AN INTERNATIONAL ORGANIZATION DEDICATED TO PROTECTING THE RIGHTS OF ALL ANIMALS

PETA

PEOPLE FOR THE ETHICAL TREATMENT OF ANIMALS

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Giovanni Caforio, M.D.
Chairman of the Board and Chief Executive Officer
Bristol-Myers Squibb
Via email: Giovanni.Caforio@bms.com

Dear Dr. Caforio,

On behalf of People for the Ethical Treatment of Animals (PETA) and our more than 6.5 million members and supporters, I am writing to ask that Bristol-Myers Squibb (BMS) discontinue use of the Forced Swim Test (FST) in its behavioral experiments involving animals.

Since 2008, BMS has published at least seven manuscripts and submitted at least three patent applications that describe the use of the FST in experiments involving mice and rats, and gerbils. I have listed these references below. In publications, BMS-affiliated authors have described the FST as a "depression model"[i] indicative of "depression-like behavior,"[ii] and as a test capable of demonstrating "antidepressant-like"[iii] effects of compounds. However, the applicability of an animal's behavior during the FST to their mood, or to human depression, or to the utility of a compound for treating human depression has been substantially refuted. A thorough discussion of this matter is presented in the document, "The Invalidity of the Forced Swim Test" (attached).

In brief, animals, typically mice or rats, are made to swim in a cylinder of water. They swim frantically, trying to find an escape, until they stop struggling and subsequently float. The claim is that when mice spend more time floating, they are deemed to be more "depressed." This claim is made in spite of the evidence that floating is actually a learned and adaptive behavior, one that saves energy and is beneficial for survival.[iv] Individual animals who are quicker to float also save energy and are less likely to sink, meaning that animals who more rapidly pick up on this reality, and spend less time struggling, are simply learning this adaptive behavior more readily.

Some claim that the forced swim test is a screening tool for antidepressant activity, since, sometimes, mice who are given drugs like fluoxetine will swim more and float less. However, the immobility response also occurs after treatment with drugs that do not have antidepressant effects at all, such antihistamines and other miscellaneous drugs.[v] Time spent swimming vs. floating is also influenced by the genetic strain of an animal and experimental variances, such as water depth or temperature.[vi]

Six[vii] compounds identified in BMS' published animal experiments have been tested in humans. For only one[viii] of these compounds did the authors' *interpretation* of an animal's behavior during the FST predict a *potential* efficacy or inefficacy of the compound's antidepressant-like action in humans; however, *none* of the compounds identified is currently approved as a treatment for human

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depression. For the remaining five of the compounds identified, the authors' interpretation of what an animals' behavior during the FST means for humans, or the efficacy of the compound in human depression, was *not* corroborated in human trials. **This data suggest that, in your studies, a *certain interpretation* of an animal's behavior during FST will predict the *potential* efficacy of a compound for use in human depression only 17 percent of the time, which is far less than chance (50 percent), and has a zero percent chance of predicting the successful use of a compound for human depression**.

There is a clear need to develop new therapeutics to treat human depression. Only small numbers of patients respond to available treatments, which themselves have severe shortcomings.[ix] However, the use of animal experiments in an effort to generate these treatments has been criticized as a major contributor to failure rates in this area.[x] Animal models of human depression lack many important aspects of model validity. Hendrie and Pickles argue that multiple failures on the part of animal experimenters are to blame for lack of progress in this field, namely falling trap to "logical flaws" and "false assumptions."[xi]

The FST is so traumatic to animals that it is often used as a stressor in itself,[xii] in an effort to create a sense of helplessness. To quote Dutch animal behaviorists Franz Josef van der Staay, Saskia S. Arndt, and Rebecca E. Nordquist, "If evidence accumulates that the intended goal/purpose cannot be reached, then one should consider abandoning further development of the model."[xiii] This group also pointed out that in all cases, "benefits must outweigh the ethical costs of the animals. These costs include pain and suffering, distress and death."[xiv]

In summary, the FST does not reliably predict successful treatments for human depression—nullifying any scientific justification for carrying out the test; and it causes acute suffering and distress to the animals who are used—presenting a compelling ethical argument against using the test. We therefore ask that BMS immediately discontinue its use of the FST in behavioral experiments involving animals.

May we meet to discuss this important matter?

Sincerely,

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Use of the Forced Swim Test by Bristol-Myers Squibb

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