

MINUTES OF THE FORTY EIGHTH DRUGS TECHNICAL ADVISORY BOARD MEETING HELD ON JULY 8, 1999 AT NEW DELHI

The Member Secretary, welcomed the members to the 48th meeting of DTAB and explained the overall objectives of the meeting.

Chairman, Dr, S.P. Agarwal, DGHS thanked the members for attending the meeting and for their keen interest. He emphasized the importance of the role which the Board has to play in examining various technical and policy issues in the context of proper use of safe, effective and quality drugs in the country. He, further stressed upon the need for holding regular meetings of DTAB.

Chairman informed the members that for ITEM NO. 3 on mentioning of words “V (Vegetarian) and NV (Non-Vegetarian)” on the label of drugs/cosmetics and Supplementary Agenda on “Banning of Oxytocin Injection”, officials/representatives of Deptt. of Consumer Affairs have been invited to participate in the deliberations.

Sh. Praful Seth, as per rule, was elected to function as Chairman of DTAB in the absence of DGHS-Chairman DTAB, who was called by Minister of State for urgent meeting in connection with the ongoing LRS T.B. Hospital strike.

ITEM NO. 1

- (a) **Confirmation of the minutes of the last meeting of DTAB held on October 27, 1998.**

The Minutes were confirmed.

- (b) **Action Taken Report on the various Agenda items of the last DTAB meeting held on October 27, 1998.**

Action taken report on the various Agenda items of 47th DTAB was passed by the Board.

It was noted that some of the issues pertaining to ATR has been taken up as fresh agenda in this meeting.

Dr. S.D. Seth, however, pointed out that in regard to ITEM NO. S-1, guidelines for Good Clinical Trial Practices, it is necessary to have the captions serially numbered like the guidelines issued by International Conference on Harmonization (ICH).

The suggestion was accepted.

ITEM NO. 2

Review of provision related to labeling in respect of vaccines.

The Member Secretary explained that certain provisions of Rule 109 can be interpreted differently especially about the date of manufacture of vaccines. The members agreed to the need for review of existing Rule 109 of the Drugs and Cosmetics Rules, 1945, in respect of labeling of vaccines.

It was decided, that a group of vaccine Experts under the Chairpersonship of Dr. (Mrs.) Ira Ray, (Addl. DG) should examine the relevant provision and suggest the specific amendments/modification required to be made in Rule 109. This group would consist of representative of NIB, ICMR and CRI, Kasauli.

ITEM NO. 3

Proposal to amend Drugs and Cosmetics Rules, 1945 to require mention of words V(Vegetarian) and NV (Non Vegetarian) on labels of drugs/cosmetics.

Ministry of Social Justice and Empowerment nominated Shri Devdas Chhotray, Joint Secretary, Ministry of Food Processing and Shri S.R. Khanna, representative from an NGO, VOICE for acquainting the Board Members with their views on this subject.

Sh. Chhotray, explained regarding his Ministry's concern about the killing of animals and consumer's Right for Information. He stated that some consumers may like to avoid use of any product containing material from animal source if they have recourse to such information and this need of consumer requires to be respected.

It was, therefore, proposed that the provision for labeling 'V' and 'NV' on every food/drug product depending on its vegetarian or non-vegetarian aspects may be introduced in the Drugs and Cosmetics Rules.

Dr. S.R. Khanna also, in detail, stressed upon consumers rights to such information and desired a mandatory provision to indicate the source of drug in terms of 'V' and 'NV'.

The Chairman explained that while respecting the consumers Rights to Information, the issues of V & NV markings need to be examined in wider perspectives of medical treatment and critical importance of certain drugs products like vaccines, hormones, biotech products etc. which are of life saving nature and could be traced to animal origin. (Unlike food, drugs are not taken by choice or for the purpose of gratification).

He, however, suggested that in the context of general understanding of vegetarianism such drugs where macroscopic portion of animal tissues like animal blood, liver extract etc. are present in oral preparations may be considered by the Board for marking NV on the label of such drugs.

1. Prof. Jindal opined that drugs may be labeled to indicate their source i.e. synthetic sources, Bio-source and animal source.

This suggestion was however, not found practicable.

