape, e-Sheesha, e-Nicotine, Flavoured Hookah and the like products are used as a tobacco cessation product and functions for nicotine delivery for reasons including nicotine de-addiction. Hence these devices and products fall under the definition of "drug" as defined under Section 3(b) of the Drugs and Cosmetics Act, 1940.

Nicotine is a Drug and has official monographs in various international pharmacopoeias BP, USP, EP dictating the standards and specifications and also comes under the definition of 'Drug' as defined under section 3(b) of Drugs and Cosmetics Act, 1940. Manufacturing licenses for Nicotine drug products, COPPs for export purpose have been issued to various firms after satisfactory joint inspections by State and Central Licensing Authority. It was observed by the Board that, under the provision of Drugs and Cosmetics Act, 1940, any product intended to be used as aid for smoking cessation is covered under the definition of drugs and various drugs have been approved as aid for smoking cessation under the said Act and Rules made thereunder.

Various Nicotine containing preparations such as Nicotine Transdermal Patches 36 mg, 78 mg, 114 mg; Nicotine Lozenges 2mg, 4mg; Nicotine ploacrilex lozenges are approved by DCG(I) under Drugs and Cosmetics Act and rules made thereunder for the indication to reduce withdrawal symptoms including nicotine craving associated with quitting of the smoking, chewing of tobacco and guthka containing tobacco.

Nicotine Chewing gums and Lozenges up to 2 mg of 'Nicotine' are exempted from the provisions of chapter IV of the Drugs and Cosmetic Act and Rules made thereunder which require them to be covered by a sale licence subject to the condition that such a product has been manufactured under a valid drug manufacturing licence.

Nicotine is prohibited in food products, under regulation 2.3.4 of the Food safety and Standard (Prohibition and Restrictions on sales) Regulations, 2011 and Act, 2006, the excerpts of which are reproduced below:

> *"Product not to contain any substance which may be injurious to health: Tobacco and nicotine shall not be used as ingredients in any food products."*

Further 'Nicotine' is also included in list of insecticides under the Schedule of The Insecticide Act, 1968. The State of Haryana has also notified 'Nicotine in its pure chemical form' as 'Poison' vide notification No. S.O.152/C.A.12/1919/S.2 and 8/2015 dated 15.10.2015 at S.No. 20 under the Poisons Act.

DTAB deliberated the matter in detail and obtained the insights on various aspects of ENDS and associated health hazards, socio-economic issues etc. from Dr. Mohammad Shaukat, Advisor (NCD) and Dr. L. Swasticharan, CMO (NCD) the subject experts of National Tobacco control programme. Dr. L. Swasticharan made a detailed presentation on different categories of ENDS & like devices and its adverse effects on human health and suggested to ban the ENDS & like products in larger public interest. Uncontrolled consumption of Nicotine (more concentrated Nicotine

liquid, deep inhalation, prolonged inhalation which may extend beyond traditional one cigarette use etc.) from such devices may result in more worsened health hazards due to increased total nicotine intake.

Further DTAB examined the minutes of the Sub-Group meeting held on 26.04.2019 under the Chairmanship of Sh. Vikas Sheel, JS, MoHFW on Legal implications on ENDS and report of the Sub-Group on Health Effects of Electronic Nicotine Delivery System (ENDS)/ Electronic Non-nicotine Delivery System (ENNDS) and Heated Tobacco Products (HTPs) and the-like devices forwarded by the Ministry vide OM No. P.16012/13/2019-TC dated 07.06.2019. The Sub-Group in its report has concluded that ENDS and the like products, including HTPs and HnBs, are harmful for health of their users and that presence of these products in their current form has a net negative impact on Public Health and recommends that the ENDS and like devices should be banned in the larger public interest

DTAB after deliberation recommended that the manufacture, sale (including online sale) and distribution of Electronic Nicotine Delivery System (ENDS) including E-cigarette, Heat-Not burn devices, Vape, e-Sheesha, e-Nicotine, Flavoured Hookah and the like products shall be prohibited under Section 26A of the Drugs and Cosmetics Act, 1940 as well as their import (including personal purpose) shall also be prohibited under Section 10A of the said Act.

