# Indian Centre for Plastics in the Environment

(An Autonomous National Body Registered Under Societies Act)
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**October 28, 2014**

The Under Secretary (Drugs)
Room No. 523 – A,
Ministry of Health and Family Welfare
Government of India,
Nirman Bhawan,
New Delhi 110011

**Sir,**

**Sub: Draft Rules in the Notification No. G.S.R. 701 (E) dated 29 September 2014 proposing to prohibit use of Polyethylene Terephthalate or Plastic Containers for primary packaging of liquid pharmaceutical formulations**

This is with reference to the Notification No.G.S.R. 701(E) dated 29th September, 2014 wherein the draft rules with regard to use of PET and Plastic Containers for primary packaging of liquid pharmaceutical formulations have been issued. We have thoroughly examined the above rules and submit below our comments & objections.

It is stated (in the said Notification) that the Notification has been published on the recommendation of Drugs Technical Advisory Board (DTAB). In order to study the recommendations of DTAB, ICPE had sought copy of the recommendation from the Ministry of Health and Family welfare.

(ICPE letter dated October 10, 2014 and also the printout of the ICPE email to the Ministry is enclosed)

This was not provided. However we were advised by the Ministry to refer to the document:

"MINUTES OF THE 65TH MEETING OF DRUGS TECHNICAL ADVISORY BOARD HELD ON 25TH NOVEMBER, 2013 IN THE CHAMBER OF DGHS, NIRMAN BHAWAN, NEW DELHI – 110002" (MOM), available in the website.

We were also informed that the Recommendations of ICMR Expert Group on PET bottles for Pharmaceutical Applications could be obtained from the PET Bottles Manufacturers' Association,

Based on a study of the above two documents, we are submitting our objections and suggestions.




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1. We observe that the said Notification has been issued on the basis of a representation given by The HIM JAGRITI Uttaranchal Welfare Society, Dehradun and Subsequent discussions recorded in the "MINUTES OF THE 65TH MEETING OF DRUGS TECHNICAL ADVISORY BOARD HELD ON 25TH NOVEMBER, 2013 IN THE CHAMBER OF DGHS, NIRMAN BHAWAN, NEW DELHI – 110002" (MOM) and another document titled "Recommendations of ICMR Expert Group on PET bottles for Pharmaceutical Applications", - marked as Annexure I in another document which is not available to us.

2. We also observe that while the meeting was attended by officials of the medical departments, no official of the Bureau of Indian Standards, the Regulatory Body which is responsible for laying down the Standards for various materials including the use of plastic materials for use in contact with foodstuffs, pharmaceuticals and drinking water, was present. It was also noticed no representative of PET/Plastic Manufacturers was also called.

3. It is clear that the Drug Technical Advisory Board did not consult the Competent Authority which is Bureau of Indian Standards and the concerned Pharmaceutical Companies who use the PET / Plastic Containers for packaging the liquid pharmaceutical formulations or the manufacturers of the basic plastic materials, who obtain necessary regulatory approvals for using the basic plastic materials in direct contact with foodstuffs, pharmaceuticals and drinking water. As a result DTAB did not have proper technical and scientific information, nationally and globally, regarding use of PET/Plastic containers for use in primary packaging of liquid pharmaceutical formulations.

4. Our primary observation is that Drug Technical Advisory Board did not provide scientific advisory to the Ministry of Health and Family Welfare on the issue and arbitrarily recommended to ban use of PET and Plastic Containers for the packaging of liquid oral pharmaceutical formulations for a wide range of patients, merely on the representation of an activist NGO without any scientific examinations and verification.

5. For using any primary packaging material in direct contact with any food products, pharmaceuticals and drinking water, prior approval of the competent authority is mandatory by the packers / users on the safe use of such materials. The competent authority relies on the specific approvals conferred by scientific bodies based on National and International Standards. These Standards are devised based upon prolonged studies and research over a period of time and after due process of deliberations and validation in International / National Forums and thereafter adopted by the Government Authorities in the respective countries.

