Date of Hearing: March 14, 2023

ASSEMBLY COMMITTEE ON JUDICIARY
Brian Maienschein, Chair
AB 357 (Maienschein) – As Amended March 7, 2023

As Proposed to be Amended

SUBJECT: ANIMAL TEST METHODS: ALTERNATIVES

KEY ISSUE: SHOULD THE PROVISIONS OF CALIFORNIA'S LANDMARK LAW THAT PROHIBITS ANIMAL TESTING WHEN AN ALTERNATIVE EXISTS BE REVISED AND RECAST TO BETTER PROTECT ANIMALS AND REFLECT THE 23 YEARS OF IMPROVEMENTS IN SCIENCE AND TECHNOLOGY SINCE THAT MEASURE WAS FIRST ADOPTED?

SYNOPSIS

In 2000, California enacted a landmark law to limit unnecessary testing on animals when a viable alternative exists. In the two decades since the passage of that act, scientific testing technology has improved dramatically and the efficacy of animal testing has come under increasing scrutiny. This modest measure seeks to update the 2000 law by revising and recasting several definitions, most notably eliminating references to medical testing and replacing them with references to biomedical testing. Additionally, this bill enhances the reporting requirements for a manufacturer or contract testing facility to submit to the Attorney General regarding the use of animals in various scientific tests, and provides greater public transparency surrounding the use of animal testing in California.

This measure is sponsored by the Humane Society of the United States and is supported by a coalition of animal rights organizations. The proponents of this measure highlight the need to modernize California's existing animal testing laws to reflect improvements in science and best practices utilized in the testing industry. This measure is opposed by California Life Sciences, Biocom California, and Animal Health Institute, who argue that this bill may jeopardize testing on emerging medications that require various federal approvals, and that an exception for testing products to be used by animals may be necessary. Proposed amendments appear to address some of the opposition's concerns. However, it seems likely some unresolved issues may remain and the author pledges to continue working with the various stakeholders.

SUMMARY: Updates the provisions of California's landmark legislation that prohibited testing on animals when an alternative exists. Specifically, **this bill**:

1) Defines "alternative test method or strategy" to mean a test method, including a new or revised method, that fulfills all of the following criteria:

    a) Does not use animals;

    b) Provides information of equivalent or better scientific quality and relevance compared to traditional animal test methods and includes, but is not limited to, computational toxicology and bioinformatics, high-throughput screening methods, testing of categories of chemical substances, tiered testing methods, in vitro studies, and systems biology; and

c) Has been identified and accepted for use by a federal agency or program within an agency responsible for regulating the specific product or activity for which the test is being conducted.

2) Defines "biomedical research" to mean the investigation of the biological processes and causes of disease or research conducted to increase fundamental scientific knowledge, and to expand the understanding about how processes in living organisms develop and function but does not include traditional animal test methods done to assess the safety or efficacy of chemicals, ingredients, drugs, medical devices, vaccines, product formulations, or products.

3) Defines "traditional animal test method" to mean a process or procedure using animals to obtain information on the characteristics of a chemical or agent and that generates information regarding the ability of a chemical or agent to produce a specific biological effect under specified conditions.

4) Prohibits manufacturers and contract facilities from using traditional animal test methods within this state for which an appropriate alternative test method or strategy exists, or a waiver has been granted by the agency responsible for regulating the specific product or activity for which the test is being conducted.

5) Requires, when an alternative test method or strategy does not exist, manufacturers and contract testing facilities to use a traditional animal test method using the fewest number of animals possible and reducing the level of pain, suffering, and stress of an animal used for testing to the greatest extent possible.

6) Provides that nothing in the bill prohibits the use of any nonanimal test method or strategy for the testing of any product, product formulation, chemical, drug, medical device, vaccine, or ingredient, as specified.

7) Provides that nothing in this bill prohibits the use of traditional animal testing to comply with requirements of state or federal agencies.

8) Deletes references in existing law to alternative animal tests scientifically validated and recommended by the Inter-Agency Coordinating Committee for the Validation of Alternative Methods and adopted by the relevant federal agency or agencies and the definition of the Inter-Agency Coordinating Committee for the Validation of Alternative Methods

9) Deletes the existing definition of "medical research."

