MINUTES OF THE 85TH MEETING (VIRTUAL) OF DRUGS TECHNICAL ADVISORY BOARD HELD ON 29.07.2020 AT DGHS, NIRMAN BHAWAN, NEW DELHI

Dr. V.G. Somani, DCG(I), Member-Secretary, DTAB welcomed the Board members under the Chairmanship of Dr. Rajiv Garg, DGHS and in presence of Dr. Sunil Kumar, OSD, DGHS for the first virtual meeting of DTAB and thanked all the Board members for their participation.

Thereafter, the Chairman 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 84th DTAB MEETING HELD ON 27.08.2019

The Action Taken Report (ATR) on the recommendations of DTAB in 84th meeting was approved with the following considerations:

i) With regard to point No. 2 of ATR regarding provisions for door step delivery of drugs published vide G.S.R. 220(E) dated 27.03.2020 under Section 26B of the Act, the Board suggested to include provisions that the drugs are required to be shipped and delivered under the respective recommended storage condition.

ii) With regard to point No. 3 of ATR regarding incorporation of definition for "stem cell derived product" under the New Drugs and Clinical Trials Rules, 2019, Board recommended that, the matter relating to issuance of the clarification for such products as already decided, needs to be expedited considering the urgency.

iii) With regard to point No. 10 of the ATR on the agenda which was deferred in the 84th meeting, relating to delegation of powers of the licensing authority i.e. DCG(I) to sign licences and registration certificates etc to any person under his control by an order in writing, the Board considered the agenda for deliberation in light of multi disciplinary licensing activities, increased man power and their wide spread work locations across the Country, transfers of the officers and urgent disposal of the relevant applications/files. The Board felt that, quick delegation is the need of the hour for early disposal under the Drugs and Cosmetics Rules, 1945 and also to adhere timelines as specified in Medical Devices Rules, 2017, New drugs and Clinical Trials Rules, 2019 and various 'Ease of Doing Business' regulatory initiatives.

The Board deliberated the matter in detail and recommended that, for smooth administration and legal convenience, provisions shall be amended to enable DCG(I) to delegate his power as Licensing Authority (LA), Central Licensing Approving Authority (CLAA) and Central Licensing Authority (CLA) to his eligible sub-ordinate officers promptly on need basis for which approval of the Central Government may not be required. Accordingly, 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 Trial Rules, 2019 should be amended.

AGENDA No. 2

Consideration of recommendation made by Sub-committee regarding examining the issue of safety and efficacy of fixed dose combination of Flupenthixol + Melitracen for human use as per DTAB recommendations

DTAB was apprised that, the Board in its 84th meeting held on 27.08.2019 after deliberation, agreed that the Phase IV Clinical Trial protocol should be referred to the Sub-Committee of DTAB chaired by Dr. Nilima Kshirsagar.

Accordingly, the sub-committee held its meeting on 29.11.2019. M/s. Mankind Pharma made a detailed presentation before the Sub-Committee with respect to the Phase IV clinical trial protocol submitted by the firm.

The Sub-committee after going through the presentation as made by the firm and also taking into account the relevant scientific literature* and after having a detailed deliberation made the following suggestions:-

1. Under inclusion criteria, patients with comorbid depression & anxiety disorders shall be enrolled in the study (committee observed that same indication has been approved by DCGI for the FDC of Escitalopram + Clonazepam which is a comparator in the proposed study.
2. The treatment should continue as long as recommended by the treating Psychiatrist but at least 16 weeks (usual minimum duration of treatment for such cases) and the patient should be followed after discontinuation of the treatment for 04 weeks with respect to both the arms. Further blinding should not be broken till the completion of the study.
3. Checklist of the side effects with mention of 'any other' to be incorporated in the Case Report Form (CRF) for monitoring AEs.
4. Patients with HAM-A greater than 25 and HAM-D greater than 9 should be excluded.
5. Follow-up visits and dispensing of drugs should be on monthly basis after 12 weeks.
6. ECG with QTc value should be done at the base line and at the end of the study.
7. Include the standard scale for neurological such as abnormal involuntary movement, etc. adverse event monitoring.
8. General Physician shall not be taken as investigators.
9. The trial shall be conducted as per the provision of the New Drugs and Clinical Trial Rule 2019.
10. The Principal Investigator should be MD/Diploma in Psychiatry.
11. The Sponsor shall also include some Government sites.

*(references:-Kaplan & Sadock's Comprehensive textbook of Psychiatry Tenth edition)

The Sub-committee recommended that firm should revise the Protocol no. CRB/CT-001/2018 Version 2.1 dated 07 Jun 2018 after incorporating above suggestions and submit to CDSCO for further necessary action.

DTAB deliberated the matter and opined that, the revised protocol, as submitted by the firm shall also be forwarded to the Sub-committee for its examination and recommendation in the matter.

AGENDA No. 3

Consideration of the report of the expert committee of DTAB to review the rationality & safety of 294 FDCs marketed in the country

The Board was apprised that, the matter was discussed in 68th DTAB meeting held on 16.02.2015 and recommended that, the following 03 FDCs can be considered for further examination by Subject Expert Committees constituted by Ministry of Health and Family Welfare.