2. Prof. Kokate and Mrs. Muthuswamy, representative of ICMR, felt that what may be appropriate in case of food may not necessarily be appropriate in case of drugs which are prescribed for relief from diseased conditions are many a times in life threatening situation. To introduce the concept of Vegetarian and Non Vegetarian by marking V or NV in drugs, may not be in the overall interest of the consumers.
3. Sh. Praful Seth agreed with views of Chairman about the possibility of considering the proposal for a limited number of non-critical drugs that is oral tonics etc. having obvious animal tissues. He also explained that alternate formulations are also available and the physician may advice/educate consumers about it.
4. Prof. S.D. Seth, and Sh. R. Anand Raj Sekhar, opined that if at all proposal to mark NV has to be considered, it may be discussed only for Non-essential drugs.
5. Dr. Prem Agarwal, representative of IMA, opposed any move to bring in the concept of V/NV in the field of medicines and also stated that it would not be rational to further classify drugs as ‘essential or non essential’ for the purpose of marking NV on the labels.
6. Drugs Controller, Karnataka, was in agreement to the extent of marking NV on non-essential drugs taken orally and containing obvious animal tissues but did not favour the concept of marking V or NV in the field of drugs.
7. The president MCI, Dr. Ketan Desai, was of the opinion that marking products as NV is not relevant for medicines and no attempt should be made to differentiate them as essential one. The proposal may be considered for food products and not for drugs.
8. Dr. Bhargava, representative of Medical Council of Indian, Dr. Gupta, Director, CDRI, Lucknow and Mr. M.V. Kumar, expressed strong views against introducing the requirement for marking drugs products with NV.

The matter was discussed in great details and the other members did not favour any labeling of NV or V on the medicines.

In view of the above, labeling of drugs “V/NV” or “from animal source”, as proposed in the agenda, was not accepted.

ITEM NO. 4

Proposal to reconsider the rationality and continued marketing of Fixed Dose Combination of four anti TB drugs.

Member Secretary briefed the members about the subject and about the deliberation held earlier by the Board in its previous meetings.

In view of the new facts claimed by M/s. Lupin Labs., DTAB members agreed to allow M/s. Lupin Laboratory, Mumbai to make presentation before the Board in respect of the marketing of FDC of four anti TB drug formulation. Dr. D.S. Bakhle made a detailed audio-visual presentation on behalf of the firm.

Explaining the epidemiological data on TB in India and trends in multi drug resistance, etc. reference was made to the WHO TRAC Report 1998 according to which FDC of four anti TB drugs is now recommended to be used.

It was argued that FDC would ensure improved compliance and convenience of administration. The firm claimed that they have developed the necessary know-how to manufacture stable formulation of four anti TB drugs and have undertaken R&D studies to ensure batch to batch bioequivalence of their product.

The members enquired about the stability of formulation containing ethambutol which is hygroscopic in nature. They also wanted to know about the analytical protocols adopted by the manufacturer to test the combination; profile of invitro dissolution pattern corresponding to the parameters of bioavailability protocols need to be furnished.

Dr. G.R. Khatri, DDG (TB), special invitee, referred to WHO paper reporting significant variation in bioavailability patterns of FDC formulation. The 1999 publication of the International Union Against Tuberculosis and Lung disease (IUATLD) regarding assessment of FDC's was also brought to the notice of members.

It was explained by Prof. S.D. Seth, that in the context of Pharmacokinetic profile of drugs in question and the mechanism of anti TB action, it would suffice to have efficient bioavailability studies done.

Members were in agreement to this approach and suggested for such studies to be undertaken at well established centers.

After consideration of all relevant aspects, the Board decided that manufacturers will be asked to get fresh Bioavailability studies conducted with FDC of 4 anti TB drug formulation at NIPER Chandigarh and TRC Chennai after getting the protocols approved from the Dte. General of Health Services. Stability study reports and analytical protocols would also be furnished by the manufacturing firms.

Reports and data generated following these studies should be placed before the Board in its next meeting for deciding the issue. Status quo to be maintained till such time.