10) Requires, commencing January 1, 2025, and annually thereafter, a manufacturer or contract testing facility in this state using traditional animal test methods to report to the Attorney General the number and species of animals used, the type and number of alternative test methods or strategies used, the number of waivers used, and the purpose of the use of the traditional animal tests, alternative test methods or strategies, and waivers.

11) Requires the Attorney General to publish the information submitted pursuant to 10) in a publicly available manner on its internet website.

12) Provides that a violation of this bill is enforceable through a civil action by the Attorney General, the district attorney of the county in which the violation is alleged to have occurred,

or a city attorney of a city or a city and county having a population in excess of 750,000 and in which the violation is alleged to have occurred.

13) Provides that if the court determines that the Attorney General or district attorney is the prevailing party in the enforcement action, the official may also recover costs, attorney's fees, and a civil penalty not to exceed five thousand dollars ($5,000) in that action.

EXISTING LAW:

1) Requires a depositary of living animals to provide the animals with necessary and prompt veterinary care, nutrition, and shelter, and treat them kindly, and provides that a failure to do so may result in civil penalties, as specified. (Civil Code Section 1834.)

2) Prohibits manufacturers and contract testing facilities from utilized animal tests when an appropriate alternative test method has been scientifically validated and recommended by the Inter-Agency Coordinating Committee for the Validation of Alternative Methods, and the alternative test has been approved by the relevant federal agency or agencies or program within an agency responsible for regulating the specific product or activity for which the test is being conducted. (Civil Code Section 1834.9 (a).)

3) Provides that nothing in 2) prohibits the use of any alternative nonanimal test method for the testing of any product, product formulation, chemical, or ingredient that is not recommended by the Inter-Agency Coordinating Committee for the Validation of Alternative Methods. (Civil Code Section 1834.9 (b).)

4) Provides that nothing in 2) prohibits the use of animal tests to comply with requirements of federal agencies when the federal agency has approved an alternative nonanimal test, and federal agency staff concludes that the alternative nonanimal test does not assure the health or safety of consumers, or when an animal test is required by a state agency. (Civil Code Section 1834.9 (c).)

5) Provides that the prohibition in 2) does not apply to medical research. (Civil Code 1834.9 (e).)

6) Defines several terms related to the prohibition on animal testing set forth in 2). (Civil Code Section 1834.9 (f).)

7) Provides that a violation of the prohibition in 2) is enforced by a civil action for injunctive relief brought by the Attorney General, the district attorney of the county in which the violation is alleged to have occurred, or a city attorney of a city or a city and county having a population in excess of 750,000 and in which the violation is alleged to have occurred. (Civil Code Section 1834.9 (d).)

8) Prohibits a testing facility from conducting a canine or feline toxicological experiment in this state to achieve discovery, approval, maintenance of approval, notification, registration, or maintenance of a pesticide or chemical substance, except as specified. (Civil Code Section 1834.9.3 (b).)

9) Prohibits a manufacturer from importing for profit, selling, or offering for sale in this state, any cosmetic, if the cosmetic was developed or manufactured using an animal test that was

conducted or contracted by the manufacturer, or any supplier of the manufacturer, as specified. (Civil Code Section 1834.9.5.)

FISCAL EFFECT: As currently in print this bill is keyed fiscal.

COMMENTS: In 2000, California became the first state in the nation to enact a widespread prohibition on needless testing of consumer products on animals when the Legislature enacted SB 2082 (O'Connell) Chap. 476, Stats. 2000. That measure prohibited animal testing if an alternative test were approved by the Interagency Coordinating Committee on the Validation of Alternative Methods. In the intervening years, the Interagency Coordinating Committee on the Validation of Alternative Methods has ceased validating alternatives to animal testing. Also, new methods and strategies for alternatives to animal testing developed. Accordingly, this measure revises, recasts, and updates the 2000 law to ensure that no animals will needlessly suffer because of an antiquated statutory prohibition on animal testing. In support of this measure, the author notes:

> California is a scientific and technological leader in non-animal alternatives. Science is rapidly moving away from outdated animal tests as many faster, less expensive, and more human-relevant alternative methods become available. This legislation would ensure that companies in California are taking advantage of these new testing strategies as soon as they are available and appropriate for use.
>
> AB 357 would require companies and their contract testing facilities to use test methods that replace animal testing when they are available and provide information of equivalent or better scientific quality and relevance for the intended purpose. The bill would also require a manufacturer or contract testing facility using traditional animal testing methods to report annually to the Attorney General information regarding their use of animal testing.