S. No.	Name of the FDC	S. No. as per DCG(I) consolidated list
1	Atenolol + Losartan + Hydrochlorothiazide	162
2	Duloxetine + Mecobalamin	293
3	Mecobalamin + Vit-B6+Folic acid	136

The FDCs were discussed by Subject Expert Committee (SEC), recommendations of the SEC are as follows:-

S. No.	Name of the FDC	Details of SEC meeting	Recommendations of SEC
1	Atenolol+Losartan+ Hydrochlorothaizide	57thSEC (Cardiovascular & Renal) dated 27.11.2018	The committee deliberated the matter & recommended that the use of Beta blocker-Atenolol in this FDC with diuretic (Ref: ASCOT-BPLA trial) is not appropriate. However the applicant may present their scientific justification with supportive evidence if any for further consideration.
		71st SEC (Cardiovascular & Renal) dated 06.12.2019	In light of recommendation of committee dated 27.11.2018, the firm presented justification for the FDC. After detailed deliberation, the committee recommended for continued manufacturing and marketing of the FDC subject to the condition that it should be indicated for stage-II hypertension with co-morbidities like CAD and Post MI.
2	Duloxetine + Mecobalamin	41st SEC (Neurology & Psychiatry) dated 14.11.2018	The FDC was deliberated by the committee. After detailed deliberation the committee opined that this particular FDC should be restricted only for the following indication: For the management of painful peripheral neuropathy with coexistent vitamin B12 deficiency.
3	Mecobalamin + Vitamin B6 + Folic Acid	58th SEC (Cardiovascular & Renal) dated 18.12.2018	After detailed deliberation, committee opined that the FDC can be permitted for continued manufacturing & marketing of only for the strengths which are already approved by DCGI.

S. No.	Name of the FDC	Details of SEC meeting	Recommendations of SEC
		70th SEC (Cardiovascular & Renal) dated 07.11.2019	The committee reviewed its earlier recommendation and after detailed deliberation, committee opined that the FDC can be permitted for continued manufacturing and marketing.

As these FDCs have been declared as rational and recommended by SECs. It is proposed that NOCs for continued manufacturing and marketing of these FDCs may be issued.

DTAB examined and agreed to the recommendations made by the SECs. Further, Board, in general, suggested that while granting approval to any new FDCs, the indication of such FDCs need to be specified.

AGENDA No. 4

Consideration of the proposal for review of prophylactic doses mentioned under Schedule 'V' of Drugs & Cosmetics Rules, 1945 vis-a-vis the doses prescribed under Food Safety and Standards (FSS) Act, 2006

DTAB was apprised that, a proposal has been received from FSSAI proposing that Drugs & Cosmetics Rules,1945 may be amended to delete the preparations containing the prophylactic doses under Schedule 'V' considering the provisions of doses under Section 22 of FSS Act, 2006 especially products formulated in Tablets, Capsules, Liquids, etc. meant for oral administration.

As per Section 22 of FSS Act, 2006 it is evident that the products in drug type matrix (i.e. Tablets, capsules etc.) covered under FSS Act which are containing vitamins below RDA also falls under prophylactic and some of the therapeutic doses prescribed in schedule V of the Drugs and Cosmetics Rules, 1945. FSSAI has also proposed for amending the Schedule K (10) for revising the scope of substances which are used both as articles of food as well as drugs so that same are exempted from the provisions of Chapter IV of the Drugs and Cosmetics Act and Rules made there under.

Accordingly, DCC in its 52nd DCC meeting held on 18.09.2017 deliberated the proposal and recommended that a provision may be incorporated in Drugs and Cosmetics Rules, 1945 especially in Schedule 'V' and Schedule 'K' to exclude multivitamin preparations containing vitamins in a strength which is lower than Recommended Daily Allowance (RDA) for Indians as recommended by ICMR and FSSAI, from the provisions of Drugs and Cosmetics Rules, 1945.

The DTAB deliberated the matter in its 78th meeting held on 12.02.2018 and opined that the matter may be referred to DG, ICMR for their recommendations.

The said matter was then referred to Director-General (DG), ICMR and a reply in the form of D.O. letter dated 10.06.2019 addressed to DCG(I) has been received along with comments from DG, ICMR. Further, ICMR made another communication vide letter no. 65/04/2019-BMS dated 14.10.2019 to the FSSAI on the same matter.

DTAB examined the ICMR recommendations and recommended that vitamins with doses up to one RDA should be regulated under FSSI Act. Other vitamin preparations

having prophylactic and therapeutic claims should be regulated under the Drugs and Cosmetics Act, 1940 and Rules, 1945 including Schedule 'V' of the Rules. Accordingly, Schedule 'V' of the Drugs and Cosmetics Rules, 1945 should be amended by incorporating provisions clearly that vitamins with doses up to one RDA shall be regulated under FSS Act. Further, the Board proposed that necessary review of doses specified under Schedule 'V' may be undertaken subsequently.

AGENDA No. 5

Consideration of the proposal for providing an opportunity of being heard to Shri. Dhirendra Singh before the DTAB as per the direction of Hon'ble Supreme Court of India w.r.t. FDC of Chlorpheniramine Maleate + Codeine Syrup bearing S.O. No 909(E) and FDC of Codeine + Chlorpheniramine + Alcohol syrup bearing S.O. No 920(E)

DTAB was apprised that, as per the judgment of the Hon'ble Supreme Court dated 15.12.2017, the matter related 344 FDCs +05 FDCs was already deliberated in Drugs Technical Advisory Board (DTAB) in its 78th meeting and the Board recommended for constituting a sub-committee under the Chairmanship of Dr. Nilima Kshirsagar. Further, it was decided to give the hearing to all appellants/ petitioners including All India Drug Action Network (AIDAN) as per the direction of Hon'ble Supreme Court.

