MINUTES OF THE 84TH MEETING OF DRUGS TECHNICAL ADVISORY BOARD HELD ON 27.08.2019 AT DGHS, NIRMAN BHAWAN, NEW DELHI

PRESENT

1.	Dr. A. K. Saxena Director General of Health Services, Nirman Bhawan, New Delhi	Chairman
2.	Dr. V.G. Somani Drugs Controller General (India), FDA Bhawan, New Delhi	Member Secretary
3.	Shri C. Hariharan Director (I/C), Central Drugs Laboratory, Kolkata	Member
4.	Dr. A. K. Tahlan Director, Central Research Institute, Kasauli, Himachal Pradesh	Member
5.	Dr. P. Dhar IVRI, Izatnagar	Member
6.	Dr. Pallavi Jain Govil Principal Secretary, Health, M.P.	Member
7.	Prof. M. D. Karvekar Bengaluru	Member
8.	Shri. Pankaj Patel Chairman and Managing Director, Zydus Cadila Group, Ahmedabad	Member
9.	Dr. Nilima Kshirsagar Chair in Clinical Pharmacology, ICMR, Mumbai	Member
10.	Dr. R.N. Tandon Past Honorary Secretary General, IMA, New Delhi	Member
11.	Prof. Dr. T.V. Narayana President , IPA, Bengaluru	Member
12.	Shri. M.S Lokesh Prasad Scientific Officer & Govt. Analyst, Bengaluru, Karnataka	Member
13.	Dr. Vaishali N Patel Govt. Analyst, Food & Drugs Laboratory, Vadodara, Gujarat	Member

CDSCO REPRESENTATIVES

1. Dr. K. Bangarurajan,
   JDC(I), CDSCO (HQ), New Delhi
2. Shri. A. K. Pradhan
   DDC(I), CDSCO (HQ), New Delhi
3. Dr. Santosh Indraksha
   ADC (I), CDSCO (HQ), New Delhi
4. Shri. Asheesh Kaundal
   Drugs Inspector, CDSCO (HQ), New Delhi
5. Shri. G. Raghuvaran
   Drugs Inspector, CDSCO (HQ), New Delhi
6. Shri. Rajesham Pambala
   Drugs Inspector, CDSCO (HQ), New Delhi

The President, Pharmacy Council of India, New Delhi; President, Medical Council of India, New Delhi; Director, CDRI, Lucknow; Drugs Controller (I/C), Assam and Elected member by MCI could not attend the meeting because of their other commitments.

Dr. V.G. Somani, DCG(I), Member-Secretary, DTAB welcomed the Board members under the supervision of new chairman Dr. A. K. Saxena, DGHS. All members were introduced to the Chairman. The Chairman then 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 83rd DTAB MEETING HELD ON 11.06.2019

The Action Taken Report (ATR) on the recommendations of DTAB in 83rd meeting was approved with the following considerations:

i) With regard to recommendation of the DTAB for banning of Electronic Nicotinic Delivery Systems (ENDS) including E-Cigarettes (EC) etc. one of the members mentioned that legality of considering such products as “drug” needs to be looked into and if required, the same should be defined under the Drugs and Cosmetics Act, 1940 before their banning. The DTAB noted the concern and recommended that the same may be communicated to the Government.

ii) With regard to recommendation of the DTAB for finalization of the draft rules on e-pharmacy, some of the members mentioned that such regulation on e-pharmacy should be robust and appropriate to address the various issues such as, misuse of prescription, confidentiality of the patient data, maintaining proper storage conditions during supply of the drugs, need for counseling the patients/ consumers by the suppliers during supply of the

drugs about how to take the drugs and other precautions, etc. DTAB noted the concerns and recommended that the same may be communicated to the Government.

AGENDA NO. 2

CONSIDERATION OF PROPOSAL TO INCORPORATE THE PROVISION IN THE DRUGS AND COSMETICS RULES, 1945 TO ENABLE DOOR STEP DELIVERY OF MEDICINES BY RETAILER

The Board was apprised that, under the provisions of Drugs and Cosmetics Act, 1940 and Rules thereunder, the licencee shall sell, stock or exhibit or offer for sale or distribute the drugs by retail in the licensed premises only.

A significant number of patients mainly geriatrics suffering from chronic diseases requires continued medication. As these patients are unable to visit the pharmacy retail outlets for purchasing drugs frequently, it may be considered to incorporate provisions under the Drugs and Cosmetics Rules, 1945 to enable the retail outlets for door step delivery of medicines to the patients on prescription presented either in physical or on the e-mail ID of the licencee duly registered with licensing authority. Accordingly, draft rules for the proposed amendment was placed before the DTAB.

DTAB after detailed deliberation agreed to the proposal and further recommended that provisions should also be included in the draft rules to ensure following:

1) The drugs are supplied at the door step of the patients located within the same district where the licencee is located.

2) In case of chronic diseases, the prescription should be dispensed only if it is presented to licencee within 30 days of its issue. However, in case of acute cases, the prescription should be dispensed only if it is presented to licencee within 7 days of its issue.

