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CONSUMER PRODUCT SAFETY COMMISSION

[Docket No. CPSC-2012-0037]

16 CFR Part 1500

Codification of Animal Testing Policy

AGENCY: Consumer Product Safety Commission.

ACTION: Proposed Statement of Policy on Animal Testing

SUMMARY: The Consumer Product Safety Commission (CPSC or Commission) proposes to codify its statement of policy on animal testing, as amended, which was previously published in the *Federal Register*. The amended statement of policy on animal testing is intended for manufacturers of products subject to the Federal Hazardous Substances Act (FHSA) to find alternatives to animal testing and reduce the number of animal tests under the FHSA.

DATES: Written comments and submissions in response to this notice must be received by [**insert date that is 75 days after publication in the Federal Register**].

ADDRESSES: You may submit comments, identified by Docket No. CPSC-2012-0037, by any of the following methods:

Electronic Submissions

Submit electronic comments in the following way:

Federal eRulemaking Portal: http://www.regulations.gov. Follow the instructions for submitting comments.

To ensure timely processing of comments, the Commission is no longer accepting comments submitted by electronic mail (e-mail) except through www.regulations.gov.

Written Submissions

Submit written submissions in the following way:

Mail/Hand delivery/Courier (for paper, disk, or CD-ROM submissions), preferably in five copies, to: Office of the Secretary, Consumer Product Safety Commission, 4330 East West Highway, Bethesda, MD 20814; telephone (301) 504-7923.

Instructions: All submissions received must include the agency name and docket number for this proposed statement of animal testing policy. All comments received may be posted without change, including any personal identifiers, contact information, or other personal information provided, to http://www.regulations.gov. Do not submit confidential business information, trade secret information, or other sensitive or protected information electronically. Such information should be submitted in writing.

Docket: For access to the docket to read background documents or comments received, go to http://www.regulations.gov.

FOR FURTHER INFORMATION CONTACT: Leslie E. Patton, Ph.D., Project Manager, Office of Hazard Identification and Reduction, U.S. Consumer Product Safety Commission, 4330 East West Highway, Bethesda, MD 20814; telephone (301) 504-7848; lpatton@cpsc.gov.

SUPPLEMENTARY INFORMATION:

The Federal Hazardous Substances Act (FHSA), 15 U.S.C. 1261–1278, requires appropriate cautionary labeling on certain hazardous household products to alert consumers to the potential hazards that a product may present. Among the hazards addressed by the FHSA are products that are toxic, corrosive, irritants, flammable, combustible, or strong sensitizers. The FHSA and the Commission regulations at 16

CFR part 1500 provide certain test methods related to testing on animals to determine the existence of the hazards addressed by the FHSA.

On May 30, 1984, the Commission adopted an animal testing policy that minimized the number of test animals required for toxicity testing and clarified when animal testing might be needed (1984 Policy) published in the *Federal Register* on May 30, 1984 (49 FR 22522). These guidelines advised product manufacturers to use alternatives to animal testing whenever possible, including: (1) prior human experience, (2) existing animal or limited human test results, and (3) expert opinion. The 1984 Policy stated:

> it is important to keep in mind that neither the FHSA nor the Commission's regulations require any firm to perform animal tests. The statute and its implementing regulations only require that a product be labeled to reflect the hazards associated with that product. While animal testing may be necessary in some cases, Commission policy supports limiting such tests to the lowest feasible number and taking every feasible step to eliminate or reduce the pain or discomfort that can be associated with such tests….The Commission resorts to animal testing only when the other information sources have been exhausted. Furthermore, the FHSA regulations, at 16 CFR 1500.4, clearly state that reliable human experience shall take precedence over different results from animal data.