A public notice dated 12.03.2018 was published on CDSCO website requesting all the Petitioners/Appellants/AIDAN for submitting the information in the prescribed format which contained detailed information with respect to the subject FDC. Further, CDSCO has issued a public notice on 24.05.2018 inviting the concerned Applicants 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, letters were also sent to all the Petitioners/Appellants/AIDAN individually including petitioner vide CDSCO letter dated 28.05.2018.The Petitioners through said letter, were informed that in compliance to the direction of Hon'ble Supreme Court, it has been proposed to give hearing for deliberation by the sub-committee. Accordingly, it was also requested to regularly visit the CDSCO website and avail the opportunity of hearing on given date. It was also informed that no separate letter will be sent for the hearing schedule.

After providing the hearing to all the Petitioners/Appellants/AIDAN these 344 + 05 FDCs were examined by the DTAB Sub-Committee and report was submitted before DTAB. DTAB in the 79th meeting held on 16.05.2018 deliberated the matter and final report was submitted to Ministry. After considering the recommendations of DTAB, and the direction of Hon'ble Supreme Court the Central Government vide Gazette notifications S.O. number 4379(E) to S.O. number 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.

One of the petitioner, Mr. Dhirendra Singh had approached to the Hon'ble Supreme Court and filed the Contempt petition for not providing hearing related to FDC of Chlorpheniramine Maleate + Codeine Syrup bearing S.O. No 909(E) and FDC of Codeine + Chlorpheniramine + Alcohol Syrup bearing S.O. No 920(E). In this regard, the Hon'ble Supreme Court in its order dated 09.01.2020 in the Contempt Petition (C) No. 842/2019 in transferred case (C) No. 39/2017, ordered that petitioner should have been given an opportunity of hearing before the Drugs Technical Advisory Board.

In view of above, Mr. Dhirendra Singh was invited to present the case before the Board. Accordingly, he placed his contentions in detail regarding addiction of younger generations to the codeine containing preparations, widespread trafficking of such drugs, and voluminous seizures made by enforcement agencies like NCB across the country and pleaded that the esteemed Board may consider for taking action to address the issue in light of grave repercussions due to continued manufacturing and marketing of such products.

DTAB heard the appeal of Mr. Dhirendra Singh.

The matter was then deliberated by the Board in detail. It was noted by the Board that as per records, one of the product i.e. FDC of Codeine + Chlorpheniramine + Alcohol syrup is already under prohibition of the Central Government vide S.O. No. 4581 dated 07.09.2018.

As regard to the other product i.e. FDC of Codeine + Chlorpheniramine Maleate syrup, Board noted that the relevant part of Judgment of Hon'ble Supreme Court dated 15.12.2017, which is reproduced below.

> *"37. insofar as the drugs that have been banned and which were manufactured pre 21st September, 1988, a list of 15 such drugs has been given to us by Mr. Kapil Sibal, learned senior counsel for the respondents. We set aside the Central Government notifications banning them as these cases were never meant to be referred to the Kokate Committee. It will be open, however, for the Central Government, if it so chooses, do novo, to carry out an inquiry as to whether such drugs should be the subject matter of a notification under Scetion 26A of the Drugs Act."*

Accordingly, the Board recommended that for FDC of Codeine + Chlorpheniramine Maleate syrup, appropriate course of action may be taken under the above judgment of the Hon'ble Supreme Court.

AGENDA No. 6

Consideration of the proposal to examine the requirement of Form CT-11/14/15 and Form 29 as prescribed in the New Drugs and Clinical Trials Rules, 2019 and Drugs and Cosmetics Rules, 1945 respectively

Board was apprised that, earlier, as per Drugs and Cosmetics Rules, only Form 29 NOC, irrespective of BE and Non-BE purpose, was required to be obtained for grant of Form 29. But as per New Drugs and Clinical Trials Rules, 2019, permission in Form CT-11/14/15 needs to be obtained for grant of Form 29.

In this regard, Representatives of Indian Pharmaceutical Alliance (IPA) have raised the concern stating that India is having such stringent and excessive requirements for developing product for examination, test, analysis, CT or BE study. Because of these excessive requirements, Industries are facing difficulties in registration of their product in India as well as globally. Whereas internationally, organizations are allowed to manufacture drugs for Clinical trial, bioequivalence study, examination, test or analysis purpose without obtaining any license from drug regulatory authority. This hinders the Research and Development of drugs in India, severely impacting availability of new drugs to Indian patients It was suggested that in line with International Practices, requirements of Form CT-11/14/15 and Form 29 should be abolished. Alternatively, only one requirement i.e., Form-29 should be mandated.

DTAB deliberated the issue and recommended that provision may be made for notification of information by the applicant relating to manufacture of new drug for test and analysis under Form CT-10/12/13 except for batches manufactured for clinical trial or BA/BE studies. With regard to grant of license in Form-29, timeline may be specified as 7 working days for its issuance by Licensing Authority, failing which it shall be considered deemed approved. In both the cases, however the facility shall remain open for regulatory inspections. Accordingly, the necessary amendments should be made in the Drugs and Cosmetics Rules, 1945 and the New Drugs and Clinical Trials Rules, 2019.

AGENDA No. 7

Consideration of the proposal to cancel the licenses of the manufacturers who does not deposit the penalty within the prescribed time limit given by NPPA under DPCO and similar action on retailers who indulge in overcharging of pricing of drugs/ medical devices

Board was apprised that, Hon'ble Parliamentary Standing Committee (PSC) in its 54th Report, regarding 'Pricing of Drugs with special reference to Drugs (Prices Control) Order, 2013' of the Ministry of Chemicals and Fertilizers (Department of Pharmaceuticals) has stated that for violation of Drug Price Control Order (DPCO), 2013 with respect to overcharging, the National Pharmaceuticals Pricing Authority had issued various Demand Notices but the actual amount recovered from manufacturing firms is too meager in comparison to the amount due to be recovered.