This amendment may be made applicable both in case of presentation of prescriptions physically and through email.

AGENDA NO. 3

CONSIDERATION OF PROPOSAL TO INCORPORATE DEFINITION FOR “STEM CELL DERIVED PRODUCT” UNDER THE NEW DRUGS AND CLINICAL TRIALS RULES, 2019

DTAB was apprised that, the Ministry of Health & Family Welfare, Government of India has notified the New Drugs and Clinical Trials Rules, 2019 vide G.S.R. 227(E) dated 19.03.2019 under the provisions of the Drugs and Cosmetics Act, 1940.

These rules are applicable to all new drugs, investigational new drugs for human use, clinical trial, bioequivalence study, bioavailability study and Ethics Committee.

As per, Rule 2 (1) (w) in the Chapter I of the said rules, new drug, amongst others, includes following:-

> *"(v) a vaccine, recombinant Deoxyribonucleic Acid (r-DNA) derived product, living modified organism, monoclonal anti-body, stem cell derived product, gene therapeutic product or xenografts, intended to be used as drug;"*

In light of above definition, various representations have been received to clarify the meaning of "Stem cell derived product". Various stem cell related activities/ surgeries/ practices, which are not actually products, should not be covered under these rules.

Two court cases are also are going on in Hon'ble Delhi High Court against these new rules praying that they have been affected by the New Drugs and Clinical trials Rules 2019 as the clinic providing their treatment with stem cell therapy has stopped the treatment until such time the clarification is obtained by the clinic as per these New Drugs and Clinical trials Rules 2019,

In view of the above, it was proposed to clarify the *Stem Cell Derived Product* as follows:

> *"Stem Cell Derived Product means a drug which has been derived from processed stem cells and which has been processed by means of substantial or more than minimal manipulation with the objective of propagation and / or differentiation of a cell or tissue,' cell activation, and production of a cell-line, which includes pharmaceutical or chemical or enzymatic treatment, altering a biological characteristic, combining with a non-cellular component, manipulation by genetic engineering including gene editing & gene modification.*
>
> *For the purpose of this clause:*
>
> *(i) Substantial or more than minimal manipulation means ex-vivo alteration in the cell population (T-Cell depletion, cancer cell depletion), expansion, which is expected to result in alteration of function.*
>
> *(ii) The isolation of tissue, washing, centrifugation, suspension in acceptable medium, cutting, grinding, shaping, disintegration of tissue, separation of cells, isolation of a specific cell, treatment with antibiotics, sterilization by washing or gamma irradiation, freezing, thawing and such similar procedures, regarded as minimal manipulations and are not considered as processing by means of substantial or more than minimal manipulation.*
>
> *(iii) Stem cells removed from an individual for implantation of such cells only into the same individual for use during the same surgical procedure should not*

undergo processing steps beyond rinsing, cleaning or sizing and these steps shall not be considered as processing."

DTAB deliberated the matter in length and in principle, agreed to the proposal and further recommended that it is given to understand that ICMR/ DHR is making guidelines for this and therefore, while considering the issuance of such clarification on stem cell derived products, those guidelines to be published by the ICMR may be considered.

DTAB also recommended that, the routine practices/ transplantations/ surgeries/therapies undertaken by doctors involving stem cell for treatment of their own patients and not for commercialization of the same outside their own hospitals/clinics fall outside the purview of Drugs and Cosmetics Act, 1940 and the New Drugs and Clinical Trials Rules, 2019. Therefore, shall be dealt outside the said regulation.

Further, DTAB recommended that, till such time the clarification about stem cell derived product is brought out by ICMR etc., communication should be issued to the State Licensing Authorities and other stake holders that the overall issue is under process and it is inappropriate to intervene from regulatory angle on routine practices/therapies/surgeries/transplantations undertaken by Registered Medical Practitioners/ physicians / doctors in their clinics/hospitals involving such stem cells for the treatment of their patients based on their medical expertise.

AGENDA NO. 4

CONSIDERATION OF THE PROPOSAL FOR AMENDMENT OF THE EXEMPTIONS PROVIDED UNDER SCHEDULE K REGARDING SUPPLY OF MEDICINES BY REGISTERED MEDICAL PRACTITIONERS TO THEIR PATIENTS

DTAB was apprised that, Registered Medical Practitioners (RMP) can supply different categories of medicines including vaccines to their patients as per the exemption provided with certain conditions under Schedule K of the Drugs and Cosmetics Rules, 1945.

Currently, there is no specific category which can be supplied by RMP to their patients and therefore, it was proposed to incorporate the certain additional conditions under the conditions of exemption to prevent the misuse of the exemption.

DTAB deliberated the matter and rejected the proposal, as it is not in line with the reality and rights of RMPs for prescribing medicines as per their experience and expertise.