Animal testing frequently subjects animals to needless suffering and produces poor quality results. There is no doubt that the use of animals in scientific and product research has significantly benefitted human beings. However, many product developers and scientific observers are increasingly concerned that animal experimentation is based on scientifically flawed premises and that in many cases, animal testing retains its acceptability only because clear alternatives have not been identified. For example, dramatically rising costs and extremely high failure rates in drug development have led many to re-evaluate the value of animal studies. A study found that only about 12 percent of pharmaceuticals pass preclinical testing to enter clinical trials. Of those, only 60 percent successfully complete phase I trials. Overall, approximately 89 percent of novel drugs fail human clinical trials, with approximately one-half of those failures due to unanticipated human toxicity. (Gail Van Norman, *Limitations of Animal Studies for Predicting Toxicity in Clinical Trials: Is it Time to Rethink Our Current Approach?* (November 2019) JACC: Basic to Translational Science, at p. 849.)

One prominent, and recent, example of the potential deficiencies in using dogs to test the safety of products can be found in the EPA's most recent review of the herbicide Glyphosate, more commonly known as Round Up. In 2017, the EPA required both 90-day and chronic toxicity tests on dogs; and based on the results, the EPA eventually permitted the product to keep its registration. (U.S. EPA Office of Pesticide Programs Draft Human Health Risk Assessment in Support of Registration Review (Dec. 12, 2017) at. pp. 30-31.) That same year, however, the California Office of Environmental Health Hazard Assessment required Round Up to be added to the list of chemicals necessitating a warning pursuant to Proposition 65 due to the

carcinogenic risks posed by the product. (https://oehha.ca.gov/public-information/press-release/press-release-proposition-65/glyphosate-be-added-proposition-65.) Although the state and federal government are presently contesting the validity of various agency findings, the ongoing debate would seem to validate the studies that call into question the veracity of the results obtained by testing the chemicals on dogs.

Further, despite the deeply rooted assumption that animal models accurately predict human toxicity, even cursory examination of the concordance of animal and human trials raises concerns. An analysis of 2,366 drugs concluded that, "results from tests on animals (specifically rat, mouse and rabbit models) were highly inconsistent predictors of toxic responses in humans." Similar results were found for nonhuman primates and dogs, where the author argued that canine data indicating an absence of toxicity would only increase the probability that the compound would show no toxic effects in humans from 70 percent to 72 percent - a very small, almost negligible effect that comes at huge costs. (Bailey, et. al, An Analysis of the Use of Animal Models in Predicting Human Toxicology and Drug Safety, (2014), Alternatives to Laboratory Animals Journal, available at https://journals.sagepub.com/doi/abs/10.1177/026119291404200306.)

Perhaps most troubling about the ongoing use of animal testing is that in many cases, non-animal tests could produce better results. For example, "tissue chips" are being developed that have the potential to generate 3D replicas of nearly a dozen types of human cells, including brain, liver, and skin cells. (https://ncats.nih.gov/tissuechip/chip.) One study noted that the use of these chips and similar human-like samples were actually better at predicting human skin sensitivities than animal tests. (Kleinstreuer NC et al., *Non-animal methods to predict skin sensitization (II): an assessment of defined approaches.* (2018) Critical Reviews in Toxicology, at pp. 359-374.) Indeed, ongoing studies by the National Institutes of Health are rapidly developing new and better methods to test a wide array of products for human consumption using non-animal methods.

Given the inadequacy of many animal tests, California has been a national leader on eliminating unnecessary tests on animals. Recognizing the need to move away from cruel and inaccurate tests on animals, California has been a national leader in eliminating needless animal testing. As noted in 2000, the state was a national leader in prohibiting most animal tests when an alternative existed. Building upon that legislation, in 2018 California enacted SB 1249 (Galgiani) Chap. 899, Stats. 2018 to prohibit the use of animal testing in the development of cosmetic products starting in 2020. Additionally, last year the Legislature approved SB 879 (Wiener) Chap. 551, Stats. 2022, to prohibit unnecessary toxicological testing on dogs and cats. Furthermore, California was a national leader in ending the practice of sending shelter pets to be used for animal research, thus ensure these pets could be adopted to loving homes and not used to test consumer products. (AB 2269 (Waldron) Chap. 568, Stats. 2016.)