The PSC firmly felt that unless DPCO rules are made stringent and effectively implemented, the unfair market practices by pharma companies may continue to hamper the availability of affordable medicines to the people. Since overcharging of drugs/medicines is a violation of consumer's right to basic healthcare, the Committee strongly recommend that if the manufacturer does not deposit the demanded amount within the prescribed time limit given by NPPA, cancellation of licenses of such companies to manufacture that medicine/drug may be considered. Similar action may also be taken on retailers who indulge in overcharging of drugs/medical devices.

The Board was further apprised that earlier, the said proposal to cancel the licenses of the manufacturers for overcharging of prices was deliberated in the 82nd meeting of the Board held on 02.04 2019. However, the Board did not agree to the proposal which was considered and Action Taken Report (ATR) on the recommendation of the Hon'ble PSC was submitted by the Government accordingly.

In response to the ATR, the PSC recommended that the relevant provision of DPCO, 2013 and Drugs and Cosmetics Act, 1940 and its rules should be revisited by the Ministry and necessary action should be taken for the amendment of these orders/ Acts/ Rules so as to make these provisions more stringent and effective.

Subsequently, the matter was placed for deliberation by the Drugs Consultative Committee (DCC) in its 58th meeting held on 14.07.2020, wherein the DCC did not agree to the proposal, as the objective of the Drugs and Cosmetics Act is to regulate the import, manufacture, distribution and sale of drugs to ensure their quality, safety and efficacy.

DTAB considered the recommendation of the DCC and deliberated the matter in detail and agreed to the opinion of the DCC as the objective of regulation under the Drugs and Cosmetics Act, 1940 and Rules made there under is to ensure the quality, safety and efficacy of drugs and activities related to it. Further, pricing and its regulation is mandated under the Essential Commodities Act (ECA) and therefore, it is not appropriate to incorporate provision relating to punitive actions for overcharging or pricing related violations in the Drugs and Cosmetics Act, 1940 and Rules thereunder.

AGENDA No. 8

Consideration of the proposal for exemption of audit of manufacturing site for grant of license or loan license, by the registered notified body for manufacturing of Class-A devices

Board was apprised that, as per rule 20 of the Medical Device Rules-2017, the applicant needs to submit the application in Form MD-3 for licence or in Form MD-4 for loan licence for the grant of licence in Form MD-5 or loan licence in Form MD-6, as the case may be, to manufacture Class A medical devices.

The State Licensing Authority after scrutiny of documents and on being satisfied that the requirements of these rules have been complied with, grants a licence in Form MD-5 or loan licence in Form MD-6, as the case may be, to manufacture Class A medical devices.

Further, the audit of the manufacturing site by registered Notified Body in the manner as specified in the Third Schedule of MDR-2017 is required to be carried out within one hundred and twenty days from the date on which the licence was granted by the State Licensing Authority.

Since the Class- A medical devices are least risk prone, it was proposed to remove the requirement of audit of manufacturing site by the registered Notified Body. However, the manufacturer should submit the self certification of the compliance of all the submitted documents to State Licensing Authority for grant of licence to manufacture Class A medical devices.

DTAB after detailed deliberation agreed to the proposal.

AGENDA No. 9

Consideration of the proposal to Include American Standard Test Method (ASTM) in the product standards for Medical Devices under Rule 70 of MDR-2017

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.
The rule 7 of the Medical Device Rules-2017 provides Product standards for medical device. The extracts of the rule 7 is as under:

(1) The medical device shall conform to the standards laid down by the Bureau of Indian Standards established under Section 3 of Bureau of Indian Standards Act, 1985 (63 of 1985) or as may be notified by the Ministry of Health and Family Welfare in the Central Government, from time to time.
(2) Where no relevant standard of any medical device has been laid down under sub-rule (1), such device shall conform to the standard laid down by the International Organisation for Standardization (ISO) or International Electro Technical Commission (IEC), or by any other pharmacopoeial standards.

(3) In case of the standards which have not been specified under sub-rule (1) and sub-rule (2) the device shall conform to the validated manufacturer's standards.

Since the American Standard Test Method (ASTM) is accepted globally, it was proposed to include the ASTM in the sub-rule (2) of the rule 70 of MDR-2017.

DTAB after detailed deliberation, agreed to the proposal and recommended for necessary amendment in the Medical Devices Rules, 2017 in this regard.

AGENDA No. 10

Consideration of proposal to amend rule 43A of the Drugs and Cosmetics Rules, 1945 to notify Inland Container Depot Tihi, Indore in Madhya Pradesh as port of entry for drugs

Board was apprised that, representation had been received from the Chief Manager, Container Corporation of India Ltd. (CONCOR), a PSU under Ministry of Railways to include Inland Container Depot (ICD), Tihi, Indore in the approved list of ICD for import of drugs/pharmaceuticals under Rule 43A of the Drugs and Cosmetics Rules, 1945.

CONCOR has shifted its ICD operations to ICD at Tihi, Indore. ICD, Tihi is the largest ICD catering to Industries of Indore, Pithampur, Dewas, Ratlam and Ujjain regions, including all Pharma industries in these regions. Therefore, considering the volume of business handled at ICD, Tihi and its strategic location with respect to surrounding industrial zones, Inland Container Depot (ICD), Tihi, Indore should be included in the approved list of ICD for import of drugs/pharmaceuticals under Rule 43-A of the Drugs and Cosmetics Rules, 1945.