6. Poly Ethylene Terephthalate (PET) and other plastics materials like Polyethylene (PE) and Polypropylene (PP) etc. are such materials which are approved for use in contact with food products, pharmaceuticals and drinking water as per National and International Standards and Specifications like Bureau of Indian Standards (BIS) in India and International Organisations of Standards (ISO) adopted in more than 150 countries Globally including India. Reference of such Standards are given in the following clauses.

7. IS 12229:1987 – Reaffirmed 2000 titled: "Positive list of constituents of Polyalkylene Terephthalate (PET & PBT) for their safe use in contact with Foodstuffs, Pharmaceuticals and Drinking Water" specifies the permissible constituents of PET and PBT, the allowable migration limits as per Standard Test Methods and other parameters.

(Copy of IS 12229:1987 – Reaffirmed 2000 is enclosed)

8. Indian Standard IS 12252 – 1987 (Reaffirmed 2005) titled: "SPECIFICATION FOR POLYALKYLENE TEREPHTHALATES (PET AND PBT) FOR THEIR SAFE USE IN CONTACT WITH FOODSTUFFS, PHARMACEUTICALS AND DRINKING WATER" specifies the requirements and methods of sampling and test for Polyalkylene Terephthalate (PET and PBT) also known as thermoplastic saturated polyesters polymer materials for the manufacture of plastic items used in contact with foodstuffs, pharmaceuticals and drinking water.

(Copy of IS 12252 – 1987 – reaffirmed 2005 is enclosed)

9. It is customary for any user / packer to get the particular product tested by the approved authority for its compliance with the specifications laid down in the Standards. In India, Central Food Technological Research Institute (CFTRI), Mysore, one of the premier CSIR institutions and a NABL Accredited Laboratory, has conferred such Test Certificate for PET as conforming to Indian Standard IS 12252 – 1987.

(CFTRI Test Report is enclosed)

10. It is observed in the 'Results and Discussions' part of the CFTRI Report that "The migration values ranged from a minimum of 0.044 mg/dm² (0.44 ppm) in n-Heptane (38° C / 0.5h) to a maximum of 0.53 mg/dm² (5.3 ppm) in 3% Acetic Acid (121° C/2h) which are the specified tolerance limits of 10 mg/dm² and 60 ppm as per IS: 12252-1987 (2005). Similarly the migration values ranged from a minimum of 0.004 mg/in² in n-Heptane (49° C/24h) to a maximum of 0.032 mg/in² in 95% Ethanol (49° C/24h) which are within the specified tolerance limits as per US-FDA:177-1630(2011).

CFTRI Test Report giving the details of the tests conducted and the test conditions thereof for a popular PET grade of one of the largest PET Material Manufacturers in the world used for packaging of "Foodstuffs, Pharmaceuticals and Drinking Water" is enclosed.

11. It is alleged that 'Antimony leaches from PET Bottles'.
Similar allegations were made in Andhra Pradesh High Court also, as intimated by The Ministry of Environment and Forests in their letter to ICPE – ref: letter no. F. No. 11-27/2013-HSMD dated 30th December, 2013.

(Copy enclosed)

ICPE response to the above letter is also enclosed.
(Refer ICPE Letters dated January 27, 2014 and February 4, 2014).

Our observations on the issue of Antimony leaching are as below:

In a PIL one complainant produced a copy of test certificates issued by National Test House (Western Region) showing the presence of Antimony in the Migration Test. In the instant case, the NGO – Him Jagriti also makes a statement that "PET leaches Antimony" without any documentary evidence elaborating the actual result.

The Test Certificate of National Test House does not mention the Method of Testing. It only mentions –"As per standard procedure". This is not an accepted protocol of reporting and does not carry any conclusion. A Test Report must clearly state the method of testing, range of acceptable test results and also gives its comments on the tested values. However, in the Test Certificate of National Test House no such indications were provided. It just declared the Test Values, and it appears that Drug Technical Advisory Board also simply concluded, on the basis of such incomplete Test report, that 'Antimony was detected', which is a misleading statement.