AGENDA NO. 3

CONSIDERATION OF THE PROPOSAL OF REGULATION OF SALE AND DISTRIBUTION OF DRUGS OVER INTERNET (E-PHARMACY) IN LIGHT OF CONCERNS RAISED IN VARIOUS FORA

DTAB was apprised that, the Department of Health and Family Welfare has issued a draft notification vide G.S.R. 817(E) dated 28.08.2018 proposing to amend the Drugs and Cosmetics Rules, 1945 by incorporating separate part for the regulation of e-Pharmacies in the Country.

In response to the draft notification a large number of comments have been received. However, a number of PILs have been filed in various Hon'ble High Courts of the country at Delhi, Madras, Mumbai, etc. The Hon'ble High Courts have issued various directions with regards to the regulation of sale of drugs over internet. Keeping in view of above matter, Central Government has also decided to carry out wider consultations before finalizing the draft notification.

DCC in its 56th meeting held on 01.06.2019 deliberated the issue of finalization draft notification vide G.S.R. 817(E) dated 28.08.2018 and recommended to include the provision for uploading the e-prescription in the rules on e-pharmacy which is to be finalized.

DTAB in its 81st meeting held on 29.11.2018 deliberated and agreed for amendment of the Drugs and Cosmetics Rules, 1945 for regulation of sale of drugs by E-Pharmacy and asked CDSCO to bring the final version of the notification to DTAB for review.

Accordingly, the draft for final notification, as available with CDSCO, was placed before the DTAB.

DTAB after detailed deliberations, recommended for finalization of the draft rules considering the suggestions/ comments of stakeholders.

AGENDA NO.4

CONSIDERATION OF THE PROPOSAL OF CONCEPT OF DOSSIER APPROVAL FOR FORMULATION DEVELOPMENT AND FOR GRANT OF MANUFACTURING LICENCE

DTAB was apprised that, the Drugs and Cosmetics Rules, 1945 have been amended vide G.S.R. 327(E) dated 03.04.2017 mandating the submission of BA/BE studies for grant of manufacturing licence. As per the GSR 327(E), applicant shall submit the result of bioequivalence study along with the application for grant of manufacturing licence of oral dosage form of drugs falling under the Category II and Category IV of the Biopharmaceutical Classification System.

The Rules have also been amended vide G.S.R. 360(E) dated 10.04.2018 making it mandatory to submit evidences of stability, safety of excipients, etc. to State Licensing Authority along with application before grant of product manufacturing licences.

In this context DCC in its 56th meeting held on 01.06.2019 deliberated the concept of the “Dossier Approval” in respect of formulation development data, including stability data and BA/BE data, generated under the valid licence under the Drugs and Cosmetics Rules, 1945.

It was deliberated that any person/ institution can develop a drug formulation and can generate dossier of the product development containing detailed data on formulation development, BA/BE study data, stability data, excipients compatibility, etc, and submit to the licensing authority for approval. Once such dossier is approved by licensing authority under Drugs and Cosmetics Rules, 1945, the same may be submitted by a manufacturer under an agreement for technology transfer etc. between the person/institution who has developed the formulation and the manufacturer for seeking grant of manufacturing licence for the same product subject to submission of following:

1. Equivalency report showing the similarity of raw materials, API and excipient source and specifications, packaging materials specifications, SOPs, testing methods, manufacturing and packaging processes, equipment design and principle, batch size and finished product specifications between manufacturers product and the product developed by the person/institution.
2. Comparative evaluation data including multimedia comparative dissolution profile to show the similarity between the two products.
3. Six months accelerated and long term stability data for the drug formulation generated at the applicants manufacturing site.

Accordingly, Drugs and Cosmetics Rules may be amended to make necessary provisions in this regard.

DTAB deliberated the issue and recommended for amendment of the Drugs and Cosmetics Rules, 1945 regarding dossier of approval and submission of the same for grant of manufacturing licence for drugs. Further, DTAB opined that in such cases the technology followed at manufacturing site must be same as that approved through dossier approval.

The Board also recommended that appropriate guidelines shall be issued for the applicability of these provisions for modified release dosage forms, products involving complex or special manufacturing technology.