DTAB deliberated the matter and recommended for amendment of Rule 43A of the Drugs and Cosmetics Rules, 1945 allowing import of drugs into the country through Inland Container Depot Tihi, Indore in Madhya Pradesh.

AGENDA No. 11

Consideration of proposal to amend the Drugs and Cosmetics Rules, 1945 for declaring the batch number on label of the trade pack (final packed unit) for vaccines containing multicomponent in separate final container

Board was apprised that M/s GSK Pharmaceutical Limited, GSK House, Dr. Annie Besant Road, Worli, Mumbai vide their application No. RA/393/2018 dated 25th July 2018 requested clarification regarding Batch Numbers to be declared on Trade Packs for vaccines containing two components in a separate final container based upon observation raised by the CDL, Kasauli during the testing of Hexavalent vaccine of GSK Pharmaceutical limited (Trade name- InfanrixHexa) (DTaP-HBV-IPV+ Hib) vaccine.The CDL had stated that the company had not mentioned the combination batch number on the product pack even though the same was mentioned on the summary lot protocol submitted to them with samples for lot release.

InfanrixHexa comprises DTaP+HBV-IPV Pentavalent liquid suspension in PFS and freeze dried Hib component in vial. The firm in their letter clarified following points-

1. For packs containing two components, e.g., freeze dried vaccine in vial + diluent in PFS or freeze dried vaccine in vial+ liquid suspension of second vaccine in PFS, firm is declaring the batch number, manufacturing date & expiry date of both the component on the carton and the individual label of vial/PFS. For such vaccine which contains two components, the firm additionally maintains a combination batch number i.e. the batch number assigned to the final packaged unit of the freeze dried vaccine+ liquid vaccine or freeze dried vaccine+diluent combo pack. This packaged lot number (Combined batch number) is not declared on the label but mentioned on the company's Batch Release Certificate & Summary Lot Protocol.

2. Global practice followed by the firm for marketing of the said product in countries like EU, Australia, Canada, etc, for the declaration of batch number is as follows-

   In the Inner label of vial of Hib component,-batch number of the Hib component is declared

   In the Inner label of PFS of DTaP+HBV+IPV component, batch number of the DTaP+HBV+IPV component is declared.

   In Outer carton, batch number of the combined DTaP+HBV_IPV/Hib vaccine is declared.

3. There is no specific international guideline on declaring batch no. on trade packs of vaccines containing two components.

   It is submitted that there is no specific rule in Drugs & Cosmetic Rules 1945 or guidelines for declaration of batch number on label of the trade pack (Final packed unit) for vaccine containing multi-component in separate final container.

   In view of the above, this CDSCO has clarified to the firm that in case of multi component vaccines, the outer carton of vaccine should contain combined batch number & expiry date of component of shortest expiry date. However, primary label of individual component may contain their respective batch number & expiry date. Also the firm is needed to have proper record & traceability for said combined batch number.

DTAB after deliberation agreed to the proposal for appropriate amendment in the Drugs and Cosmetics Rules, 1945**.**

AGENDA No.12

Consideration of proposal to examine the requirements of permission from Central Government for the export of the drugs 'Oseltamivir phosphate' and 'Zanamivir' or any preparation based thereon, etc under the Gazette Notification issued vide G.S.R. 144(E) dated 17.02.2017

Board was apprised that the Ministry of Health and Family Welfare had published the Gazette notification vide G.S.R. 144(E) dated 17.02.2017 under the Drugs and Cosmetics Act, 1940.

The Gazette Notification G.S.R. 144(E) inter-alia mandates that:

> *"... no person shall manufacture for sale or distribution or sale or stock or exhibit or offer for sale or distribute any preparation containing the drug 'Oseltamivir Phosphate' and 'Zanamivir except in the following manner:*
>
> *"(b) the conditions specified in the Drugs and Cosmetics Rules, 1945 in respect o f the drugs specified under Schedule H I to that rules shall apply to the drugs 'Oseltamivir Phosphate' and Zanamivir' or any preparation based thereon.*
>
> *Provided that the Drugs Controller General (India) may allow export of the drug 'Oseltamivir Phosphate and 'Zanamivir or any preparation based thereon for reasons to be recorded in writing and in consultation with the Central Government."*

Thus, permission by the Central Government is required to be given each time for the export of these drugs as per the above notification.

DCC in its 58th meeting held on 14.07.2020 deliberated the matter and recommended for revoking the Notification G.S.R. 144(E) dated 17.02.2017 by considering the aspect in the current context. However, the Committee also recommended that simultaneously, these drugs should be notified under Schedule H1 of the Drugs and Cosmetics Rules, 1945 for the regulation of their sale in the Country.

DTAB after detailed deliberation recommended for revocation of the G.S.R. 144(E) dated 17.02.2017 and inclusion of these drugs in Schedule H1 of the Drugs and Cosmetics Rules, 1945.

AGENDA No.13

Consideration of proposal for inclusion of provisions related to the registration of standalone Bioanalytical laboratories in the ND & CT Rules, 2019

Board was apprised that the Ministry of Health & Family Welfare, Government of India had 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.

Bio-analytical laboratory is the laboratory meant for analysis of biological samples received from the BA/BE Study Centres. Bioanalytical laboratory involved in analysis the biological samples of BA/BE studies are part of BA/BE Study Centre and hence need to regulated along with the BA/BE Study Centres.

As per the Rule 2(g) of New Drugs and Clinical Trial Rules 2019, "Bioavailability and bioequivalence study centre" is defined as below:

"Bioavailability and bioequivalence study centre" means a centre created or established to undertake bioavailability study or bioequivalence study of a drug for either clinical part or for both clinical and analytical part of such study.