ITEM NO. 5

Proposal to amend part of the entry no. 27 of gazette notification GSR 578 (E) dated 10/8/1989 relating to “.....and all Fixed Dose Combination injectables preparations containing synthetic Oestrogen and Progesterone.”

The representative of DG, ICMR, Dr. (Mrs.) Muthuswamy, explained the proposal brought before the Board.

The issue relates to previous notification GSR 578 (E) dated 10/8/1989 which restricts the FDC of injectables preparation containing synthetic Oestrogen and Progesterone. The earlier decision made by the Expert committee, was based on the possible misuse of the drug as pregnancy detection injection. Such misuse is however, no more a concern due to easy availability of pregnancy detection kits. Such combination is in use in various countries excluding India as a very promising contraceptive. In view of this, ICMR plans to undertake clinical trials in the country with the drug as once a month injectables contraceptive. However, the earlier notification needs modification to pave the way for ICMR to undertake trials. ICMR would import the drug for the proposed trials and evaluation. Once the clinical trials are found satisfactory and accepted, the drug may get marketing approval.

Most of the members which deliberated the issue were in favour of ICMR trials. Dr. Prem Agarwal opined that in the context of Indian situation, it would be appropriate if ICMR is allowed to conduct the study on fast track basis.

Board recommended that the proposed clinical trials under ICMR could continue without disturbing the present prohibitory status and the drug would be imported for limited purpose of clinical trials. Once the results are accepted, the notification may be modified to allow the marketing of the FDC.

ITEM NO. 6

Adoption of guidelines for generating pre-clinical and clinical data for recombinant DNA based Vaccines, Diagnostics and other Biologicals.

Member Secretary explained that the Deptt. of Biotechnology has prepared a set of guidelines to be adopted for generating pre-clinical and clinical data for recombinant DNA based vaccines, diagnostic kits and other products.

Chairman observed that the Committee which had undertaken this task consisted of renowned experts and the similar guidelines being followed in various developed countries have been taken into consideration. Board may consider to recommend to adopt these guidelines for industry and regulatory authorities or alternatively may consider to introduce the same as annexure to Schedule Y of the Drugs and Cosmetics Rules.

Prof. Seth pointed out some typographical errors and a few clarification needs to be provided.

After deliberation, the Board was of the opinion that as of now it would be appropriate to adopt it as DTAB approved guidelines and recommended to circulate these after making corrections as suggested by Prof. S.D. Seth.

ITEM NO. 7

Proposal to consider the amendment to the Drugs and Cosmetics Rules for regulating the collection, processing, storage, distribution and transportation of blood and operations of blood banking in the country as per direction of the Supreme Court of India – publishing of final notification.

The Member Secretary explained that as per the recommendations made by previous Board concerning finalization of the rules on Blood Banking System, the finalized Rules were published by Notification in the Official Gazette by the Ministry of Health, vide GSR 245 9E) dated April 5, 1999, and are being placed before this Board.

Dr. Prem Agarwal invited attention of the Board to Part-II of notification related to “Blood Donation Camps” under which three organizations have been authorized to hold Blood Donation Camp. He desired that provision be made to allow organization of such camps by “A Licensed Blood Bank” rather than “A Licensed Govt. Blood Bank” with a view to mobilize vast resources to collect blood from voluntary donors through Camps.

Drugs Controller, Karnataka proposed that Voluntary or Charitable Blood Bank Organizations may also be permitted to organize Blood Donation Camps subject to the condition that these are duly approved by the respective State Blood Transfusion Council.

Drugs Controller, Kerala felt that there was no need to make any changes in provisions relating to authorization of organizations which have been permitted to hold blood donation camps.

After deliberations, the Board, while endorsing notification published on April 5, 1999 by the Govt., agreed to suggest to National Blood Council for allowing all licensed blood bank to organize blood donation camps with the condition that the same shall be approved and monitored by the concerned State Blood Transfusion Councils.

ITEM NO. 8

Deleting of 'Schedule W' of the Drugs and Cosmetics Rules in pursuance of the directions issued by the Supreme Court of India in the case of Hoechst India limited v/s. Union of India.