AGENDA NO. 5

CONSIDERATION OF PROPOSAL FOR INCLUSION OF PROVISIONS ON GOOD DISTRIBUTION PRACTICES (GDP) OF PHARMACEUTICAL PRODUCTS IN THE DRUGS AND COSMETICS RULES, 1945

The DTAB was apprised that, the objective of the quality control over drugs is to ensure that the patients get quality drugs. For this purpose it is necessary to ensure the quality and identity of pharmaceutical products during all aspects of the distribution process which includes procurement, purchasing, storage, distribution, transportation and associated documentation/ record keeping practices. Each activity in the distribution system is required to be carried out in accordance to the principles of Good Distribution Practices (GDP). The involvement of unauthorized entities in the distribution and sale of pharmaceutical products is a matter of concern as it leads to introduction of spurious drugs in the supply chain. It is the responsibility of all parties involved in the distribution of pharmaceutical products to ensure that the quality of pharmaceutical products and the integrity of the distribution chain are maintained throughout the distribution process.

The said matter was deliberated earlier in 47th Drugs Consultative Committee held on 30.07.2014 and 31.07.2014 wherein report of the sub-committee constituted for preparation of Guidelines on GDP of Pharmaceutical Products was considered. The matter was also deliberated in 54th meeting of DCC held on 30.07.2018 and the DCC suggested to take necessary provisions to impart legal sanctity to the suggested guidelines as a Schedule to the Drugs and Cosmetics Rules, 1945 to penalise the offenders.

Subsequently, a notice was issued to all State/UT Drugs Controllers and stake holders on 25.09.2018 inviting comments/ suggestions on the draft guidelines. Comments/ suggestions have been received and are compiled.

DTAB in its 81st meeting held on 29.11.2019 deliberated on the issue and agreed to incorporate GDP guidelines as a separate Schedule in the Drugs and Cosmetics Rules, 1945.

Further this issue of incorporation of GDP guidelines as a separate Schedule was deliberated in 56th DCC meeting held on 01.06.2019 and it is recommended to

make necessary provisions for Good Distribution Practice under the Drugs and Cosmetics Rules, 1945.

DTAB deliberated the matter and recommended to amend the Drugs & Cosmetics Rules, 1945 for provisions for Good Distribution Practices (GDP) of pharmaceutical products.

AGENDA NO. 6

PROPOSAL FOR AMENDMENT IN SCHEDULE H OF DRUGS AND COSMETICS RULES TO PROVIDE EXEMPTION FROM LABELLING REQUIREMENTS AS PER SCHEDULE H FOR THE CHEMICAL CONTRACEPTIVE MENTIONED UNDER ENTRY NO. 15 OF SCHEDULE K OF THE DRUGS AND COSMETICS RULES, 1945

DTAB was apprised that, "Schedule K" of the Drugs and Cosmetics Rules, under the entry no. 15 provides exemption from taking a sale licence for chemical contraceptive having the following composition per tablet:

(1) DL-Norgestrel-0.30 mg,
Ethinyloestradiol-0.30 mg

(2) Levonorgestrel-0.15 mg,
Ethinyloestradiol-0.03 mg

(3) Centchroman-30 mg

(4) Desogestrel-0.150 mg,
Ethinyloestradiol-0.03 mg

(5) Levonorgestrel-0.1 mg,
Ethinyloestradiol-0.02 mg

However, drugs centchroman and ethinyloestradiol are specified in the Schedule H of Drugs and Cosmetics Rules, at the entry no. 101 and 186 respectively.

A representation has been received from HLL Lifecare Limited mentioning that the company is manufacturing and supplying regular oral contraceptive pills to the Ministry of Health and Family Welfare under National Family welfare Programme since 1993 under various brand names of contraceptive like Mala N, Mala D, Apsara, Choice, Ecroz, Khushi, Sunheri etc. containing drug composition Levonorgestrol I.P. 0.15 mg, Ethinyloestradiol I.P. 0.03 mg, combo packed with Ferrous Fumarate I.P. 60 mg.

The firm has submitted that labelling of the above said products were initially done by mentioning "Schedule K" on all the packing material as these products are covered under the "Schedule K" of Drugs and Cosmetics Rules, 1945.

However, objections have been raised by one of the State Drugs Controller Office on the labelling of these products with following remarks:

1. "Labelling part of above products shall be in line with Schedule H requirements: viz., printing of Rx, red box and Schedule H warning in the primary and secondary packages of the products.

2. The labelling shall not include “Schedule K” as this is not a labelling requirement.”

Accordingly, the company has implemented the labelling requirements as per “Schedule H” in its packing artwork.