However, this existing definition is not covering stand alone analytical laboratories.

Therefore, it was proposed to amend the said Rules to include the provision of registration of stand-alone Bio-analytical laboratories in the New Drugs and Clinical Trial Rules, 2019 by inserting the word analytical part in the definition as under;

"Bioavailability and bioequivalence study centre" means a centre created or established to undertake bioavailability study or bioequivalence study of a drug for either clinical part ***or analytical part*** *or for both clinical and analytical part of such study.*

DTAB after deliberation agreed to the proposal to amend the definition.

AGENDA No.14

Consideration of proposal for inclusion of Tapentadol in Schedule H1 of the Drugs and Cosmetics Rules, 1945

Board was apprised that, a representation had been received from National Commission for Protection of child rights to examine the issue of notifying the drug Tapentadol under Schedule H1 of Drugs and Cosmetics Rules, 1945.

In the representation, the Commission has stated that one of the members of the Commission, during his visit to Tamil Nadu found that an opioid drug named TAPENTADOL having similar atomical chemical formula components of Tramadol is being abused by the school children of Pudukkottai, Tamil Nadu which is made available to them by local vendors.

In light of the above fact, the Chairperson, National Commission for Protection of Child Rights on behalf of Commission u/s 13(1) of CPCR Act, 2005 recommended to examine the issue to notify the drug Tapentadol under Schedule H1 of Drugs and Cosmetics Rules, 1945.

DTAB after deliberation agreed for inclusion of Tapentadol in Schedule H1 of the Drugs and Cosmetics Rules, 1945.

AGENDA No.15

Consideration of proposal on merger of Pharmacopoeial Laboratory for Indian Medicine (PLIM) and Homoeopathic Pharmacopoeia Laboratory (HPL) with Pharmacopoeia Commission of Indian Medicine & Homoeopathy (PCIM&H), Ghaziabad

Board was apprised that, Pharmacopoeial Laboratory for Indian Medicine (PLIM) and Homoeopathic Pharmacopoeia Laboratory (HPL) are the subordinate organizations of Ministry of AYUSH with specific provisions in the Drugs & Cosmetics Act and rules as Appellate Laboratory. Regulatory provisions for PLIM and associated matters pertaining to Ayurveda, Siddha and Unani drugs are given under Rules 163-A to 166 and for HPL and associated matters pertaining to Homoeopathy drugs are given in rules 3 and 3-A(7) of the Drugs and Cosmetics Rules, 1945.

Pharmacopoeia commission of Indian Medicine & Homeopathy (PCIM&H) is an autonomous organization under the Ministry of AYUSH established since 2010 (Homoeopathy was included in 2014) with mandate to lay down, revise and harmonize the Standards and SOP of Ayurveda, Siddha, Unani and Homoeopathy (ASU&H) drugs and publish respective Pharmacopoeias and Formularies.

The proposal of merger of PLIM and HPL with PCIM&H has been deliberated in a meeting held under chairmanship of Secretary-AYUSH with DGHS and DCGI on 03.01.2020. In the meeting it was deliberated that, presently, the infrastructural capacity of PCIM & H is inadequate to deliver the desired outcomes for

standardization of work of ASU & H drugs. It is therefore intended to bring the two appellate laboratories i.e. Pharmacopoeial Laboratory for Indian Medicine (PLIM) and Homoeopathic Pharmacopoeia Laboratory (HPL) under umbrella of Pharmacopoeia Commission of Indian Medicine & Homoeopathy (PCIM&H), Ghaziabad to work in syncytium with the objective of augmenting the functional capacity to meet the standardization needs of ASU&H drugs and publication of monograph of their quality standards with a focused approach in time bound manner. Finally, it was resolved in the meeting that consultation is required for recommendation or concurrence of both ASUDTAB and DTAB for making amendment in Drugs & Cosmetic Rules about the proposed merger of PLIM and HPL with PCIM&H.

Accordingly, Member Secretary, DTAB had requested all the members of DTAB vide letter AYUSH/Misc-54/2019-DC dated 14.02.2020 for providing the recommendations through mail.

DTAB deliberated the matter and concurred the decision taken for merging PLIM and HPL with PCIM&H.

AGENDA No.16

Consideration of proposal to include FD&C Red # 40 Aluminum Lake (E129) Allura Red Colour in the list of approved colours under rule 127 of the Drugs and Cosmetics Rules, 1945

Board was apprised that a representation had been received from one manufacturing company that currently Conjugated Estrogen Tablets USP are being manufactured by them in a white tablet format using Opadry white as the colouring agent. Now the company wants to change the colour coat of Conjugated Estrogen Tablets USP from white to maroon coat utilizing colour pigment FD & C Red # 40 Aluminum Lake (E129) Allura red.

The Opadry Maroon colour coat contains HPMC 2910/ Hypromellose [6cP], Titanium Dioxide, FD&C Red # 40 Aluminum Lake (El29) (Allura red) PEG 400/ Macrogol and FD&C Blue #2 Aluminum Lake (El32). Allura Red AC is a coal tar colour which is red azo dye compound derivative of naphthalene. This term coal tar is an older nomenclature for synthetic chemical that started out with coal tar as the precursor. The colour FD&C Red 40 is a synthetic chemical and is also referred to as coal tar colours.