AGENDA NO. 5

CONSIDERATION OF THE PROPOSAL TO AMEND G.S.R 390 (E) DATED 24/04/2018 ISSUED UNDER SECTION 10A PROHIBITING IMPORT OF OXYTOCIN TO ALLOW IMPORT OF OXYTOCIN REFERENCE STANDARDS EXCLUSIVELY FOR TEST AND ANALYSIS PURPOSE

The Board was apprised that, the Ministry of Health and Family Welfare had published the Gazette notification vide GSR No.390 (E) dated 24.04.2018 under section 10A of Drugs and Cosmetics Act, 1940 prohibiting the import of Oxytocin and its formulation in any name or manner.

Subsequently the Ministry of Commerce and Industry vide notification number 19/2015-2020 dated 12/07/2018 had prohibited the import of Oxytocin.

However, various representations have been received from different firms regarding import of the Oxytocin reference standard for the purposes of examination, test or analysis. The firms involved in manufacture of the drug are facing difficulties in import of the Oxytocin reference standard.

In view of above, it was proposed that the Gazette notification vide G.S.R 390 (E) dated 24/04/2018 issued under section 10A may be amended to allow import of Oxytocin reference standards exclusively for test and analysis purpose, while import of Oxytocin API for manufacturing commercial batches shall continue to be prohibited.

DTAB deliberated that reference standard is necessary for test and analysis purpose before carrying out commercial manufacturing of the drug and therefore agreed to the proposal to amend the said notification to allow import of Oxytocin reference standards exclusively for test and analysis purpose.

AGENDA NO. 6

CONSIDERATION OF PROPOSAL FOR AMENDMENT OF RULE 121 PERTAINING TO TEST FOR PYROGENS UNDER THE DRUGS AND COSMETICS RULES, 1945

DTAB was apprised that, as per Rule 121A of the Drugs and Cosmetics Rules, 1945:

> *Test for pyrogens–Solution of substances intended for parenteral administration in large volumes (10 ml or more at a time) shall be pyrogen-free and tested for pyrogens. If water or any other aqueous solvent is supplied along with the substances for preparing such solutions, it shall also be pyrogen-free and tested for pyrogens.*

The above condition is applicable for products with 10ml volume or more. However there is no such provision mentioned in the Drugs and Cosmetic Act and Rules 1945 there under for pyrogen testing, for the products with less than 10ml. Hence, it becomes difficult to apply test for pyrogens as per Rule 121A in products with less than 10ml volume. As per I.P 2018, test for pyrogens is designated for products irrespective of their volume.

Therefore, in order to remove discrepancy between Rule 121A of Drugs and Cosmetic Rules 1945 and IP 2018 regarding test for pyrogen, it was proposed that rule 121A i.e., tests for pyrogens should be amended to read as follows:-

> *Test for pyrogens–Solution of substances intended for parenteral administration shall be pyrogen-free and tested for pyrogens or Bacterial Endotoxin Test (BET) as per Indian Pharmacopeia (I.P.) If water or any other aqueous solvent is supplied along with the substances for preparing such solutions, it shall also be pyrogen-free and tested for pyrogens or Bacterial Endotoxin Test (BET) as per I.P.*

DTAB after deliberation agreed to bring alignment in I.P and the Rules and consider appropriate amendments in this regard.

AGENDA NO. 7

CONSIDERATION OF THE PROPOSAL FOR AMENDMENT OF PARA 10.9 OF SCHEDULE 'M' OF DRUGS AND COSMETICS RULES, 1945 FOR WAIVER OF REQUIREMENT FOR VACCINES MANUFACTURED USING LESS THAN 60% RESIDUAL SHELF-LIFE PERIOD IN THE COUNTRY

The Board was apprised that, amendment of para 10.9 of schedule M of Drugs and Cosmetic Rules, 1945 for waiver of requirement for vaccines manufactured using less than 60 % residual shelf life period was deliberated in the 78th DTAB meeting held on 12.02.2018 and opined that the matter may be referred to Department of Biotechnology (DBT) for recommendations in respect of the effect on the product quality and shelf life. Dr. A. K. Tahlan was assigned as coordinator for deliberation with DBT.

Accordingly, the matter was forwarded to DBT. The observations of the DBT were placed before the DTAB.

Considering the observations of the DBT, it was proposed that for the manufacturers who are doing proper stability studies of formulations for assigning the shelf life, the proviso to the Para 10.9 of the Schedule M needed to be incorporated for assigning shelf life of finished formulations more than the shelf life of the active materials, if supported with the stability studies, as follows:-

> *"Provided that the Licensing Authority may permit the finished formulation to have its shelf life more than the shelf life of active raw material used in the said finished formulation, if it is supported by the stability studies using the active raw material having residual shelf life lesser than the shelf life proposed for formulation."*

DTAB after detailed deliberations agreed to the proposed amendment of the proviso to the Para 10.9 of the Schedule M as above. The DTAB also opined that Rule 31 of the Drugs and Cosmetics Rules already provides that in exceptional cases the licensing authority may allow the import of any drug having shelf life period lesser than 60 percent but before the date of expiry and therefore further changes in the regulation may not be required at this stage. However, to make the process for allowing such import hassle free, the matter may also be considered through procedural simplification.

