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Assess flame retardants with care—Response

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LETTERS

Edited by **Jennifer Sills**

Editorial expression of concern

On 14 October 2016, *Science* published the Research Article "Sustained virologic control in SIV$^+$ macaques after antiretroviral and $\alpha_4\beta_7$ antibody therapy" by S. N. Byrareddy *et al*. (*1*). The virus used in this study had a stop codon in the SIV *nef* gene. The presence of the stop codon was known by Dr. Villinger, who provided the virus, and he selected this strain intentionally as he believes it provides a better model for chronic HIV infection. However, this information was not communicated to other authors of the Byrareddy paper nor explicitly stated in the manuscript. In macaques, viral variants that can replicate more effectively because they have this stop codon corrected are selected over a period of weeks. Variability in correcting the stop codon introduces variation in the level of viral pathogenicity between different animal subjects, which may have affected the conclusions and should have been discussed in the Research Article. Byrareddy *et al*. (*1*) has been corrected to indicate that the virus used was not wild-type SIVmac239, but SIVmac239-*nef-stop*.

On 21 March 2019, *Science* published an Editorial Expression of Concern alerting readers to this error. Three studies published in this issue of *Science* have attempted to replicate this work, two using the same SIVmac239-*nef-stop* virus used in Byrareddy and one using a different SIV strain (*2*–*4*). In no case did treating with antibody against integrin $\alpha_4\beta_7$ result in robust, long-term decreases in SIV load after stopping antiretroviral therapy. In addition, a phase-1 clinical trial in humans published in *Science Translational Medicine* failed to show any significant benefit of including a similar FDA-approved antibody in an HIV treatment protocol (*5*).

We are maintaining an Editorial Expression of Concern on Byrareddy *et al*. (*1*) to alert readers that current evidence suggests that the reported result is not robust and therefore does not provide a good basis for guiding work on therapies for HIV. *Science* is not moving beyond an Editorial Expression of Concern because neither the Byrareddy authors, the authors of the attempted replication studies, nor the editors can account for the differences in results. Moreover, there is a substantial scientific basis supporting the idea that targeting the integrin $\alpha_4\beta_7$ may have a positive impact on the course of infection.

Jeremy Berg
Editor-in-Chief

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Human activities and climate change have put Florida's Indian River Lagoon in peril.

PHOTO: JEFFREY GREENBERG/UNIVERSAL IMAGES GROUP VIA GETTY IMAGES

Florida lagoon at risk of ecosystem collapse

One of North America's most biodiverse estuaries is at risk of irreversible shifts in population dynamics, community structure, and ecosystem function. The Indian River Lagoon in Florida lies at the intersection of warm-temperate and subtropical climates and has sustained human existence for at least 11,000 years (*1*). Human-induced impacts on the ecosystem have led some species, such as the smalltooth sawfish, to become endangered (*2*) and led other species, such as the dusky seaside sparrow, to go extinct (*3*).

Anthropogenic perturbations have increased within the Indian River Lagoon in recent years as a result of accelerated population growth, urbanization, habitat alteration, pollution, and toxic spills (*4*), with disastrous ecological outcomes for lagoon fish and wildlife. The synergistic effects of these anthropogenic stressors have been exacerbated by global climate change (*5*). One example of these synergistic effects is harmful algal blooms, which have caused major seagrass die-offs (*6*). Other effects include large-scale marine mammal, bird, and fish kills (*7*). Up to 70% of the U.S. Atlantic coast population of Florida manatees aggregate in the Indian River Lagoon, directly exposing them to a combination of ongoing and emerging threats (*8*, *9*). Fish in the lagoon are experiencing external health abnormalities (lesions, tumors, parasites, and diseases) at a frequency that is an order of magnitude higher than those in other Florida estuaries (*10*). Despite 40 years of

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regulation and restoration aimed at mitigating impacts in the Indian River Lagoon, ecosystem degradation has continued and is expected to worsen.

Anthropogenic activities are diminishing biodiversity and thwarting ecological dynamics in estuarine ecosystems worldwide (*11*, *12*). Advances in biodiversity-based management strategies are needed to inspire environmentally sustainable human behaviors. The Indian River Lagoon is a barometer for how human influences can affect ecological balance and human health, and it serves as a warning for increasingly burdened estuaries in a developing world. Without innovative management solutions designed to restore water quality and critical habitats, the future ecological health and sustainability of the Indian River Lagoon estuary are in jeopardy.