This colour is, however, not included in the list of approved colours as prescribed in rule 127 of the Drugs and Cosmetics Rules, 1945. However, the same is approved and used for many years by the major regulatory authorities across the world including USA, UK, Canada, Australia & Singapore as permitted colour for pharmaceutical preparations and food products. Further, the Food Safety and Standards Authority of India (FSSAI) has also approved FD&C Red # 40 Aluminum Lake (E l29) (Allura red) as colorant in food products in India. Therefore, the company has requested to include FD&C Red # 40 Aluminum Lake (E l29) Allura red

colour in the list of approved colours under Rule 127 of the Drugs and Cosmetics Rules, 1945.

DTAB deliberated the matter and recommended to amend the Rule 127 of the Drugs and Cosmetics Rules, 1945 to include FD&C Red # 40 Aluminum Lake (E l29) Allura red colour.

AGENDA No. 17

Consideration of the proposal to amend the New Drugs and Clinical Trials Rules, 2019 to include the provisions for compassionate use of unapproved new drugs

Board was apprised that, representation of Cure SMA Foundation of India had been received to frame the rules/ guidelines for Compassionate use unapproved drugs in India.

In the representation it was mentioned that the medical treatment of patients with chronic, life-threatening or seriously disabling rare diseases can be very disappointing both for the suffering patients, their families and physicians in cases where patients cannot be treated satisfactorily with currently authorized medicines. Market authorization of new pharmaceuticals in developing countries like India can take several years, which is valuable time lost from the patient's perspective.

Further, it was mentioned in the representation that the way to tackle this problem was to allow patients with chronic, life-threatening or seriously disabling rare diseases to obtain the medicines under "compassionate use" for new pharmaceuticals under clinical development for which phase-II/III studies provide acceptable safety profile in clinical trials. It was also suggested to develop a frame work for compassionate use of unapproved new drugs.

In this regard, the Central Government has published a draft notification vide G.S.R. 354(E) dated 05.06.2020 to include the provisions relating to compassionate use of unapproved new drugs under the New Drugs and Clinical Trial rules, 2019. A period of 15 days time was given from the date of publication of draft notification in the Gazette of India to all stake holders likely to be affected for submitting comments/suggestions to the Ministry.

DTAB considered the draft notification issued vide G.S.R. 354(E) dated 05.06.2020 along with objections/suggestions received from various stake holders**.**

DTAB after detailed deliberation agreed to the proposal and recommended to amend the New Drugs and Clinical Trials Rules, 2019 to include the provisions for compassionate use of unapproved new drugs.

AGENDA No. 18

Consideration of proposal to amend the Drugs and Cosmetics Rules, 1945 for exemption of BA/BE studies for the drugs manufactured solely for export purpose

Board was apprised that, during interaction of Department of Commerce with Pharma industry representatives one of the regulatory action points suggested was as under:

> 'Exemption of Bio Availability & Bio Equivalence (BA/BE) studies data for the drugs manufactured for export purpose as the manufacturers abide with the regulations of the importing countries.'

The Drugs & Cosmetics Rules, 1945 were amended vide G.S.R 327(E) dated 03.04.2017, providing that the applicant shall submit the result of bioequivalence study, along with the application for grant of a licence of oral dosage form of drugs specified under Category II and Category IV of the biopharmaceutical classification system.

As per Rule 84 of the Drugs and Cosmetics Rules, the provisions shall apply to the manufacture of drugs for sale notwithstanding that such drugs are manufactured for sale outside India. However, for export of any drug to any country, the manufacturer is required to meet the requirements of the importing country. Some country may not require BA/BE study, while some other may require BA/BE Study of specific design as per their BA/BE guidelines. Therefore, it would be appropriate to provide exemption of the BA/BE study for manufacture of drugs solely meant for export.

In view of above, it was proposed that necessary provision may be made in the Drugs and Cosmetics Rules, 1945 to exempt BA/BE studies data for the drugs manufactured for export purpose as the manufacturers abide with the regulations of the importing countries.

DTAB deliberated the proposal and recommended for amendment of Rule 74, 74B, 76, 78, 78A & 84 of the Drugs and Cosmetics Rules, 1945 to provide exemption of BA/BE studies for the drugs manufactured solely for export purpose.

AGENDA No. 19

Consideration of proposal to amend the Drugs and Cosmetics Rules, 1945 for exemption of excipients and basic chemicals for non-medicinal use from obtaining permission from licencing authority for import without registration and import licence

Board was apprised that, during interaction of Department of Commerce with Pharma industry representatives one of the regulatory action points suggested was as under:

> 'Exemption of excipients viz HPMC, Povidone, Crospovidone, lactose monohydrate, methyl cellulose etc. and basic chemicals like 2-Dimethylaminoethanol, Glycerine from the list of drugs meant for dual use issued by DCGI.'

As per Entry No. 1 of the Schedule D of the Drugs and Cosmetics Rules, 1945, it is required to obtain permission from licencing authority for import of substances for non-medicinal use without registration and import licence.

As per Sub-rule (8) of rule 24A of the Drugs and Cosmetics Rules, 1945, no import Registration Certificate is required in respect of an inactive bulk substance to be used for a drug formulation with or without Pharmacopoeial conformity.

In light of above, , the amendment in the Drugs and Cosmetics Rules, 1945 for exemption of permission from licencing authority for import of excipients which are inactive bulk substances to be used for a drug formulation and basic chemicals for non-medicinal use for which no registration and import licence are required, may be considered in present context.