AGENDA NO. 8

CONSIDERATION OF RECOMMENDATIONS OF EXPERT COMMITTEE HELD ON 20.09.2016 TO REVIEW CERTAIN FIXED DOSE COMBINATION AS PER THE DIRECTIONS OF THE HON'BLE HIGH COURT, MAHARASHTRA, NAGPUR BENCH

The Board was apprised that, the Hon'ble High Court of Judicature at Bombay, Nagpur Bench during the hearing in a petition number 18/2010 relating to Court on its own motion Vs. Union of India on 08.09.10 had directed that DCG(I), which is the authority under the Drugs and Cosmetics Act, to consider whether the following FDCs approved by them and referred to in the list are entitled to be approved with reference to the parameters set out by the Committee constituted by the Hon'ble Court.

1. Pantoprazole + Domperidone
2. Cefadroxil + Clavulanic Acid
3. Telmisartan + Amlodipine
4. Ceftazidime + Tazobactam
5. Cefipime + Tazobactam
6. Cefixime + Cloxacillin
7. Amlodipine + Metoprolol
8. Esomeprazole + Itopride
9. Cefixime + Cloxacillin + Lactobacillus
10. Trandalopril+ Verapamil
11. Rabeprazole + Itopride

The court was apprised by the Office of DCG(I) that the FDCs referred to in the order will be placed before the DTAB for its consideration.

DTAB after deliberation in its 60th DTAB meeting held on 10.10.2011 recommended that the FDCs referred to by the Hon'ble Court may be referred to the Expert Committee examining the rationality of 294 FDCs, to examine their safety and efficacy; and the Hon'ble Court apprised accordingly.

The FDCs were examined by the said expert committee and out of the 11 FDCs, 8 FDCs have been considered as rational while in the case of following 3 FDCs the committee recommended that the manufacturers may be asked produce or generate more data in respect of their safety and efficacy for further consideration.

1. Cefadroxil + Clavulanic Acid
2. Cefixime + Cloxacillin
3. Cefixime +Cloxacillin + Lactobacillus

Further, a separate expert committee to review the above three antibiotics fixed dose combinations as per the order of Hon'ble Court Bombay, Nagpur Bench was constituted in consultation with DGHS and the data received in respect of safety and efficacy was deliberated in the meeting of the expert committee held on 20.09.2016.

Subsequently, DTAB in its 75th meeting held on 03.01.2017 constituted a committee. However, the committee could not submit its report.

Since, the Committee constituted under the Prof. Kokate is already examining such similar FDCs, it was proposed that the matter may be referred to the said Committee.

DTAB after detailed deliberation recommended that the matter may be referred to the Committee constituted under the Prof. Kokate for examination as proposed.

AGENDA NO. 9

CONSIDERATION OF THE PROPOSAL FOR AMENDMENT IN THE MEDICAL DEVICE RULES, 2017 REGARDING APPLICABILITY OF VALID LICENSE FOR ANY PRODUCT ISSUED UNDER THE DRUGS AND COSMETICS RULES, 1945 VIS-À-VIS THAT ISSUED UNDER MDR-2017

DTAB was apprised that, the Ministry of Health & Family Welfare, Government of India has notified the Medical Devices Rules 2017 vide G.S.R. 78(E) dated 31.01.2017 under the provisions of the Drugs and Cosmetics Act, 1940.Said rules are effective from 01.01.2018 to regulate the Clinical Investigation, Manufacture, Import, Sale and Distribution of the medical devices in the country.

Chapter XII, Rule 97, for Clause (i) Medical Device Rules, 2017 –

> *"the licence or registration certificate, issued under the provisions of the Drugs and Cosmetics Act and Rules 1945, prior to commencement of these rules shall be deemed to be valid till its expiry or for a period of eighteen months from the date these rules are notified whichever is later under the corresponding provisions of these rules."*

Representation has been received from Association of Indian Medical Device Industry (AiMeD) regarding applicability of valid license for any product issued under the Drugs and Cosmetics Rules, 1945 vis-à-vis that issued under MDR-2017

It has been represented that there is no provision in the MDR, 2017 to permit transition period and the new license number is being actionable the day it is issued by SLA and it is unreasonably expected that manufacturer will overnight switch labelling on packaging to the new license number. This is not practical nor can old inventory be destroyed or wasted needlessly.

Therefore, the association has requested for amendment in the MDR-2017 addressing the issue.

In view of the above, it was proposed that-

A. The license issued under the provisions of these rules shall be effective before expiry of the license issued under Drugs and Cosmetics Rules, 1945 or on completion of six months from the date new license is issued under the provisions of Medical Device Rules, whichever is earlier to enable smooth transition and clearance of packaging inventory labelled with earlier Manufacturing licence number.

B. Also, for the purpose of export, in case of change of constitution or name change of the firm, the licensee shall obtain the permission from licensing

Authority to use the old name for the purpose of exhausting transition time of registration in foreign countries. Such permission will be given initially for one year and extendable for further period of one year on the request of the applicant.