Id. at 22523. The 1984 Policy also stated that if non-animal test systems for prediction of toxicity and irritancy are accepted by the scientific community as adjuncts or alternatives to whole-animal testing, "[The CPSC Directorate for] Health Sciences will incorporate the techniques into the Commission's compliance program to the extent feasible and will recommend any changes to the Commission's statutes or regulations that may become appropriate as the result of advances in testing methods that are developed." *Id.*

Since the 1984 Policy, there have been new methods accepted by the scientific community as replacements or adjuncts to animal tests for predictions of toxicity and

irritancy. Such developments in testing have been made in recent years, particularly since the National Institutes of Health Revitalization Act was passed in 1993 (Public Law 103-43, Section 1301), directing the National Institute of Environmental Health Sciences (NIEHS) to establish a method and criteria for the validation and regulatory acceptance of alternative testing methods. The NIEHS created the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM; http://iccvam.niehs.nih.gov/home.htm), which was made permanent by the ICCVAM Authorization Act of 2000, Public Law 106-545. The duties of ICCVAM are to review, optimize, and validate new, revised, or alternative test methods that encourage the reduction, refinement, or replacement of the use of animals in testing. ICCVAM has representatives from 15 federal regulatory and research agencies, including the CPSC. These agencies generate, use, or provide information from toxicity test methods for risk assessment purposes. In addition, ICCVAM provides test recommendations to federal agencies and other stakeholders to facilitate appropriate interagency and international harmonization of toxicological test protocols.

ICCVAM submits recommendations for a test method to federal agencies that require or recommend acute or chronic toxicological testing. According to Public Law 106-545, these agencies should promote and encourage the development and use of alternatives to animal test methods for regulatory purposes, and ensure that any new or revised acute or chronic toxicity test method is valid for its proposed use. Federal agencies have 180 days from the time of submission to identify any relevant test methods for which the ICCVAM test recommendations may be added or substituted, review such test recommendations, and notify ICCVAM if they will adopt the ICCVAM test

recommendations. Since 2003, the Commission has approved, where applicable, the recommendations made by ICCVAM to reduce and refine animal testing applicable to test methods under the FHSA. In order to make the ICCVAM recommendations and Commission's animal testing policy more accessible and transparent to interested parties, the Commission proposes to update its regulations on animal testing at 16 C.F.R. part 1500, published elsewhere in this *Federal Register*, and establish a Web page on the CPSC's website at http://www.cpsc.gov/businfo/animaltesting.html regarding the ICCVAM recommendations and new developments in test methods that further reduce or refine animal testing.

In addition, the Commission proposes to update its statement on animal testing policy to reflect the ICCVAM recommendations that have been reviewed and adopted by the CPSC as being appropriate tests for assessing hazards under the FHSA. In order to make this statement of policy more accessible and transparent to interested parties, the Commission proposes to codify the policy at 16 CFR 1500.232.

Since this is a statement of policy, a delayed effective date is not required. 5 U.S.C. 553(d)(2). A delayed effective date is not required for the additional reason that this policy is not a substantive rule. 5 U.S.C. 553(d)(3). Accordingly, this codification will become effective upon the publication of a final policy statement in the *Federal Register.*

List of Subjects in 16 CFR Part 1500

Consumer protection, Hazardous substances, Imports, Infants and children, Labeling, Law enforcement, Reporting and recordkeeping requirements, and Toys.

For the reasons given above, the Commission proposes to amend 16 CFR part 1500 as follows:

PART 1500 –[AMENDED]

1. The authority for part 1500 continues to read as follows:

Authority: 15 U.S.C. 1261–1278, 122 Stat. 3016; the Consumer Product Safety Improvement Act of 2008, Pub. L. 110–314, §104, 122 Stat. 3016 (August 14, 2008).

2. Add a new section 1500.232 to read as follows:

§ 1500.232 – Statement on Animal Testing Policy

(a) Summary

(1) The U.S. Consumer Product Safety Commission issues this statement of policy on animal testing and alternatives to animal testing of hazardous substances regulated under the Federal Hazardous Substances Act (FHSA). The FHSA requires appropriate cautionary labeling on certain household products to alert consumers to the potential hazard(s) that the products may present. Among the hazards addressed by the FHSA are toxicity, corrosivity, sensitization, and irritation.