This is an incomplete observation in violation of the scientific method of acceptance of any Test Report. The fact is, the migration level reported in the Test Results complies with the Regulations as stipulated in the Standards (IS: 12252 – 1987 (reaffirmed 2005).

As per the report - at 45° C, the overall migration is 0.239 ppm, at 25° C, it is 0.094 ppm and at 15 ° C it is 0.044 ppm, whereas the allowable maximum limit of overall migration as per Indian Standard IS : 12252 – 1987 (Reaffirmed 2005) is 60 ppm. Within this, the Antimony migration was tested as 0.13 ppm. Hence the migration level of Antimony is absolutely within the permissible limit and safe. Not only that,

the overall migration of all constituents taken together is very much within the permissible limit (permissible overall migration is 60 ppm and tested overall migration is 0.239 ppm, which is less than 0.4% of the threshold limit).

In this context we reproduce the relevant clauses of the BIS Standard IS 12252:1987 (reaffirmed 2005):

Quote

Clause 3. REQUIREMENTS

3.2 Other Ingredients – The material shall comply with the threshold limits of the manufacturing residues, polymerization ingredients and auxiliary items as prescribed in IS : 12229-1987 (Positive list of constituents of polyalkylene terephthalates (PET and PBT) for their safe use in contact with foodstuffs, pharmaceuticals and drinking water).

3.4 Overall Migration – The material shall comply with the overall migration limits of 60 mg/l, Max of stimulant and 10 mg/dm2, Max of the surface of the material or article when tested by the method prescribed in IS:9845-1986 (Method of analysis for the determination of specific and/or overall migration of constituents of plastic materials and articles intended to come into contact with foodstuffs (first revision).

Unquote

Thus it is clear mere presence of a material/some leaching, per se, is not a ground for banning the use of the same unless it exceeds the prescribed limits laid down in the BIS Standard.

12. We are repeating this aspect due to the fact that this is a very important parameter and Drugs Technical Advisory Board and ICMR Expert Group did not analyse the representation of the NGO – HIM Jagriti Uttaranchal Welfare Society appropriately and did not verify the scientific and Regulatory status of PET and Plastic Containers in accordance with the Regulatory Standards and had made vague statements that - "as leaching has been demonstrated in various studies, as a precautionary measure PET Bottles should not be used for drugs …"etc.

13. There are allegations that Endocrine Disruptive Chemicals were reportedly found in the leachate of PET bottles. Whereas research reports released by International Body like ILSI (International Life Sciences Institute) Europe Packaging Material

Task Force has concluded on the **Toxicological Status of PET Materials** as below:

13.1."No evidence of toxicity has been detected in feeding studies using animals. Negative results from Ames tests and studies into unscheduled DNA synthesis indicate that PET is not genotoxic. Similar studies conducted with monomers and typical PET intermediates also indicate that these materials are essentially non toxic and pose no threats to human health."

13.2. On Migration of PET Components, the Report says:

"Similar studies designed to detect metal additive migration (e.g. antimony catalyst) show only trace levels of antimony (less than 5 ppb). Oral toxicity studies using the extracted species have been completed, and in all cases no adverse effects have been observed at exposures expected to occur from the use of PET packaging system."

13.3. The Report makes a General Conclusion:

**"General Toxicity and genotoxicity studies on PET, its monomers and typical intermediates indicate that this material does not pose a threat to human health. There is a significant body of evidence demonstrating that PET shows no oestrogenic activity."**

(Copy of Report of International Life Sciences Institute enclosed)

These conclusions are sufficient to show that PET Bottles are absolutely safe for use in contact with Foodstuffs, Pharmaceuticals and Drinking Water as per laid down Government Safety Regulations.