DTAB deliberated and recommended that at any point of time, only one licenses should be made applicable. However, this choice has to be exercised by the applicant/licencee while obtaining license. In case a licencee is already holding both old licence issued under D&C Rules and new licence under MDR-2017, he should be asked to submit their choice. In case a licencee opts for old license issued under D&C Rules, to be made applicable, it should remain valid till its expiry. In case the licencee opts for new licence issued under MDR-2017, to be made applicable, he should also be allowed to use the old licence issued under Drugs and Cosmetics Rules till its expiry to enable smooth transition.

DTAB also agreed for the proposed amendment of the MDR-2017 regarding change in the constitution and name change of the firms for the purpose of export providing as under:

"In case of change of constitution or name change of the firm, the licensee shall obtain the permission from licensing Authority to use the old name for the purpose of exhausting transition time of registration in foreign countries. Such permission will be given initially for one year and extendable for further period of one year on the request of the applicant".

AGENDA NO. 10

CONSIDERATION OF THE PROPOSAL FOR AMENDMENT OF THE RULES MADE UNDER THE DRUGS AND COSMETICS ACT, 1940 PROVIDING THAT THE LICENSING AUTHORITY I.E., DCG(I) BY AN ORDER IN WRITING DELEGATE THE POWER TO SIGN LICENCES AND REGISTRATION CERTIFICATES ETC TO ANY PERSON UNDER HIS CONTROL

The Board was apprised that, as per the existing provisions, the Licensing Authority/ Central Licence Authority/ Central Licensing Approving Authority may with the approval of the Central Government by an order in writing delegate all or any of its powers to any other officers under his control under Rule 22 and Rule 68B of the Drugs and Cosmetics Rules 1945; Rule 9 of the Medical Devices Rules, 2017 and Rule 4 of the New Drugs and Clinical Trials Rules, 2019, as the case may be.

During the last ten years the manpower of CDSCO has increased by more than 5 times and there have been many changes in the Drugs and Cosmetics rules as well as notification of new rules viz Medical Device Rules, 2017 and New Drugs and Clinical Trials Rules, 2019 which prescribes various provisions including timelines for processing of applications for grant of various permissions/licences to improve transparency, accountability and predictability in the regulatory system.

In light of engagement of large manpower for discharge of multi disciplinary activities and transfer of CDSCO officers from time to time as per transfer policy, it is necessary that delegation of powers to the officers happens quickly without any time

lag to avoid any legal complication and to ensure timely disposal of various applications and also to avoid inconveniences to the public & other stakeholders.

Since such delegation to large number of officials at frequent pace is required, the timely delegation will also help adhering timelines in all cases including those specified in the Medical Devices Rules, 2017 and New Drugs and Clinical Trials Rules, 2019 for processing of various applications.

Therefore, it was proposed that for smooth administration and legal convenience, the provisions under Rule 22 and Rule 68B of the Drugs and Cosmetics Rules 1945; Rule 9 of the Medical Devices Rules, 2017 and Rule 4 of the New Drugs and Clinical Trials Rules, 2019 may be amended so as to enable DCG(I) to delegate his power as licensing authority, Central licensing authority, Central Licence approving authority to his eligible subordinate officers promptly on need basis by reducing the step of obtaining the approval from Central Government.

DTAB deferred the agenda for now as it required careful consideration and deliberation.

AGENDA NO. 11

CONSIDERATION OF THE PROPOSAL FOR AMENDMENT OF THE DRUGS AND COSMETICS RULES, 1945 FOR MAKING PROVISION ON REQUIREMENT OF CERTIFICATION FOR DECLARING PROPER STORAGE CONDITION OF THE DRUGS IN DISTRIBUTION CHANNEL AND TO MENTION THE STORAGE CONDITIONS ON THE LABEL OF DRUG PRODUCTS VIS A VIS FORM 17 UNDER SCHEDULE A

The Board was apprised that, distribution is an essential activity in the integrated supply-chain management of pharmaceutical products. Various individuals and entities involved in the distribution chain are responsible for the handling, storage and distribution of such products. It is important to have adequate controls over the entire chain of distribution. To maintain the original quality of pharmaceutical products, every party involved in the distribution chain has to comply with the applicable requirements for proper storage and distribution of drugs.

Storage of the drugs under the prescribed conditions is one of the important components for ensuring quality, safety and efficacy of the drugs. The conditions of storage of various drugs have been mentioned under the Schedule P of the Drugs & Cosmetics Rules, 1945.

The Rules 64 and Rule 65 of the Drugs & Cosmetics Rules 1945, specify the conditions to be fulfilled to sell, stock, exhibit or offer for sale or distribute of the drugs.

It has been observed in many of cases that, whenever a drug is found to be Not of Standard Quality, the concerned manufacturer challenges the Govt. Analyst report in the Court of Law by claiming that it is due to wrong handling and storage conditions of drugs in the distribution chain as well as during the drawing the samples by DIs and testing by Government Analysts.

In Form 17 (Intimation to person from whom sample is taken), there is no provision to mention the storage conditions under which the drug was found and sampled.