(2) In order to determine the appropriate cautionary labeling, it is necessary to have objective criteria by which the existence of each hazard can be determined. Hazards such as toxicity, tissue corrosiveness, eye irritancy, and skin irritancy result from the biological response of living tissue and organs to the presence of the hazardous substance. One means of characterizing these hazards is to use animal testing as a proxy for the human reaction. In fact, the FHSA defines the hazard category of "*highly toxic*" in terms of animal toxicity when groups of 10 or more rats are exposed to specified amounts of the substance. The Commission's regulations under the FHSA concerning

toxicity and irritancy allow the use of animal tests to determine the presence of the hazard when human data or existing animal data are not available.

(3) Neither the FHSA nor the Commission's regulations *require* animal testing. The FHSA and its implementing regulations only require that a product be labeled to reflect the hazards associated with that product. While animal testing may be necessary in some cases, Commission policy supports limiting such tests to a minimum number of animals, and the policy also advocates measures that eliminate or reduce the pain or discomfort to animals that can be associated with such tests. The Commission has prepared this statement of policy with respect to animal testing to encourage the manufacturers subject to the FHSA to follow a similar policy.

(4) In making the appropriate hazard determinations, manufacturers of products subject to the FHSA should use existing alternatives to animal testing whenever possible. These include prior human experience, literature sources that record the results of prior animal testing or limited human tests, and expert opinion. The Commission recommends resorting to animal testing only when the other information sources have been exhausted. At this time, the Commission recommends use of the most humane procedures with the fewest animals possible to achieve reliable results. Recommended procedures are summarized in the following statement and can be accessed on the Commission's webpage at: http://www.cpsc.gov/businfo/animaltesting.html.

(b) Statement of Policy on Animal Testing.

(1) The Commission reviews staff recommendations on alternative test methods developed by the scientific and regulatory communities. Current descriptions of test method recommendations approved by the Commission can be accessed via the Internet

at: http://www.cpsc.gov/businfo/animaltesting.html. Overall, the Commission prefers test methods that reduce stress and suffering in test animals and that use none or fewer animals while maintaining scientific integrity. The Commission strongly supports the use of validated alternatives to animal testing. The following parts of this section outline some of these alternatives. Testing laboratories and other interested persons requiring assistance interpreting the results obtained when a substance is tested in accordance with the methods described here, or in following the testing strategies outlined in this statement of policy and the regulations under 16 CFR part 1500, should refer to the Commission's animal testing webpage at http://www.cpsc.gov/businfo/animaltesting.html.

(a) Acute toxicity - The traditional FHSA animal test for acute toxicity determines the median lethal dose (LD_{50}) or lethal concentration (LC_{50}), the dose or concentration that is expected to kill half the test animals. Procedures for determining the median LD_{50}/LC_{50} are described in section 2(h)(1) of the FHSA and supplemented in §1500.3(c)(1) and (2) and the test method outlined in §1500.40. The Commission recommends using modifications of the traditional LD_{50}/LC_{50} test during toxicity testing that reduce the number of animals tested, whenever possible. Approved modifications are identified on the website at: http://www.cpsc.gov/businfo/animaltesting.html and include:

(i) *In vitro* and *in vivo* test methods that have been scientifically validated and approved for use in toxicity testing by the Commission;

(ii) Valid *in vitro* methods to estimate a starting dose for an acute *in vivo* test;

(iii) A sequential version of the traditional LD_{50}/LC_{50} tests described in §1500.3(c)(1) and (2) and the test method described in §1500.40, in which dose groups are run successively rather than simultaneously;

(iv) A limit-dose test, where the LD_{50}/LC_{50} is determined as a point estimate, which can still be used to categorize a hazard, although it gives no information on hazard dose response.