The Member Secretary explained that Hon'ble Supreme Court of India had dismissed on August 6, 1998, an SLP filed by the Govt. (in the case of M/s. Hoechst (I) Ltd. & other) against the judgement of Delhi High Court striking impugned portions of rule 96 relating to marketing of drugs only under generic or proper name as listed in Schedule 'W' to the Drugs and Cosmetics Rules, 1945.

In pursuance of the directions issued, the Govt. has initiated steps for deletion of Schedule 'W' and the impugned portions of rule 96 to the said rules.

The Board approved the action taken in the matter.

ITEM NO. 9

Revision and upgradation of Schedule 'M' to the Drugs and Cosmetics Rules, 1945 relating to GMPs on manufacture, storage, distribution of drugs including Large Volume Parenterals (I.V. Fluids).

Member Secretary explained that earlier the Board had recommended that Schedule "M", relating to Good Manufacturing Practices (GMPs) should be revised and upgraded so as to lay stricter provisions relating to manufacture of I.V. Fluids.

The Member Secretary also pointed out that National Human Rights Commission, vide its Order dated March 31, 1999, examined the issue of GMPs under the said Schedule for its harmonization to match with WHO Guidelines on manufacture, storage, distribution of I.V. Fluids and all other drugs. A comprehensive report on Schedule M has now been prepared by a subcommittee of Drugs Consultative Committee under the Chairmanship of Commissioner, FDA, Maharashtra which is also placed for consideration of the members. A copy of report was made available to the members who were requested to convey their observation/suggestion to the Member Secretary.

The Board advised that the new guidelines on GMPs be reviewed by Drugs Consultative Committee and the final draft of Schedule 'M' be made available to the Board for its consideration.

ITEM NO. 10

Consideration of the proposal to set up an Expert Committee to review the rationality of certain drug formulations moving in the market and are reported to be irrational or hazardous.

A detailed account of issues related to the agenda which explains the prevailing situation in the country in respect of market authorization of drug formulation by State Licensing Authorities, were given by the Member Secretary.

Member Secretary brought to the notice of the Board members regarding the protracted process which has to be followed by Govt. to weed out a formulation which happens to have been approved by some State Licensing Authority and is later observed to be not in conformity with parameters of therapeutic justification etc. Many a time, these matters also end up in litigation. Therefore, there is a strong need to review the systems prevailing in different States, nature of formulations, especially the combination ones approved at least in last one year and to suggest to the Govt. suitable changes in the policies and existing Rules.

Serious concern was expressed by all members on this issue. It was noted that due to present procedure, it is difficult to assess the exact number of drug formulation approved and being marketed in the country.

Some Members specifically pointed to the fact that many a times, a formulation for which approval is refused by one State is approved by another State's licensing authority for the same applicant. This leads to piquant situation as the same product then moves to the state which has refused permission. From legal point of view such products may require to be banned under section 26 A by Central Govt. This takes a long time and puts unnecessary demand on the available infrastructure.

After extensive discussion on the subject matter, the Board decided to constitute a Committee consisting of following members to undertake an in-depth study of the practices followed by State Authorities for approval of drug formulation and suggest remedial measures to be adopted to contain proliferation of drug products.

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| 1. Representative of IMA | Member |
| 2. Representative of ICMR | Member |
| 3. Representative of IPA | Member |
| 4. Two medical experts (To be nominated
by the Chairman) | Member |
| 5. Two Pharmacologists -do- | Member |
| 6. Two State Licensing Authorities -do- | Member |
| 7. DCG(I) | Member Convenor |

It was also decided that this Committee would also examine drug products referred to it and which need decision by DTAB for continued marketing etc. For this purpose, the committee may co-opt Experts depending upon the nature of drugs to be evaluated.

ITEM NO. 11

Consideration of the proposal to amend relevant rules of the Drugs and Cosmetics Rules, 1945 with regard to upward revision of fee structure prescribed for grant/renewal of sales and manufacturing licences as per Maharashtra model.

ITEM NO. 12

Consideration of the proposal to amend the provisions of the Drugs and Cosmetics Rules for curtailing the number of Licences required for stock, distribution and sale of drugs.

ITEM NO. 13

Consideration of the proposal to amend the provisions of the Drugs and Cosmetics Rules in regard to duration of various licences under the rules.