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Assess flame retardants with care

In their Perspective "Toward fire safety without chemical risk" (19 April, p. 231), J. de Boer and H. M. Stapleton discuss the safety of flame retardants as if they all belong to one class of chemicals. The authors assert that "all substitutes [used to replace older halogenated flame retardants] showed harmful effects." This generalization does not do justice to improvements in flame retardants or to the variety of chemicals available.

Recent flame retardants have been made with properties that render them safer than older alternatives. Polymeric compounds with high molecular weight can now be made with flame-retarding properties (*1*, *2*). Contrary to previously used molecules with lower molecular weight, the new versions do not migrate from the polymers to which they are added, such as clothing or upholstery, minimizing the chance of exposure (*2*). Most important, from a toxicology standpoint, these chemicals are essentially not bioavailable, meaning they are unlikely to cross epithelial membranes, enter the body, and cause harm even if exposure occurs (*2*–*4*). For example, the U.S.

As the search for the safest flame retardants continues, accurate assessment is critical.

Environmental Protection Agency (EPA) lists a butadiene styrene brominated copolymer as an alternative to the flame retardant hexabromocyclododecane (*2*).

It is inaccurate to generalize flame retardants as if they all have similar effects. At the request of the U.S. Consumer Product Safety Commission, the National Academies of Sciences, Engineering, and Medicine (NASEM) recently investigated whether the safety assessment for organohalogen flame retardants (OFR) can treat all OFRs as a single class (*5*). The committee considered 161 OFRs and attempted grouping based on functional and structural properties as well as known or predicted biological activity. The committee concluded that it is not possible to treat OFRs as a single class for hazard assessment. However, the

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committee identified 14 subclasses for which this might be feasible. In contrast with the broad statements of de Boer and Stapleton condemning all OFRs as hazardous and posing unacceptable risk, the NASEM report sets the stage for a careful, scientifically robust assessment of the safety of these important substances known to save human lives.

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COMPETING INTERESTS

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Response

Osimitz *et al.* suggest that we mischaracterized all halogenated flame retardants (FRs) by classifying them as one class of hazardous compounds. We agree that there are differences among FR classes and subclasses. However, over the past two decades, we have repeatedly observed a pattern of regrettable substitutions, in which one harmful FR was replaced by another that was later found to be potentially harmful (*1*, *2*). In each case, it took years for toxicologists to prove the harmful effects of the substitute. Meanwhile, the production of the harmful FRs continued and high volumes of these chemicals were released into our environment, resulting in human exposure to millions of people (*3*–*5*). Once ample evidence was available, a new substitute appeared on the market and the process repeated itself. Therefore, we urgently ask regulatory authorities to breach this cycle and be much more active in restricting the production of hazardous FRs.

Osimitz *et al.* propose FRs that use polymeric compounds with high molecular weight as a way forward. We mentioned the only one that has been identified, the butadiene styrene brominated copolymer, in our Perspective. Other polymeric FRs are still considered confidential business information, preventing most scientists from characterizing their toxicity and exposure potential. Indeed, such polymers are not bioavailable. However, they pose a clear disadvantage in the circular economy, as they are difficult to recycle due to the high concentration of bromine in the polymer (*6*). In addition, we do not know what will happen with those compounds later in their life; will they fall apart and degrade to more harmful halogenated substances? When these materials end up in a landfill or if they are burned, they present a risk for the formation of hazardous polybrominated dioxins and furans (*6*).

We agree that there may be one or two organohalogen FRs that are not considered toxic, but there are many more non-halogenated FRs that are considered safer, as we emphasized in our Perspective. The European research project ENFIRO generated a report documenting a series of safer alternatives, such as zinc stannate, melamine polyphosphate, and aluminium diethylphosphinate for many applications (*7*). In addition, most halogen-free FRs perform better in smoke suppression and decrease the amount of hazardous gases such as benzene and toluene released from polyvinyl chloride during combustion, which may save more lives (*8*).

There is a rational argument for using available non-halogenated alternatives such as metal-based or melamine-based FRs. Ultimately, testing for harmful effects of these chemicals before use should be carried out by industry. Chemical FRs should be "benign by design" (*9*).

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