Therefore, in order to ensure the proper handling and storage conditions of drugs at each level of distribution chain, it was proposed to amend the Drugs and Cosmetics Rules, 1945 to incorporate provisions as under:

i. The manufacturer shall mention the recommended storage conditions on the label of the innermost container of the drug or every other covering in which the container is packed.

ii. Every licence holder/ Government stores or such stores which are exempted from obtaining sale licence under Chapter IV of the Act shall ensure and mention on the invoice or bill that the drug is supplied under storage condition as per label and the recipient licencee/ Government stores or such stores which are exempted from obtaining sale licence under Chapter IV of the Act shall ensure at the time of receipt that the drug has been received under proper storage condition as per label.

DTAB after detailed deliberation, in principle agreed to the proposed amendments including the provision for mentioning in Form 17 the storage conditions under which the drugs was found and sampled by the Drugs Inspector. However, it was opined that consideration should be given to make all amendments related to labelling issues effective from single date.

AGENDA NO. 12

CONSIDERATION OF THE PROPOSAL FOR AMMENDEMENT OF THE NEW DRUGS AND CLINICAL TRIAL RULES, 2019 TO REPLACE THE WORD 'INDEPENDENT ETHICS COMMITTEE' WITH 'NON- INSTITUTIONAL ETHICS COMMITTEE'

The Board was apprised that, the Ministry of Health & Family Welfare, Government of India has notified the New Drugs and Clinical Trials Rules, 2019 vide G.S.R. 227(E) dated 19.03.2019 under the provisions of the Drugs and Cosmetics Act, 1940. These rules are applicable to all new drugs, investigational new drugs for human use, clinical trial, bioequivalence study, bioavailability study and Ethics Committee.

Whoever intends to conduct clinical trial or bioavailability study and bioequivalence study shall be required to have approval of institutional or independent Ethics Committee constituted in accordance with the provisions of Rule 7 and registered with the Central Licencing Authority under Rule 8 of the said rules.

As per Rule 25 of the said rules where a clinical trial site does not have its own Ethics Committee, clinical trial at that site may be initiated after obtaining approval of the protocol from the Ethics Committee of another trial site; or an

independent Ethics Committee for clinical trial constituted in accordance with the provisions of rule 7, provided that such committee is located within the same city or within a radius of 50 kms of the clinical trial site and other conditions.

There are two types of Ethics Committees functioning in the country. One type of EC generally called as institutional Ethics Committees are constituted by institute. Other type of Ethics Committee which are not attached to any institution are termed as independent Ethics Committee (instead of non-institutional Ethics Committee). This is creating confusion in the minds of stakeholders, whether institutional ethics committees are independent or not? as only ECs other than institutional ECs are termed as independent Ethics Committee. In reality, whether institutional or other than institutional EC, both have to be independent in their functioning.

Irrespective of whether Ethics Committee is institutional or independent, the Committee is required to oversee the conduct of clinical trial or bioavailability study and bioequivalence study independently without conflict of interest to safeguard the rights, safety and wellbeing of trial subjects in accordance with these rules, Good Clinical Practices Guidelines and other applicable regulations.

Therefore, it was proposed to replace the word 'independent Ethics Committee' with 'non-institutional Ethics Committee' in the New Drugs and Clinical Trials Rules, 2019 to give the meaning that Ethics Committee either institutional or non-institutional should be independent to approve the clinical trial or bioavailability study and bioequivalence study protocols and other related documents.

DTAB deliberated the proposal and recommended to amend the New Drugs and Clinical Trial Rules, 2019 to replace the word 'independent ethics committee' with 'non- institutional ethics committee'. The DTAB also recommended that the amendment proposed should also be informed to ICMR for their reference.

ADDITIONAL AGENDA NO. S-1

CONSIDERATION OF THE PROPOSAL TO AMEND THE MEDICAL DEVICES RULES, 2017 FOR PRESCRIBING QUALIFICATION OF PERSONS AND DRUGS INSPECTORS (MEDICAL DEVICES) TO BE DESIGNATED AS MEDICAL DEVICE TESTING OFFICERS AND MEDICAL DEVICE OFFICERS RESPECTIVELY

The Board was apprised that, the Ministry of Health & Family Welfare, Government of India has notified the Medical Devices Rules 2017 vide G.S.R. 78(E) dated 31.01.2017 under the provisions of the Drugs and Cosmetics Act, 1940.Said rules are effective from 01.01.2018 to regulate the Clinical Investigation, Manufacture, Import, Sale and Distribution of the medical devices in the country.

As per Rule 18 (1) and Rule 18 (2) of the said rules, the Central Government may designate a Government Analyst appointed under section 20 of the Act and an Inspector appointed under section 21 of the Act as Medical Device Testing Officer and Medical Device Officer respectively.

It may be pertinent to mention that, a road map has been prepared for bringing all medical devices in to regulatory control to ensure their quality and performance and accordingly additional man power including Medical Device Testing Officers and Drugs Inspectors (Medical Devices) are also being considered for strengthening proportionately for efficient regulation of such products.

