F. No. DCGI/Misc/2016-61
Directorate General of Health Services
Central Drugs Standard Control Organisation
Office of Drugs Controller General India.

FDA Bhawan, Kotla Road,
New Delhi-110002
Dated ..01-06-16.....

NOTICE

In order to examine the feasibility to replace Draize test which is applied on Rabbit eyes and skin by alternative methods for testing of eyes and skin irritation or corrosion. A committee has been constituted to give its recommendation for taking necessary action in the matter.

The committee in its first meeting held on 23rd May, 2016 deliberated the issue and perused the related literature applicable globally *vis-a-vis* Schedule-Y requirement. The committee opined that as there is international trend towards replacing tests on animals with alternatives it may be considered in Indian context, after obtaining assessment of feasibility, validation, preparedness of Indian laboratories etc.

It is further decided to seek the feedback/opinion from different stakeholders *viz.* laboratories involved in carrying out preclinical toxicity tests from public, private sector and related organisation from pharmaceutical industry before taking the final decision in the matter.

Points of discussion of minutes of meeting and Feedback Proforma for obtaining comments are attached for ready reference.

In view of above all the stake holders including testing laboratories are requested to kindly provide their comments to the undersigned within a period of two week to enable this office to take necessary action in the matter.

(Dr. G. N. Singh)
Drugs Controller General (I)

Points of Discussion of Minutes of Meeting

The committee perused the related literature applicable globally *vis-a-vis* Schedule-Y requirement. It noted that several alternative tests are being evolved and validated to different stages. The OECD guidelines have also suggested use of alternative methods. The committee also noted that US FDA and European Union have initiated the process of use of alternative methods.

The committee opined that as there is international trend towards replacing tests on animals with alternatives it may be considered in Indian context, after obtaining assessment of feasibility, validation, preparedness of Indian laboratories etc.

The main contentions are; are Indian pre clinical testing laboratories equipped for such change? have the alternative methods been validated particularly in India?, do we have adequate number of laboratories to undertake the toxicity testing of all required substances by alternative methods ?. If the answer is NO or PARTIAL, how much time and what efforts will be required for capacity building for using alternate methods?

In this regard, it was therefore decided to seek the feedback/opinion from different stakeholders *viz.* laboratories involved in carrying out preclinical toxicity tests from public, private sector and related organisation from pharmaceutical industry on the above issue. The committee decided that data in this connection may be obtained in the "Feedback from stakeholders".

Feedback proforma from stakeholders

(Response requested in 15 days)

Government of India is considering to replace the above said tests with alternative methods for eye irritation test in rabbits and Dermal toxicity tests for skin irritation/corrosion tests in rabbits and skin sensitization in guinea pigs and mice by alternative methods with respect to the approval of new drugs and therefore examining the feasibility of such replacement in Indian situation. In this regard, you are requested to provide the following information-

1. Name of the stake holder / Organization:
2. Address
   Telephone
   FAX
   E-mail
3. Name of the person and designation submitting the profile.....:
4. Whether your facility is currently conducting / has experience with Draize test/ocular toxicity test and skin irritation/corrosion tests in rabbits and skin sensitisation test in guinea pigs or mice?
5. If your facility conducts the eye and skin irritation tests on rabbit then, for what type of following pharmaceuticals/chemicals are the tests conducted? (Please provide Average number of tests done in last year)

   a. Pharmaceuticals: NO————————/year

   b. Chemicals /pesticides: ——No————————/year

   c. Chemicals / surfactants / environmental pollutants No————————/year

6. To which regulatory agency(ies), the reports are submitted?

7. Do you have facilities to carry out following *in-vitro* tests which have been adopted by the OECD?

   A. Tests for skin irritation

   a. OECD TG 430: *In vitro* trans cutaneous electrical resistance test method for skin corrosion **Y/N**

   b. OECD TG 431: *In vitro* reconstructed human epidermis test method for skin corrosion. **Y/N**

   c. OECD TG 435: *In vitro* membrane barrier test method for skin corrosion. **Y/N**

d. OECD TG 439: *In vitro* reconstructed human epidermis test method for skin irritation. **Y/N**

e. OECD Guidance Document 203: guidance document on an IATA for skin corrosion and irritation. **Y/N**

B. **Tests for Eye irritation**:

a. OECD TG 460: Fluoresce in leakage test method for identifying ocular corrosives and severe irritants. **Y/N**

b. OECD TG 437: Bovine corneal opacity and permeability test method. Y/N

c. OECD TG 438: Isolated chicken eye test method. **Y/N**

d. OECD TG 491: Short time exposure *in vitro* test method for identifying

(i) chemicals inducing serious eye damage. **Y/N**

(ii) chemicals not requiring classification for eye irritation or serious eye damage. **Y/N**

e. OECD TG 492: Reconstructed human cornea-like epithelium (RhCE) test method for identifying chemicals not requiring classification and labelling for eye irritation or serious eye damage. **Y/N**

f. Draft OECD TG: Cytosensor microphysiometer method: An in vitro Method for Identifying Ocular 3 Corrosive and Severe Irritant Chemicals as well as Chemicals not classified as Ocular Irritants. The cytosensor microphysiometer method is also recommended by the European Union Reference Laboratory for alternatives to animal testing to differentiate water-soluble ocular corrosives and severe irritants and non-irritants in a top-down and bottom-up approaches, respectively. **Y/N**

C. Test for Skin Sensitisation

a. OECD TG 442c: In Chemico Skin Sensitisation – Direct Peptide Reactivity Assay (DPRA). **Y/N**

b. OECD TG 442d: In Vitro Skin Sensitisation – ARE-Nrf2 Luciferase Test Method (Keratino SensTM). **Y/N**

c. OECD draft TG: Human Cell Line Activation Test (h-CLAT) ; final test guideline expected to be published later in 2016). **Y/N**

8. In case the eye and skin irritation tests on rabbits are replaced in Chapter-3 of Schedule-Y of Drugs and Cosmetics Act, with alternative *in-vitro* and *ex-vivo* methods, do you have preparedness? Y/N

a. If 'No, what will be the time period requirement?

9. Any other Comment?