This bill. As noted above, some aspects of California's 23-year old prohibition on animal testing when an alternative exists have become unworkable, particularly those aspects of the law which are related to the obsolete Interagency Coordinating Committee on the Validation of Alternative Methods and their approval of alternatives. This bill revises, recasts, and modernizes the 2000 law to address current scientific realities. First, this measure eliminates the references to the Interagency Coordinating Committee on the Validation of Alternative Methods and instead prohibits animal tests when a viable non-animal method or strategy exists. Furthermore, recognizing the growing prevalence of biomedical research, the bill specifically defines that term

to mean, "the investigation of the biological processes and causes of disease or research conducted to increase fundamental scientific knowledge, and to expand the understanding about how processes in living organisms develop and function but does not include traditional animal test methods done to assess the safety or efficacy of chemicals, ingredients, drugs, medical devices, vaccines, product formulations, or products."

Additionally, the bill makes several changes and updates to the codes and deletes several definitions to conform to the above-described reforms to the 2000 law. Finally, the bill implements a new reporting requirement whereby a manufacturer of consumer products or contract testing facility in this state that uses traditional animal test methods must report to the Attorney General the number and species of animals used, the type and number of alternative tests, methods or strategies used, the number of waivers issued, and the purpose served by the traditional animal tests, alternative test methods or strategies, and waivers. The bill also requires that the Attorney General must post and make available the results of this data collection on the Department of Justice's internet website. It should be noted that the Attorney General is presently vested with the power to enforce the 2000 statute. Thus, the reporting of this data to the Attorney General appears to be appropriate.

Opponents worry that this bill may prohibit some necessary tests. This bill is opposed by California Life Sciences, Biocom California, and the Animal Health Institute. One of the biggest areas of concern for the opposition is the transition from the term "medical research" to the broader term "biomedical research." This mirrors some concerns raised by the same organizations regarding the aforementioned SB 879. The opposition contends the definitional change may impact the, "life science industry's ability to ensure the safety and efficacy of numerous medical products." Indeed, the current federal Food and Drug Administration standards for the required use of animal testing can be described as opaque at best. At this time the Food and Drug Administration generally still requires submission of preclinical animal data in investigational new drug applications. However, as noted above, there is a growing body of literature demonstrating alternative methods and technologies that may have utility in improving the nonclinical drug development process. These alternative methods include the following: (1) in vitro tests using cell lines; (2) tissue samples; (3) use of alternative organisms such as bacteria; (4) 3-dimensional modeling and bioprinting; (5) in silico tests; (6) organ-on-chip technologies, such as 3-dimensional organoids; (7) computer modeling; (8) and phase 0 in-human microdosing trials.

Furthermore, it should be noted that this bill does not ban all animal testing. In the event that no alternative exists and no waiver has been given by regulators, the text of Civil Code Section 1834.9 as amended by this bill appears to allow animal testing to occur. Nonetheless, as discussed below, the author is proposing several amendments to address these concerns and pledges to continue to work with stakeholders.

Proposed author's amendments seek to address some of the opposition concerns regarding the scope of the new definitions. Seeking to ameliorate some of the concerns the author is proposing several amendments to this measure. First, and most notably, the author is proposing to revise part of the definition of "biomedical research." Thus, as amended, the term will be defined as:

(3) ~~**(A)**~~ "Biomedical research" means the investigation of the biological processes and causes of disease or research conducted to increase fundamental scientific knowledge, and to expand the understanding about how processes in living organisms develop and function ***but shall not***

include traditional animal test methods done to assess the safety or efficacy of chemicals, ingredients, drugs, medical devices, vaccines, product formulations, or products.

~~**(B) Notwithstanding subparagraph (A), "biomedical research" shall not include testing done to assess the safety or efficacy of chemicals, ingredients, drugs, medical devices, vaccines, product formulations, or products.**~~

Additionally, the author is proposing to amend the definition of "alternative test method or strategy" as follows:

"Alternative test method or strategy" means a test method, including a new or revised method, that fulfills all of the following criteria:

(A) ~~**(i)**~~ Does not use animals.