(b) Dermal irritation/corrosivity - A weight-of-evidence analysis is recommended to evaluate existing information before *in vivo* dermal irritation testing is considered to determine appropriate cautionary labeling. This analysis should incorporate any existing data on humans and animals, validated *in vitro* test results (valid tests are identified on the Commission's animal testing website at: http://www.cpsc.gov/businfo/animaltesting.html), the substance's dermal toxicity, evidence of corrosivity/irritation of one or more structurally related substances or mixtures of such substances, data demonstrating low or high pH (≤ 2 or ≥ 11.5) of the substance, and any other relevant physicochemical properties that indicate the substance might be a dermal corrosive or irritant. If there is any indication from this analysis that the substance is either corrosive or irritating to the skin, the substance should be labeled appropriately. If the substance is not corrosive *in vitro*, but no data exist regarding its irritation potential, human patch testing should be considered. If *in vitro* data are unavailable, and human patch testing is not an option, a tiered *in vivo* animal test is recommended.

(i) In a tiered *in vivo* dermal study, a single rabbit is tested initially. If the outcome is positive for corrosivity, testing is stopped, and the substance is

labeled appropriately. If the substance is not corrosive, two more rabbits should be patch-tested to complete the assessment of skin irritation potential.

(ii) If a tiered test is not feasible, the Commission recommends the test method described in §1500.41. Note that in any *in vivo* dermal irritation test method, the Commission recommends using a semi-occlusive patch to cover the animal's test site, and eliminating the use of stocks for restraint during the exposure period, thereby allowing the animal free mobility and access to food and water.

(c) Ocular irritation - A weight-of-evidence analysis is recommended to evaluate existing information before any *in vivo* ocular irritation testing is considered. This analysis should incorporate any existing data on humans and animals, validated *in vitro* test data (identified on the Commission's animal testing website at: http://www.cpsc.gov/businfo/animaltesting.html), the substance's dermal corrosivity/irritation (primary skin irritants and corrosives are also usually eye irritants, and therefore, do not need to be tested in the eye), evidence of ocular irritation of one or more structurally related substances or mixtures of such substances, data demonstrating high acidity or alkalinity of the substance, and any other relevant physicochemical properties that indicate that the substance might be a dermal corrosive or irritant or ocular irritant.

(i) When the weight-of-evidence is insufficient to determine a substance's ocular irritation, a Commission-approved *in vitro* assay for ocular irritancy should be run to assess eye irritation potential and determine labeling.

Valid *in vitro* assays are identified at: http://www.cpsc.gov/businfo/animaltesting.html. If no valid *in vitro* test exists, the test strategy for determining dermal corrosion/irritation outlined in section (b)(ii) above can be followed to determine ocular irritation.

(ii) If the dermal test strategy outlined in section (b)(ii) leads to a conclusion of *not corrosive*, a tiered *in vivo* ocular irritation test should be performed, in which a single rabbit is exposed to the substance initially. If the outcome of this initial test is positive, testing is stopped, and the substance is labeled an eye irritant. If the outcome of this initial test is negative, one to two more rabbits are tested for ocular irritation, and the outcome of this test will determine the label. If a tiered test is not feasible, the Commission recommends the test method described in §1500.42.

(iii) When any ocular irritancy testing on animals is considered necessary, including the method described in §1500.42, the Commission recommends a threefold plan to reduce animal suffering: (1) the use of preemptive pain management, including topical anesthetics and systemic analgesics that eliminate or reduce suffering that may occur as a result of the application process or from the test substance itself; (2) post-treatment with systemic analgesics for pain relief; and (3) implementation of humane endpoints, including scheduled observations, monitoring, and recording of clinical signs of distress and pain, and recording the nature, severity, and progression of eye injuries. The specific techniques that

have been approved by the Commission can be found at:

http://www.cpsc.gov/businfo/animaltesting.html.

Dated: June 25, 2012

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Todd A. Stevenson, Secretary
Consumer Product Safety Commission

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