In view of above, it was proposed that, the **Rule 18(1)** of MDR-2017 may be amended to provide as follows:

The Central Government or as the case may be, the State Government, may designate a Government Analyst appointed under section 20 of the Act as Medical Device Testing Officer **OR** may appoint any such person, having following Qualification as Medical Device Testing Officer:

"A. Master degree in Biomedical Engineering or Chemistry/ Bio Chemistry/ Pharmaceutical Chemistry/ Microbiology/ Pharmacy/ Pharmacology/ Physiology/ Veterinary science from a recognized University or equivalent.

B. 5 Year's experience in the field of Medical Device/ *in vitro* Diagnostic testing or experimental Pharmacology or bioassay of drugs or in chemical and Physicochemical testing of drugs."

Similarly **Rule 18(2)** of MDR-2017 may be amended to provide as follows:

The Central Government or, as the case may be, the State Government, may designate an Inspector appointed under section 21 of the Act as Medical Device Officer **OR** may appoint any such person, having following Qualification as Medical Device Officer:

"A. Graduate Degree in Biomedical Engineering.

OR

Graduate degree in Pharmacy or Pharmaceutical Chemistry or in Medicine with specialization in Clinical Pharmacology or Micro-biology from recognized university established in India by Law with 03 years experience in manufacturing or testing or regulation of Medical Devices or diagnostics as per D & C Rules or in Research or designing.

A. Masters Degree in Biomedical Engineering.

OR

Post-graduate degree in Pharmacy/ Pharmaceutical Chemistry/ Bio-chemistry/ Chemistry/ Micro-biology/ Pharmacology from recognized university or equivalent with 18 months experience in manufacturing or testing or regulation of Medical Devices or diagnostics as per D & C Rules or in Research or designing.

Desirable: Post Graduate"

DTAB after deliberations agreed to the proposed amendments.

ADDITIONAL AGENDA NO. S-2

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

The Board was apprised that, the matter was discussed in 83rd meeting of DTAB held on 11.06.2019 and DTAB recommended that, the application of the firms 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.

Accordingly the Phase IV protocol was sent to Dr. Nilima Kshirsagar vide e-mail dated 13.08.2019. The chairperson vide e-mail dated 22.08.2019 has desired that matter may be placed before DTAB for guidance to place the protocol to the Sub-Committee constituted for evaluating the said FDC.

DTAB after deliberation, agreed to revise the earlier decision by mentioning that the Phase IV Clinical Trial protocol should be referred to the Sub-Committee of DTAB chaired by Dr. Nilima Kshirsagar instead of referring the same to her under the capacity of individual expert.

ADDITIONAL AGENDA NO. S-3

CONSIDERATION OF REQUEST FROM SUB-COMMITTEE OF DTAB IN RESPECT OF THE DIRECTIONS OF HON'BLE SUPREME COURT OF INDIA IN THE CASE OF 344 FDCS + 5 FDCS PROHIBITED VIDES S.O. NO. 705 (E) TO 1048 (E) DATED 10.03.2016 AND S.O. NO. 1851 (E) TO 1855 (E) DATED 08.06.2017 BY THE MINISTRY OF HEALTH & FAMILY WELFARE

The Board was apprised that, one person has filed a contempt petition (civil) vide petition no. 842 of 2019 in the Hon'ble Supreme Court of India alleging that he has not been given due hearing by the Sub-committee of DTAB.

In light of the directions of the Hon'ble Supreme Court of India and after recommendation of DTAB, a sub-committee under the Chairpersonship of Dr. Nilima Kshirsagar was constituted on 19.02.2018 to review the banned 344 FDC + 5 FDCs.

The Sub-committee provided the hearing to concerned petitioners/ appellants including AIDAN as per the direction of Hon'ble Supreme Court of India.

During the process of hearing, the Sub-committee issued a public notice on 24.05.2018 inviting the concerned appellants/ petitioners for hearing with effect from 05.06.2018 and also stated that the schedule of hearing will be published time to time on CDSCO website. Accordingly all concerned were requested to regularly visit the CDSCO website and avail the opportunity of hearing on the given date. Further, it was mentioned in the said notice that no separate letter will be sent for the hearing schedule.

Subsequently, a public notice dated 28.05.2018 was also displayed on the website of CDSCO where by all the parties were requested to make it convenient to give a presentation before the DTAB Sub-Committee as per the hearing schedule attached with the said notice. It was also mentioned in the public notice that in the event that the petitioner does not attend the hearing, the Sub-Committee reserves the right to make its decision on the basis of information before it and according to the direction of Hon'ble Supreme Court.

It may be informed that, an individual letters were also sent to all the Petitioners/ Appellants/ AIDAN including the person referred above vide CDSCO letter dated 28.05.2018. However, it has been claimed by the person that he received the invitation on 07.06.2018 and he accordingly sent an email to CDSCO requesting to give another date of hearing on FDC of Chlorpheniramine Maleate + Codeine Syrup bearing S.O. No 909(E).

The very next day on 08.06.2018, FDC of Chlorpheniramine Maleate + Codeine Syrup bearing S.O. No 909(E) was reviewed by the Sub Committee of DTAB and recommended for the prohibition. It is further submitted that as soon as it came to the notice, the petitioner was replied through return email only immediately very next day on 09.06.2018 informing to refer the public notice dated 28.05.2018.