The Member Secretary, at the onset, apprised the members that the above said proposals were interlinked and may be considered by the Board together.

A detailed background was given relating to (a) upward revision of fee structure prescribed under different forms for grant/renewal of licences to sell and manufacture of drugs and cosmetics in accordance with the Maharashtra modal. (b) to simplify licensing procedure for sale of drugs by reducing the multiplicity of licence and to prescribe a common format through re-structuring/omitting certain forms. (c) to review the period of duration of validity of licence being granted/renewed by the SLAs so as to reduce the administrative load on the Drugs Control Administrations through speed/disposal of the cases rather than following frequent renewals by Field Officers.

Members were also apprised of the deliberation already held by DCC on these matters.

After extensive deliberations, the Board agreed, in principle, for revision of licence fees envisaged in the 3 agenda on the lines of Maharashtra modal, reduction in the multiplicity of licences wherever feasible and enhancement of the duration of licences preferably after first validity of the period to 4-5 years.

Board Members felt that increase in the duration of the licences and their curtailing would mitigate the burden of SLAs concerning routine renewal etc. Such mechanism would enable them to utilize the time to concentrate on increased inspections, supervisory activities besides focusing on other enforcement related activities. The procedural provisions which, in the present day context, may not have remained relevant and if deletion/modification of such provision does not conflict with the basic objectives of Act & Rules i.e. efficacy, quality and safety of drugs, the same need to be reviewed by DCC.

In order to harmonies and rationalize the licensing structure under Rules, the Board felt that the above proposals may be deliberated in the DCC by taking into consideration all aspects involved. DCC may propose a comprehensive amendment required to be carried out under the Drugs and Cosmetics Rules, 1945, for consideration of the Board.

ITEM NO. 14

Consideration of the proposal for enhancement of the licence fees for licences in Forms 10, 10A & 11 for import of drugs.

Member Secretary explained that the licence fees for the grant of import licences in Forms 10, 10A and 11 of the Drugs and Cosmetics Rules was prescribed in 1980 and has not since been revised. The proposal for over-all increase in the fees of sale and manufacturing licences is also being considered by the Board separately. It is, therefore, considered necessary to increase the licence fee for import licence as well so as to harmonise the overall fee structure.

The Board after deliberations agreed to make the following increase in the licence fees for import licences.

- (I) The licence fee for import of drugs for the purpose of examination, test and analysis should be raised from Rs. 15/- to Rs. 75/- for single drug and for more than one drug, a fee of Rs. 15/- per drug should be charged.
- (II) The licence for import of drugs under Forms 10 & 10A should be raised from Rs. 50/- to Rs. 250/- for a single drug and for more than one drug by a fee of Rs. 75/- per item of drug from a single manufacture.
- (III) A fee of Rs. 50/- should be charged for a duplicate copy.

ITEM NO. 15

Registration of firms/products – to be imported and marketed in India.

The Member Secretary explained the registration procedures adopted by most of the countries while permitting import of drugs. It is observed that currently the Drugs and Cosmetics Rules provide for import licence only for limited category of drugs (Sch. C & C1) at a very nominal fee. Also the requirements of documents are not as extensive as being demanded in other countries. There is no formal registration of firms intending to export their drugs to India. It is, therefore, proposed for the consideration of the Board that overall mechanism for registration of drugs products as well as the manufacturing firms may be brought within the ambit of Rules. A reasonable fee structure shall be provided for processing of all import applications.

Chairman observed that since most of formulations may presently be not significant. However, keeping in view the changing scenario in the light of WTO agreements, the Board may consider for adequate provisions for registration.

After detailed deliberation, the Board agreed to the proposals, in principle, and suggested that the same needs to be studied further by the office of DCG(I) and to suggest specific fee structure as well as the procedures.

ITEM NO. 16

Consideration of the proposal for prescribing evaluation fees to be charged from pharmaceutical companies for processing New drugs approval cases – Agenda from Dr. S.D. Seth – member DTAB.

The Board agreed to the proposal, in principle, and noted that reasonable processing fee is charged in most of the countries for evaluation of extensive data pertaining to New drugs applications which also involves consultation with external Experts.