14. PET Bottles and other Plastics Containers conforming to the specifications laid down in Standards are used worldwide in contact with Foodstuffs, Pharmaceuticals and Drinking Water. The process of establishing these Standards took several years by the world scientific community including India. Scientific parameters of Indian Standards are similar to those used internationally.

15. It is alleged that 'Phthalate' leaches out from PET / plastic bottles.

It is strongly rejected that 'Phthalate' including diethylhexyl phthalate (DEHP) is in any way involved with PET material. PET is manufactured in large scale organised manufacturing facilities. Phthalates are not a part of the raw materials for the manufacture of PET neither is it generated any time during the manufacturing process

of PET. PET does not and cannot release any type of Phthalate including DEHP due to any reaction or during migration. The NGO – Him Jagriti etc. is trying to defy the fundamentals of Chemistry by claiming that "Phthalates leach from PET/plastic bottles". Other common plastic containers used for packaging of liquid drug solutions are made of Polyethylene (PE) and Polypropylene (PP). These plastics also are not in any way linked to Phthalates.

We would like to draw the attention of the Ministry to the fact that some types of Phthalates are used as plasticizers for manufacture of Flexible Polyvinyl Chloride (PVC) compounds. However, PVC is generally not used for making bottles for packaging of liquid pharmaceutical solutions. Hence we have not considered it necessary to elaborate on the details of PVC in the instant case.

16. Currently PET, Polyethylene (PE) and Polypropylene (PP) are the most widely used plastic materials for making Plastic Containers for packaging foodstuffs, pharmaceuticals and drinking water, apart from many other products. Further, PET, PE and PP are approved materials for use in contact with Foodstuffs, Pharmaceuticals and Drinking Water as per various International Standards including the Standards adopted by Bureau of Indian Standards.

    (Ref: IS 10146:1982 Reaffirmed 2003 Polyethylene for its safe use in contact with foodstuffs, pharmaceuticals and drinking water)

    (Ref: IS 10141: 1982 First Revision 2001 Positive List of Constituents of Polyethylene in Contact with Foodstuffs, Pharmaceuticals and Drinking Water)

    (Ref. IS 10910:1984: Reaffirmed 2003: Polypropylene and its copolymers for its safe use in contact with foodstuffs, pharmaceuticals and drinking water)

    (Ref: IS 10909(Part 0/Sec 0):2001: Positive list of constituents of polypropylene and its copolymers in contact with foodstuffs, pharmaceuticals and drinking water (first revision)

17. The Polyethylene materials fulfill the requirements of materials intended for use in medical applications as per various clauses in European Pharmacopoeia and United States Pharmacopoeia. Certificates from some of the popular grades of Polyethylene manufactured by one of the best known manufactures in the world are enclosed. The certificates clearly mention that no type of 'Phthalate' is used for the manufacturing of Polyethylene grades.

    (Technical Data Sheets of Polyethylene Grades)

18. While discussing the specific case of primary packaging of liquid pharmaceutical formulation for paediatric use, Polio Vaccination formulation is recognized as one of the largest single applications which are packed in Polyethylene (PE) Bottles. After a prolonged battle against the dreaded Polio disease over a period of several decades, India has ultimately been able to eradicate Polio from the country and achieved the distinction of 'Polio – Free' Country! These polio vaccines packed in Plastic Containers made of PE, are in use since the 1970's! In fact the success of India in eradicating polio owes much to the development of hygienic, simple and economic Plastic Containers for delivering the vaccine.

    We are not aware of any scientifically researched document acceptable by International Scientific Forum, which says that PE is not suitable for use as primary packaging material for paediatric drugs.

19. Intra Venous Liquid Bottles (I.V. Bottles) contain life saving drugs for patients of all ages including child, old and pregnant women and women in the reproductive age. In the 1970's, I.V. Bottles used to be made of Glass. However with the development of technology, Polyethylene (PE), which is a BIS approved material for such application, has replaced glass as the material of construction of I.V. Bottles.