DTAB deliberated the proposal and recommended for necessary amendments to exempt excipients and basic chemicals for non-medicinal use from obtaining permission from licencing authority for import without registration and import licence

AGENDA No. 20

Consideration of the proposal for amendment of the Medical Device Rules-2017 to include the provision for allowing the import of medical device having lesser shelf-life period but before the date of expiry in exceptional cases

Board was apprised that, as per the provision of rule 47 of Medical Device Rule, 2017 – the requirement of residual shelf-life on the date of import is as below:

- Any medical device, whose total shelf life claim is less than 90 days, shall not be allowed to be imported if it has less than 40% residual shelf-life on the date of import:
- Any medical device, whose total shelf life claim is between 90 days and one year, shall not be allowed to be imported if it has less than 50% residual shelf-life on the date of import:
- Any medical device, whose total shelf life claim is more than one year, shall not be allowed to be if it has less than 60% residual shelf-life on the date of import.

However, representation has been received from the associations i.e. Confederation of Indian Industry CII & Medical Devices Technology Association of India (MTaI) with the request to provide relaxation of residual shelf life requirements for medical devices and IVDs citing the reason that medical device industry is facing challenges in getting dispatches from overseas manufacturing sites, getting international cargo transportation and clearing the imported devices at port offices due to COVID-19 pandemic across the globe and in the due course the medical devices/ IVDs are losing the shelf life and getting below the threshold limits of residual shelf-life.

In view of above concerns highlighted by the associations, considering the short shelf life of In-vitro Diagnostics (IVD) and logistic issues faced by the industry in the supply of Medical Device and In-vitro Diagnostic kits/ reagents, it was proposed that the

above rule 47 of Medical Device Rule, 2017 may be amended to include the following provisions.

In the Medical Devices Rules, 2017, in rule 47, after the third proviso, the following proviso shall be inserted namely,-

“Provided also that in exceptional cases the Central Licensing Authority may, for reasons to be recorded in writing, may allow, the import of any medical device having lesser Shelf-life period, but before the date of expiry as declared on the container of the medical device”.

DTAB deliberate the proposal and recommended for the amendment of the Medical Device Rules-2017 to include the provision for allowing the import of medical device having lesser shelf-life period but before the date of expiry in exceptional cases.

AGENDA No. 21

Consideration of the proposal to examine the prohibition of Fixed Dose Combination of corticosteroid with any other drug for internal use except for preparations meant for meter dose inhalers and dry powder inhalers and amendment in G.S.R. 738 (E) dated 09.10.2009

Board was apprised that, FDC of Tamsulosin HCl 0.4mg (as film coated modified release tablet)+Deflazacort 30 mg hard gelatin capsule was approved by Prof. Kokate Committee constituted by Ministry of Health and Family welfare vide order dated 16.09.2014 for examining the safety and efficacy of FDCs which were licensed by State Licencing Authority without prior approval of DCG(I).

However, Gazette notification G.S.R. 738(E) dated 09.10.2009 under Section 26A of Drugs and Cosmetics Act, 1940 prohibits:-

> ‘14. Fixed Dose Combination of corticosteroid with any other drug for internal use except for preparations meant for meter dose inhalers and dry powder inhalers’

Subsequently, there is a PIL in High Court, Patna in the matter.

The matter has been considered by the Ministry of Health and Family Welfare in consultation with DGHS as the product has been declared rational by the Prof. Kokate Committee, for deliberation of the matter for necessary amendment in the above notification accordingly in the DTAB.

In view of above, the entry No. 14 of G.S.R. 738(E) dated 09.10.2009 to be amended and substituted by an entry and content as under:-

> ‘14. Fixed Dose Combination of corticosteroid with any other drug **[excluding FDC of Tamsulosin HCl 0.4mg (as film coated modified release tablet) + Deflazacort 30mg in hard gelatin capsule]** for internal use except for preparations meant for meter dose inhalers and dry powder inhalers’

DTAB deliberated the proposal and recommended to exclude the FDC of Tamsulosin HCl 0.4 mg (as film coated modified release tablet) + Deflazacort 30mg hard gelatin capsule from the prohibition under vide GSR 738(E) dated 09.10.2009. Further, Board, in general, suggested that while granting permission to any new FDC, indication need to be specified.

Meeting ended with a vote of thanks to the Chair.

LIST OF PARTICIPANTS

1. Dr. Rajiv Garg — Chairman
   Director General of Health Services,
   Nirman Bhawan, New Delhi
2. Dr. V.G. Somani — 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. Shri. H.N. Mahanta — Member
   Joint Drugs Controller (I/C), Assam
6. Dr. Pallavi Jain Govil — Member
   Principal Secretary, Health, M.P.
7. Shri. Pankaj Patel — Member
   Chairman and Managing Director,
   Zydus Cadila Group, Ahmedabad
8. Dr. Nilima Kshirsagar — Member
   Chair in Clinical Pharmacology,
   ICMR, Mumbai
9. Dr. R.N. Tandon — Member
   Past Honorary Secretary General, IMA, New Delhi
10. Prof. Dr. T.V. Narayana — Member
    President, IPA, Bengaluru
11. Shri. M.S Lokesh Prasad — Member
    Scientific Officer & Govt. Analyst,
    Bengaluru, Karnataka
12. Dr. Vaishali N Patel — Member
    Govt. Analyst, Food & Drugs Laboratory,
    Vadodara, Gujarat

INVITEES

1. Dr. Sunil Kumar,
   OSD, DGHS
2. Shri. Dhirendra Singh
   Petitioner

CDSCO REPRESENTATIVES

1. Shri. A. K. Pradhan
   DDC (I), CDSCO (HQ), DCC-DTAB Division, New Delhi
2. Dr. Santosh Indraksha
   ADC (I), CDSCO (HQ), DCC-DTAB Division, New Delhi

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