It was suggested that the office of the DCG(I) in consultation with representatives of research based Pharma industry, ICMR and other experts may suggest specific provisions in this regard.

ITEM NO. 17

Consideration of the proposal to exempt approved Centers from the provision of sale licences under Drugs and Cosmetics Rules in respect of supply and distribution of Morphine tablets.

Drugs Controller, Kerala introduced the agenda and explained to the members the urgent need to simplify the procedure for procuring Morphine tablets and its easy availability for Palliative treatment of terminally-ill Cancer patients. One of the proposals was to amend the relevant rules to provide for supply of Oral Morphine tablets by approved Centres without the obligation of taking out drug licence.

Member Secretary, briefed the Board about a recent order of Delhi High Court in a Public Interest Case, directing the Govt. to simplify relevant rules to enable easy availability of Morphine tablets to needy patients. It was explained that the Deptt. of Revenue has already requested the State Govt. to amend State Excise Rules under NDPS Act for this purpose.

After deliberations, the Board approved the proposal to make a relevant entry under Schedule 'K' of the Drugs and Cosmetics Rules exempting identified and approved Pain and Palliative care Centers by the Licensing Authorities. The stocks of the said drugs shall be kept in the custody of a Medical Officer who shall maintain proper records of purchase, supply and distribution of Oral Morphine tablets by the approved Centres.

SUPPLEMENTARY AGENDA

Consideration of banning of Oxytocin injection.

The Broader issues related to the agenda were explained by Member Secretary. In view of the reports about continued misuse of Oxytocin Injection in milch animals and possibility of deleterious effect due to such milk consumed by citizens, Hon'ble MOS for Consumer Affairs and Social Justice, Smt. Maneka Gandhi, has suggested for imposing a general ban on manufacturing of this drug. The Board was also briefed about the action earlier initiated by regulatory authorities to check its indiscriminate use.

Prof. S.D. Seth, clarified that Oxytocin is a polypeptide and gets destroyed in stomach. Moreover, it is also secreted in lactating mothers on teat stimulation during suckling. The possibility of its causing cancer, growth retardation, cardiovascular disease etc. is therefore, not based on sound medical facts. Representative of IVRI clarified that Inj., Oxytocin is an important drug in Vet. practice and is very economical. However, its misuse for non-medical purpose, needs to be strictly stopped.

Members opined that the drug, because of its specific requirements, in medical field has been included in the Essential drugs list.

Sh. Devdas Chhotray, Jt. Secy. Ministry of Food Processing, (Invitee to the meeting) suggested that perhaps, restricting the manufacture of this product to PSUs and thereafter, keeping a track on its distribution may be considered.

Representative of Deptt. of Consumer Affairs, agreed that the whole issue of use and misuse of Oxytocin Injection requires an in-depth examination and suggested to prepare a paper based on the outcome of such study.

Board recommended the formation of the following group.

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| 1. Representative of NDDB | Member |
| 2. Representative of ICMR | Member |
| 3. Representative of Dept. of AH&D | Member |
| 4. Two State Drugs Controllers | Member |
| 5. Representative from Consumer Association | Member |
| 6. A senior Gynaecologist (to be nominated
by the Chairman) | Member |
| 7. DCG(I) or his representative | Member Convenor |

ANY OTHER MATTERS WITH THE PERMISSION OF THE CHAIRMAN

Prof. C.K. Kokate invited attention of the Board on the representation made by the Pharmacy Council of India on the draft Notification published, vide GSR 316 (E) dated May 5, 1999 by the Union Ministry of Health to elicit suggestions and objections on substitution of sub-rule (2) of rule 64 on the qualifications of a competent person for the purpose under the said sub-rule.

Member Secretary explained that the intention of the proposed legislation was not to exclude the qualification already laid for the purpose but to re-structure the qualifications and experience parameters in the said sub-rule which is inclusive of persons holding qualifications as Matriculate or equivalent or Degree holders of a recognized University having proportionate experience in dealing with drugs besides Registered Pharmacists.

After detailed discussion, the Board asked the Member Secretary to consider observation made in the representation received from the Pharmacy Council of India while finalizing the draft notification by the Govt.

The meeting ended with thanks to the chair.