20. Disposable Injection Syringes being used to inject life saving drugs to patients of all ages and all categories are made of Polypropylene (PP), a plastic material approved as per Standards.

21. As stated in above clauses, PET and other Plastics Materials like PE, PP etc are approved material for use in contact with Foodstuffs, Pharmaceuticals and Drinking Water. However, pharmaceutical companies, before selecting a particular grade of plastic container / material for the packaging of a specific type of drug formulation manufactured by them, conduct long term 'Stability Studies' as per test procedures laid down in various pharmacopeias like USP, IP or EP. Hence use of PET and other Plastics Materials for packaging of different types of drugs is based on science established by various scientific bodies and accepted by Regulatory Bodies across the world including India. These Standards and procedures have been established by continuous research work over years by the entire scientific community world over.

22. Billions of PET bottles are being used worldwide for packaging of Drinking Water, Soft Drinks and Pharmaceuticals including in India since decades. As explained earlier, these uses are allowed only after compliance with Standards and Regulations laid down in India and abroad. Billions of IV (Intra Venous) injectable fluid bottles

made of Polyethylene (PE) have been and are being used worldwide including India, for the life saving treatment of human as well as animals. Billions of PE flexible pouches have been and are being used in India for packaging of liquid milk. Billions of Disposable Injection Syringes made of Plastics have been and are being used worldwide including India.

In all these applications, glass was replaced by different plastics materials – PP, PE and PET etc. It will not be out of context to bring it to the notice of the Government of India that recently there was a spurt of PIL in different courts in India against the use of PET Bottles for packaging of liquors. It was alleged that packaging of liquors in PET bottles was not safe for human consumption and also with the allegation that PET bottles are not recycled and create environmental pollution. All these PIL cases were dismissed by the respective High Courts. The petitioner of PIL had made appeal to the Supreme Court of India against the judgment of the Madhya Pradesh High Court. The Supreme Court of India dismissed the appeal saying that "We do not find any legal and valid ground for interference".

(Copy of Supreme Court judgment is enclosed along with some other judgments)

23. We would like to draw the attention of the Ministry of Health and Family Welfare that the Ministry was not provided with the correct information and scientific report on the issue, which otherwise is a well studied and accepted subject nationally and internationally. The observation of Drug Technical Advisory Board (as mentioned in the said MOM) that
Quote
"As leaching has been demonstrated by various studies, as a precautionary principle PET bottles should not be used for drugs meant for use in vulnerable groups such as pediatric age group and for pregnant women. For these groups glass bottles should be preferred for dispensing pharmaceuticals"
Unquote

is wrong and is devoid of any scientific and technical basis. In Clause No. 7 above, we have explained the issue of leaching with the documentary evidence of actual test reports. This suggestion of DTAB without any scientific basis is required to be rejected outright by Government of India.

24. Doubts have been raised about the ability of PET / other Plastic Containers to withstand the robust environmental conditions and rough terrains of India. It is also alleged that in some parts of India temperature during the summer goes up to 48° C at which the leaching of the constituents may rise inside the bottles.

The correct position is that as evidenced in the CFTRI Test Certificates, migration tests are carried out at higher than normal temperatures, some being even more than 100° C. Hence this doubt does not stand against the use of PET / Plastic Containers.

Important applications like Intravenous Solutions packed in PE bottles are sterilized at 110° C for one hour. When the bottle is made of PP Copolymer, the sterilization temperature is 120° C for half an hour.

We must remember that the storage conditions of any drug are clearly mentioned on the level of the bottle. Higher storage temperature would impair the drug quality itself.