(B) ~~**(ii)**~~ Provides information of equivalent or better scientific quality and relevance compared to traditional animal test methods ***and includes, but is not limited to, computational toxicology and bioinformatics, high-throughput screening methods, testing of categories of chemical substances, tiered testing methods, in vitro studies, and systems biology***.

(C) ~~**(iii)**~~ Has been identified ~~**by a validation body, such as the Interagency Coordinating Committee on the Validation of Alternative Methods or the Organization for Economic Co-operation and Development,**~~ and accepted for use by a federal agency or program within an agency responsible for regulating the specific product or activity for which the test is being conducted.

~~**(B) "Alternative test method or strategy" includes, but is not limited to, computational toxicology and bioinformatics, high-throughput screening methods, testing of categories of chemical substances, tiered testing methods, in vitro studies, and systems biology.**~~

Finally, the proposed amendments make two technical changes to replace references to "animal tests" with references to "traditional animal test" for consistency through the bill's drafting. Although the proposed narrowed definitions appear to address some of the opposition concerns, it remains unclear if the amendments are sufficient to address all of the opposition's issues.

ARGUMENTS IN SUPPORT*:* This bill is sponsored the Humane Society of the United States and is supported by a half-dozen animal rights organizations. The Humane Society notes:

It is estimated that more than 50 million animals are used in experiments each year in the United States. Thousands may be used for a single test, and experiments are often excruciatingly painful for the animals and can vary in duration from days to months to years. In some instances, animals are not given any kind of pain medication to help relieve their suffering or distress during or after the experiment on the basis that it could affect the experiment. Animals are often killed once an experiment is over so that their tissues and organs can be examined, although it is not unusual for animals to be used in multiple experiments over many years.

Animal testing is costly, time-consuming, and often poorly predictive of toxicity in humans. Non-animal alternatives can provide more efficient as well as more effective chemical safety

assessments. Human cell-based tests and advanced computer models, for example, deliver human-relevant results in hours or days, unlike some animal tests that can take months or years.

By minimizing animal testing and focusing on the use of faster, cost effective, and more reliable testing methods, companies can save lives, time, and money. This legislation would ensure companies take advantage of those new testing strategies as soon as they are approved for use.

***ARGUMENTS IN OPPOSITION**:* As noted this bill is opposed by several biomedical and biotechnical research organizations. In opposition to the bill California Life Sciences and Biocom California jointly write:

AB 357 removes the exemption in current law for "medical" research and replaces it with an exemption only for "biomedical" research, and as such would prohibit animal testing for drug, device, vaccine, or chemical development when 1) an alternative test method exists and 2) such testing is not required by a state agency or a federal agency that has said the existing alternative method does not assure the health or safety of consumers. Furthermore, animal testing that is conducted would need to be reported to the state and would be publicly published.

The use of animals in testing for drug, device, vaccine, or chemical development products has long been a matter of public debate. The life sciences industry, however, is unable to fully eliminate the use of all animals in research. While the life science industry adheres to both the 3Rs principles and rigorous ethical guidelines governing the use of laboratory animals – including review of all activities by an Institutional Animal Care and Use Committee (IACUC), as mandated by PHS (Public Health Service) Policy, USDA Regulations, and voluntary accreditation bodies, such as AAALAC international – its reliance on some degree of animal research is indispensable for ensuring the safety and efficacy of drugs, medical devices, and vaccines. By excluding these forms of safety testing from its definition of "biomedical research", AB 357 would hamstring the life sciences industry's ability to ensure the safety and efficacy of these medical products.

REGISTERED SUPPORT / OPPOSITION:

Support

The Humane Society of the United States (sponsor)
American Society for the Prevention of Cruelty to Animals
Animal Legal Defense Fund
Cruelty Free International
Humane Society Veterinary Medical Association
Marin Humane
National Anti-Vivisection Society
Physicians Committee for Responsible Medicine
Rise for Animals
Social Compassion in Legislation

Opposition

Animal Health Institute
Biocom California
California Life Sciences

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