The EPA's Developmental Neurotoxicity Test:

Inhumane and Ineffective

Without providing public notice or an opportunity for comment, the Environmental Protection Agency (EPA) established a new series of animal-based chemical-testing guidelines in December 2000.[1] Among these is a developmental neurotoxicity test (DNT), which is intended to assess nervous-system effects in newborn rodents. In this test, female rats are force-fed chemicals throughout their pregnancies and while they nurse their newborn pups. The pups are then subjected to a series of behavioral tests and are later killed and their brains examined. The DNT has been the subject of widespread criticism, on both scientific and humane grounds, for reasons such as the following:

Massive Animal Use

The DNT kills between 1,200 and 2,500 animals every time the test is performed. The EPA is currently requiring that this test be conducted on pesticides and may require its widespread use as part of its "Voluntary Children's Chemical Evaluation Program." Remarkably, the EPA has made little to no effort to develop or use non-animal test methods, despite their promising potential. This approach also defies a recommendation of the National Research Council that "existing *in vitro* [non-animal] methods be exploited more extensively than at present."[2]

Failure to Validate

Numerous scientists have gone on record stating that the DNT has not been validated (i.e., shown to be reliable, reproducible, and relevant for its intended purpose) and that its use for regulatory purposes is premature. In fact, the EPA's own Science Advisory Panel concluded that "developmental neurotoxicity testing must be further refined to develop more sensitive endpoints which are relevant to significant outcomes in humans" and that "the current form of the DNT guideline is not a sensitive indicator of toxicity to the offspring."[3] In addition, a panel of experts at the 18th International Neurotoxicology Conference—including three EPA officials—acknowledged that they did not know how to interpret the results of the DNT.[4] They also agreed with a National Research Council report that questioned whether the rat was the correct "model" for the DNT.[5] One EPA official even stated that the agency's reliance on rats was "like being in a bad marriage—you know you should get out but you don't because there is so much history there."[4]

In its animal welfare factsheet, the EPA states that "scientific validation is an essential step in determining the adequacy of new alternative test methods."[6] Why is rigorous validation so important for non-animal tests yet so unnecessary for animal tests?

The EPA demonstrates a clear and arbitrary double standard by requiring all non-animal tests to pass through the rigorous validation process established by the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM), while not requiring the same of nonvalidated animal tests, such as the DNT. In the absence of appropriate scientific validation studies, the EPA cannot conclude that the results of DNT studies are in any way relevant to the assessment of chemical risks to human infants and children.

Meaningless Results

Laboratory tests used to evaluate animals "differ markedly" from those used to assess effects in people.[7] The DNT, for example, relies heavily on measures of the animals' behavior, rather than other, more objective physiological measures, which has raised concerns about the potential for extreme variability of test results and the subjectivity of their interpretation.[8,9,10] In fact, one EPA scientist has acknowledged that "the outcome of a study can depend on the inherent variability of a test measure."[11]

In addition, the EPA allows investigators remarkable "flexibility" in their choice of methods of behavioral testing for the species and strain of animal to be used in the DNT,[1] even though a consistent and standardized test protocol is essential for proper validation. Scientists have also acknowledged that the toxic effects experienced by the poisoned mother animal affect her ability to raise her young, thereby confounding the results.[8,12]

Finally, the fact that different animal species are born at developmentally different stages[8] and metabolize chemicals differently than humans[11,13,14] makes DNT results virtually

meaningless for the purpose of estimating a chemical's risk to human infants or children. Studies have documented vastly different species responses to such well-characterized developmental neurotoxicants as lead[14,15] and PCB's.[11,14,16] The DNT even failed to detect the known neurotoxic effects of amphetamine.[17] In fact, EPA officials who attended a workshop on the comparability of human and animal developmental neurotoxicity reported an "up to 10,000-fold difference" in DNT results between species.[12]

Public Left Unprotected

Despite killing tens of thousands of animals in these tests, the EPA has never lowered the permissible exposure levels for any chemicals on the basis of DNT data. This has led scientists at the American Industrial Health Council to conclude that the "EPA's level of confidence in the ability of extensive developmental neurotoxicity testing to lead to greater protection of children's health is simply overstated and unsupported by the evidence."[18] In fact, the EPA has at its disposal the authority to add a safety factor for any chemicals suspected of harming infants and children. Yet it chooses to leave infants and children unprotected for years while DNT studies are performed.

Conclusion

The DNT has no place in regulatory tests guidelines and should be withdrawn by the EPA. The agency must reexamine its double standard regarding the validation requirements of both animal and non-animal test methods and take steps to reduce the unconscionable number of animals killed in EPA-mandated toxicity tests.

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