CONFEDERATION OF INDIAN PHARMACEUTICAL INDUSTRY (SSI) (Regd.)

(Registered Office : A-3/314, First Floor, Paschim Vihar, New Delhi-110063)

Mailing Add. : 128, Lok Vihar Appts., Vikaspuri, New Delhi - 18. Fax : 011-28538801, E-mail : sk_aries2001@yahoo.co.in, Website : www.cipi.in
Chairman Office : **BELCO PHARMA** 515, MIE, Bahadurgarh-124507, Haryana E-mail : pkgupta_cipi@yahoo.in

Chairman :	*Co-Chairman :*	*Secretary General :*	*Treasurer :*
P. K. Gupta	**Dr. A.M.D. Nambudiri**	**B. Sethuraman**	**R.K. Jain**
Cell : 09811106606	Cell : 09847030460	Cell : 09444083286	Cell : 09312285623

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Bahadurgarh Pharmaceuticals Mfrs. Association, Bahadurgarh-124507

Ref. No.: CIPI/2014/512
28th October 2014

Shri K. L. Sharma,
Joint Secretary,
Ministry of Health & Family Welfare,
Nirman Bhawan,, New Delhi-110 011

Sub: Gazette Notification No. GSR 701 (E) dated 29.9.2014 – use of PET containers as primary packing of drug formulations – objections / suggestions

Sir,

This has reference to the Gazette Notification No. GSR 701 (E) dated 29.09.2014 of the Ministry of Health & Family Welfare containing draft rules to amend the Drugs & Cosmetics Rules, 1945 to prohibit the use of PET containers for packing of liquid oral formulations for pediatric use as well as formulations meant for geriatrics, women in reproductive age and pregnant women.

We here under now submit our objections / suggestions to the said notification as desired therein.

We understand that the amendment is being proposed on the basis of the representation from the Him Jagriti Uttranchal Welfare Society, Dehradun to the Hon'ble Health Secretary, Ministry of Health & Family Welfare and to the Drugs Controller General. The issues raised by the Him Jagriti are as under:

i) that PET may yield endocrine disrupters,
ii) that phthalates leach from PET / plastic bottles, and
iii) that antimony leaches from PET bottles

This matter was also deliberated by the Expert Committee of DTAB constituted to examine the said issue and in their meeting held on 12.07.2013, the Expert Committee had opined that information provided in the representation of Him Jagriti and according to the available literature, it is not sufficient enough to establish a definitive correlation of causality of plastic containers for pharmaceutical products and adverse health effects.

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We fail to understand the reason behind the above said notification when the expert committee of the Ministry itself has found that PET containers for pharmaceutical products have not found to have adverse health effects. The instant notification is not supported by any authentic scientific data or studies to establish the health risks to the patients using drug formulations packed in PET containers which has compelled the Government to impose a ban on the use of such containers.

The pet bottles are being used worldwide for packing of liquid oral formulations and nowhere in the world there exists any restriction for their use for packing of liquid oral formulations for pediatric use as well as formulations meant for geriatrics, women in reproductive age and pregnant women.

The Indian Pharmacopoeia 2010 provides for use of plastic containers under General Chapter 6 covering plastic containers for non-parenteral preparations, for parenteral preparations and for ophthalmic preparations which are followed by the Indian Pharmaceutical Industry, The US Pharmacopeia also contains guidelines for plastic containers under chapter 661which are also followed by the Industry wherever required.

Further BIS has specified under IS 12252-1987 the specifications for polyalalkylene terephthalates (PET & PBT)for their safe use in contact with food stuffs, pharmaceuticals and drinking water which are followed by the Industry and are accepted by the Drug Regulatory Authority of the Country.

As regard the arguments being advocated that (i), PET may yield endocrine disrupters,(ii) phthalates leach from PET / plastic bottles, and iii) antimony leaches from PET bottles, we respond with the following scientific facts:

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1) Endocrine Disruptor:

(i) PET material has been assessed by International Life Sciences Institute (ILSI), Europe and has confirmed that general toxicity and genotoxicity on PET indicate that the material does not pose a threat to human health. The extract of the finding is reproduced below:

"There has been increasing public concern that certain man-made chemicals, if absorbed into the body, can act like a female hormone estrogen disrupting the normal endocrine cycle and causing genetic disorders or adverse reproduction effects like reduced male sperm contents. It is important to stress that the chemistry of the compounds that are used in the manufacture of PET shows no evidence of estrogenic activity. There is significant body evidence that demonstrates that the use of PET is not a concern and is perfectly safe in this respect. PET and its components have no links with any reported endocrine disrupters."