Afterwards, based on the recommendation of Sub-committee of DTAB and after acceptance of this report by the DTAB, the Central Government vide Gazette notifications S.O. No. 4379 (E) to S.O. No. 4706(E) dated 07.09.2018 prohibited 328 FDCs for manufacture, sale or distribution. Further the Central Government notifications S.O. number from 4707(E) to 4712(E) dated 07.09.2018 restricted 06 FDCs for manufacture, sale or distribution with certain conditions.

However, it may be noted that based on the direction of Hon'ble Supreme Court order dated 15.12.2017 and 07.09.2018 15 FDCs including the FDC of Chlorpheniramine Maleate + Codeine Syrup claimed to have been manufactured prior to 1988, were kept out of the purview of prohibition by the Central Government.

As desired by the Chairperson of Sub-committee of DTAB, the matter was placed before the DTAB and has also requested to permit 3 lawyers on the Sub-committee for reviewing.

DTAB deliberate and noted the status on the matter. However, DTAB further opined that the sub-committee is primarily a technical committee and hence further such inclusion may not be in line with the spirit of the committee as enshrined in the Act.

ADDITIONAL AGENDA NO. S-4

CONSIDERATION OF THE PROPOSAL TO INCLUDE MEDICAL/ SURGICAL GLOVES UNDER THE PURVIEW OF SECTION 3 (B) (IV) OF THE DRUGS AND COSMETICS ACT, 1940 AS MEDICAL DEVICES

DTAB was apprised that, representation had been received from All India Medical Gloves Manufacturers Association (MeGMA) to notify medical gloves as medical devices under MDR-2017 by considering the reasons as under:

- Lack of quality check of medical gloves may be risky in the context of prevalence of several infectious diseases spread by contact.
- As importers of gloves also participate in centre/state lenders, use of unhygienic and substandard gloves in government hospitals is also a threat.

Other concerned department has also requested to consider the request of the MeGMA for notification of medical/surgical gloves as medical devices under Medical Devices Rules, 2017

DTAB deliberated the proposal & recommended to notify the medical/surgical gloves under the purview of section 3(b) (iv) of the Drugs and Cosmetics Act, 1940 as medical devices based on the representation.

ADDITIONAL AGENDA NO. S-5

CONSIDERATION OF THE PROPOSAL TO AMEND THE DRUGS AND COSMETICS RULES, 1945 FOR MAKING A PROVISION FOR IMPORT OF DRUGS FOR TREATMENT OF PATIENTS SUFFERING FROM RARE DISEASE WHICH IS LIFE THREATENING OR CAUSING SERIOUS PERMANENT DISABILITY FOR WHICH THERE IS NO THERAPY

The Board was apprised, Rule 36A of the Drugs and Cosmetics Rules, 1945 provides that, small quantity of drugs received in donation by a charitable hospital for the purpose of treatment of the patients in the said hospital may be imported provided the drugs are given or administered to the patients free of cost. Further, the drugs shall not be prohibited for import and permitted to be marketed in the country with residual shelf life of one year or more.

Further, Rule 87 of the New Drugs and Clinical Trials Rules, 2019 provides for grant of import licence for import of unapproved new drug by Government hospital and Government medical institution, which has not been permitted in the country, but approved for marketing in the country of origin for treatment of a patient suffering from life threatening disease or disease causing serious permanent disability or disease requiring therapies for unmet medical needs.

There are lot of concerns about accessibility and affordability of new drugs available in other countries but not approved/ available in India, for various rare diseases like Gaucher and Fabry diseases, Spinal Muscular Atrophy, Duchenne Muscular Dystrophy etc.

In order to improve access of such new drugs indicated for treatment of patients suffering from rare disease which is life threatening or causing serious permanent disability for which there is no therapy, it is proposed to have provision so that small quantity of drugs received in donation may be imported hassle-free for treatment of patients suffering from such diseases, in such case the importer at the time of import should submit declaration to DCG(I) as well as to the concerned port office of CDSCO that the drug is approved in other country and it is not prohibited for import into the country and the drug has been received in donation and it will be given or administered to the patients at free cost.

Accordingly, it was proposed to amend the Drugs and Cosmetics Rules, 1945 to incorporate a new rule 36AA as under:

> "**36AA** *Import of drugs for treatment of patients suffering from rare disease which is life threatening or causing serious permanent disability for which there is no therapy.*—(1) Small quantity of drugs received in donation can be imported by a person for the purpose of treatment of the patients suffering from rare disease which is life threatening or causing serious permanent disability for which there is no therapy.
>
> (2) The importer at the time of import shall submit declaration to the licensing authority as well as to the concerned port office of CDSCO that the drug is approved in other country and not prohibited for import into the country and the drug has been received in donation to be given or administered to the patient at free cost."

DTAB deliberated the proposal & recommended that notwithstanding anything contained in the Rules made under Drugs and Cosmetics Act, 1940, the Drugs and Cosmetics Rules, 1945 should be amended as above to include the provision for import of drugs for treatment of patients suffering from rare disease which is life threatening or causing serious permanent disability for which there is no therapy.

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

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