25. It is completely incorrect to say that introduction of plastic bottles for the packaging of pharmaceuticals formulations in place of glass bottles were made without proper studies. From the early part of 1970's, there has been a steady shift towards the use of plastics replacing the conventional glass materials. Examples are well known:
    - I V Bottles
    - Disposable Syringes
    - Liquid Pharmaceutical Formulations

    For each of these applications series of tests were conducted worldwide and scientific approvals were obtained before actual implementation. Copies of Standards of different plastic materials for use in contact with Foodstuffs, Pharmaceuticals and Drinking Water have been enclosed, as mentioned in earlier paragraphs.

26. On Environmental issues, Plastics including PET are among the most environment friendly materials. When we compare the properties of PET / Plastic Containers with Glass, Aluminium etc. as packaging materials, we find that there is minimum impact on environment during entire life cycle of PET / Plastic Containers compared to alternatives.

    The advantages of PET Bottles are:

    i). Superior packaging to product ratio, PET containers being 63% and 47% more energy efficient than glass bottles and aluminium containers respectively.

ii). PET Bottles are 32% more energy efficient than glass bottles during delivery of 1000 gallons of soft drinks. (The result is extrapolated for glass bottles carrying pharmaceutical liquids also).

iii). Glass Bottles generate 230% more atmospheric emissions compared to PET.

iv). 100 Kgs oil is required to produce 1000 – one litre PET bottles as against 230 Kgs of oil for equivalent glass bottles.

v). PET / Plastic Containers help in fuel saving (during transportation) due to their lesser weight.

vi). Breakage Issue:

- Due to fragile nature, glass bottles break in large numbers during transportation and handling.
- Source (material) reduction is possible thereby adding 'less material to environment'. This is an important part of 'Packaging Waste Regulation'.

(Source: CFTRI and other published literature on the subject)

vii). Green House Gas emissions are much less in use of plastic packaging compared to Glass Packaging.

(McKinsey study in 2006)

viii). Plastics including PET are 100% recyclable. Glass is also recyclable; however recycling process of Glass consumes more energy compared to that of Plastics.

27. We are bringing all these before the Government, as we have reason to believe that all these baseless allegations and PIL are being raised on behalf of manufacturers of other packaging materials, notably glass bottles manufacturers, for commercial reasons. We submit that Government of India should not yield to any such pressures, but decide the issue strictly on scientific and accepted international standards.

    We submit that PET Bottles and other plastic containers are absolutely safe for use as per the BIS and the test reports of approved laboratories. There is no valid reason for the Ministry of Health and Family Welfare to even consider a ban on use of PET and other Plastic containers as packaging material for pharmaceutical liquid formulations in contravention of existing established Rules and Standards.

28. At the end we would like to mention that the DTAB Committee itself concluded that information provided in the representation of HIM JAGRITI and according to the available literature, is not sufficient to establish a definite correlation of

casualty of Plastic Containers for Pharmaceutical products and adverse health effects.

The DTAB Committee also felt that scientific evidence needed to be generated in a time bound manner through systematic studies to arrive at answers to the issues of leachbility from plastic container, types of toxicants leached and health hazard due to exposure of the leached toxicant.

29. We feel that all the above issues have already been studied scientifically over years by the scientific community of the world and due approvals were conferred for usage of such plastic containers for use in contact with food stuffs, pharmaceuticals and drinking water. The National and International Standards have already been published, as referred in the earlier paragraphs and also enclosed. However, if DTAB/GOI desire to conduct further studies on the subject matter, we do not have any objection to such initiative. Such a study should be conducted in a National Lab / CSIR institution involving all stakeholders following the scientific route and recording the outcome in a transparent manner before arriving at any conclusion. Till such time, there must not be any ban on the use of PET/Plastic Containers for use in contact with any type of pharmaceutical formulations, which are already approved as per law. The Government cannot take any action to ban packaging of any type of pharmaceutical formulations in the country merely on the representation of a NGO without any proven or established scientific basis.

Should the Government desire, ICPE will be ready to discuss the issue in detail and provide clarifications.

Thanking you

Yours truly
For Indian Centre for Plastics in the Environment

**S.K.Ray**
**Hon. Secretary/Member – Executive Committee**