(ii) PET material is not listed as a potential endocrine disrupter in the list of chemicals identified by the United States Environment Protection Agency (USEPA).

(2) Phthalates:

A type of phthalate (orthophthalate precisely) is often used to make plastics, other than PET, more flexible. It is also called a plasticizer. A plasticizer is never used in the manufacture of PET material. We reproduce hereunder the clarification issued by Health & Safety FAQS, NAPCOR, USA on this matter:

"Do I need to worry about phthalates in PET? No. Phthalates (pronounced as THA-lates) are a class of chemicals that includes three subsets, each with different properties. PET or polyethylene terephthalate belongs to on of these phthalate subsets, but not the one most commonly associated with the term.

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Orthophthalate is the phthalate subset most commonly referenced and discussed in popular literature and on internet sites; it has been to some negative press, often used to make various plastics more flexible, this type of phthalate is also called a plasticizer.

PET does not contain plasticizers or orthophthalates. Plasticizers are never substituted for terephthalate used in manufacture of PET, nor are the two ever mixed.

PET packaging is selected by companies for a wide variety of product applications because it is safe, strong, shatter-proof and recyclable" when PET bottles do not contain a phthalate, the question of leaching of phthalates is irrelevant and misleading.

(3) Leaching:

Only those substances which are having low molecular weight or are volatile have tendency to leach or migrate. PET materials contain very high molecular weight substances which do not leach or migrate. We here under reproduce a text from the study conducted by ILSI, Europe on this subject:

"Food grade PET essentially contains only very high molecular weight species with little or no migration propensity, so actual migration is minuscule. However the slightest interactions are now detectible by sophisticated analytical techniques and monitoring is relatively easy. Many studies have been made on PET and have always given a reassuring picture.

It may be noted that PET is safe even when exposed to higher temperatures in regard to leaching involving liquids at higher temperatures. In this regard we mention the test conditions recommended under USP 231

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USP 231 (661)
Dist tiled Water (49°C/10 days)
25% Ethanol (49°C / 10 days)
50% Ethanol (49°C / 10 days)
n-Heptane (49°c / 10 days)

(4) Antimony

One particular widely used additive, antimony trioxide, has given cause of concern. However a new and very comprehensive and detailed animal feeding study concludes that there is no risk arising from the use of antimony trioxide in PET products. A diet containing up to 20g/kg of antimony trioxide has no detectable toxic effects. Genotoxicity tests were also negative."

Keeping in mind the above studies and clarification, it may be stated that the claim about the severe adverse effects on human health by drug formulations in PET bottles is unfounded. The proposed ban on use under the said notification has not been substantiated by any authentic and robust scientific data.

Further the drug formulations packed in PET bottles are subjected to stability testing like other formulations as per D&C Act, 1940 and the Rules framed there under. The requirement for stability testing is that the drug be tested in the same container-closure system as that in which the drug is marketed. The requirement is also for accelerated testing at high temperature and relative humidity. Submission of accelerated and real time stability data is one of the basic requirements of the regulator before marketing permission for a drug formulation is given. The Drug formulations using PET bottles as primary packaging have met all these requirements. As per our members so far no adverse reports have come to their notice for the reasons attributable to PET bottles.

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Further we wish to bring to your kind notice that 5 PILs filed in the different High Courts of the Country against the use of PET containers (including for drug formulations) have been dismissed by the respective High Courts. Finally a SLP filed before the Supreme Court was also dismissed. The Apex Court observed that the petitioners have failed to produce any scientific studies or details against the use of PET packaging.

Now our request is that the Gazette Notification No. GSR 701 (E) dated 29.9.2014 containing the draft rules to prohibit the use of PET containers for packing of liquid oral formulations for pediatric use as well as formulations meant for geriatrics, women in reproductive age and pregnant women may be re-examined in view of the above facts and shall be withdrawn. Its implementation will have ramifying affects. On close reading of the draft rules it can be said that standard formulations which are administered to the above category of population with adjustment in the doses will also be affected.

Instead of banning the use of PET containers, the Ministry may re-examine the present specifications and standards of PET containers for packing liquid oral preparations in line with international practices and may revise them wherever necessary to be followed by the Industry.

Thanking you,

For Confederation of Indian Pharmaceutical Industry

P.K. Gupta
Chairman

cc: Dr. Harsh Vardhan, Union Minister for Health and FW
Mr. Lov Verma, Secretary, MOHW