However, the company is facing difficulties to sell and supply these products under various schemes of MoHFW due to following constraints:

a. “Schedule H drug cannot be advertised, which is very essential for Social Marketing to educate the people about proper use of the product.
b. Schedule H drug can only be sold with a prescription of a registered medical practitioner whereas Social marketing products are meant for providing affordable contraceptive in the remotest area of the country where availability of registered medical practitioners is a constraint.
c. The selling of Schedule H drug requires proper retail licence for selling medicines which is not possible for Social marketing Organization, as their products are sold under Govt. schemes through Over the Counter (OTC) and not through prescription.”

In this regard, the HLL Lifecare Limited has requested to make necessary amendment in the Drugs and Cosmetics Rules, 1945 to remove “Schedule H” labelling requirements on products containing;

(i) Levonorgestrol I.P. 0.15 mg, Ethinylestradiol I.P. 0.03 mg
(ii) Centchroman 30 mg

Therefore, it is proposed to make the following amendments in respect of item no.101 & 186 in “Schedule H” of the Drugs and Cosmetics Rules, 1945:

“101. Centchroman (except for strength 30 mg in Tablet)
186. Ethinyloestradiol (except for strength Ethinyloestradiol I.P. 0.03 mg in combination with Levonorgestrol I.P. 0.15 mg in Tablet)”

DCC in its 56th meeting held on 01.06.2019 deliberated and agreed to amend ‘Schedule H’ of the Drugs and Cosmetics Rules, 1945 to exempt Centchroman 30mg tablets and Ethinyloestradiol I.P. 0.03 mg in combination with Levonorgestrol I.P. 0.15 mg in Tablet from schedule H.

DTAB deliberated the proposal and recommended for amendment of the Drugs and Cosmetics Rules, 1945 to exempt Centchroman 30mg tablets and Ethinyloestradiol I.P. 0.03 mg in combination with Levonorgestrol I.P. 0.15 mg in Tablet from Schedule H.

ADDITIONAL AGENDA NO. S-1

CONSIDERATION OF THE PROPOSAL TO EXAMINE THE ISSUE OF SAFETY AND EFFICACY OF FIXED DOSE COMBINATION OF FLUPENTHIXOL + MELITRACEN FOR HUMAN USE AS PER DTAB RECOMMENDATIONS

DTAB in its 81st meeting held on 29.11.2018 deliberated the issue relating to ban of fixed dose combination of Flupenthixol + Melitracen for human use in light of

orders of High Court of Karnataka dated 14.08.2013 & 24.07.2017 and recommended for constitution of a sub-committee under the chairpersonship of Dr. Nilima Kshirsagar, Chair in Clinical Pharmacology, ICMR, Mumbai to examine the issue.

Accordingly, a Sub-Committee of DTAB was constituted vide O.M F. No. 18-76/2018-DC dated 21.12.2018 under the Chairmanship of Dr. Nilima Kshirsagar in the subject matter.

The Sub-Committee held its meeting on 06.02.2019 and as per the recommendations of the Committee, a public notice was put on the website of CDSCO on 13.02.2019 requesting all the concerned stakeholders to submit the information in the prescribed format.

However, M/s. Mankind Pharma Ltd., filed W.P. No. 11330 of 2019 before the Hon'ble High Court of Karnataka Bengaluru and challenged this office Notice dated 13.02.2019. In this regard, the Hon'ble Court vide its order dated 15.03.2019 has directed that no decision in pursuance to the impugned public notice dated 13.02.2019 shall be taken by the respondents until and unless powered Phase- IV Clinical trial is conducted, after taking due approval from DCG(I) till the next date of hearing.

DTAB noted the Hon'ble High Court order and recommended that, the firm's application to conduct Phase-IV Clinical Trial should be evaluated by CDSCO for which comment on the Phase-IV Clinical Trial protocol may be obtained from Dr. Nilima Kshirsagar.

ADDITIONAL AGENDA NO. S-2

CONSIDERATION OF THE PROPOSAL TO AMEND SUBRULE (1) OF RULE (63) IN MEDICAL DEVICES RULES, 2017 REGARDING THE PROVISIONS FOR PERMISSION TO IMPORT OR MANUFACTURE MEDICAL DEVICE WHICH DOES NOT HAVE ITS PREDICATE DEVICE

The Board was apprised that, Rule 63 of Chapter VIII in the Medical Devices Rules 2017, specifies the provisions for permission to import or manufacture medical device which does not have its predicate device. As per fourth proviso of Sub rule 1 of Rule 63-

> *"the results of clinical investigation may not be required to be submitted where the investigational medical device is approved by the regulatory authorities of either the United Kingdom or the United States of America or Australia or Canada or Japan and the said device has been marketed for at least two years in that country and the Central Licensing Authority is satisfied with the data of safety, performance and pharmacovigilance of the device, and,-*
>
> *(a) there is no evidence or theoretical possibility, on the basis of existing knowledge, of any difference in the behavior and performance in Indian population;*
>
> *(b) the applicant has given an undertaking in writing to conduct post marketing clinical investigation with the objective of safety and performance of such*

investigational medical device as per protocol approved by the Central Licensing Authority."

Further, it is pertinent to mention that during the meeting of India-EU Sub-commission on trade held on 6th June, 2018 in New Delhi, the EU side pointed out that for the regulation of new products, the new regulations stated that clinical investigation may not be required to be submitted where the investigational medical device is approved by regulatory authorities of US, UK, Australia, Canada or Japan but does not include the EU.

In view of the above, it is proposed to include EU in the provision specified under Rule 63(1) in the Medical Devices Rules, 2017 in respect of the waiver of clinical investigation.

DTAB deliberated and agreed to amend Rule 63(1) of the Medical Devices Rules, 2017 in this regard.

ADDITIONAL AGENDA NO. S-3

CONSIDERATION OF THE PROPOSAL TO AMEND FORM MD-11 UNDER THE MEDICAL DEVICES RULES 2017

The Board was apprised that, Chapter IV in the Medical Devices Rules, 2017 specifies the provisions for manufacture of medical devices for sale or for distribution.

As per clause (vii) of Rule 26- "the licence holder shall maintain an audit or inspection book in Form MD-11 to enable the Notified Body or Medical Device Officer to record his observations and non-conformity, if any."

Form MD-11 specifies the form in which the Audit or Inspection Book shall be maintained.

Form MD-11 specifies the following:

"(B) (i) The pages of the audit or inspection book shall be serially numbered and duly stamped by the Central Licensing Authority*/State Licensing Authority*. The pages, other than the first and the last pages shall have the following particulars:-

Name and designation of the auditor or medical device officer who audited or inspected the premises:

Date of audit or inspection _____

Observations of the auditor or medical device officer _____

Signature of the auditor or medical device officer"

Therefore, in order to streamline the procedure, it is proposed to amend the Form MD-11.

Therefore, it would be appropriate that (B)(i) may be amended as follows:-

"(B) (i) The pages of the audit or inspection book shall be serially numbered .The pages, other than the first and the last pages, shall have the following particulars:-

Name and designation of the auditor or medical device officer who audited or inspected the premises:

Date of audit or inspection _____

Observations of the auditor or medical device officer _____

Signature of the auditor or medical device officer"

Also, it is proposed that said Form MD-11 should be with seal or stamp by licensing authority.

DTAB deliberated the proposal and agreed to amend Form MD-11 in the Medical Devices Rules, 2017.

ADDITIONAL AGENDA NO. S-4

CONSIDERATION OF THE PROPOSAL TO INCLUDE THE PROVISION FOR IMPORT CONDITIONS TO BE COMPLIED WITH BY LICENCE HOLDER FOR SUSAR REPORTING WITHIN 15 DAYS IN MEDICAL DEVICES RULES, 2017

The Board was apprised that, Clause (ii) under Rule 26 in Chapter IV (manufacture of medical devices for sale or for distribution) of the Medical Devices Rules, 2017 specifies that

> *"the licence holder shall inform the State Licensing Authority or the Central Licensing Authority, as the case may be, of the occurrence of any suspected unexpected serious adverse event and action taken thereon including any recall within fifteen days of such event coming to the notice of licence holder."*

However, there is no provision for Import Conditions to be complied with by Licence holder for SUSAR reporting within 15 days in under Rule 38 in Chapter V (Import of medical devices) Medical Devices Rules, 2017.

Therefore, it is proposed to include the provision of SUSAR in Rule 38 (Conditions to be complied with by Licence holder) in Chapter V by inserting the following clause-

> *"the licence holder shall inform the Central Licensing Authority of the occurrence of any suspected unexpected serious adverse event and action taken thereon including any recall within fifteen days of such event coming to the notice of licence holder."*

DTAB deliberated the proposal and agreed to amend the Medical Devices Rules, 2017 to incorporate necessary provision, making it mandatory for import licence holders to inform about the SUSAR and action taken thereon to the licensing authority.

The meeting ended with a vote of thanks to the Chair.

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