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# Congress of the United States

House of Representatives  
Washington, DC 20515-2201

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May 25, 2001

Dr. Janet Woodcock  
Director  
Center for Drug Evaluation and Research  
Food and Drug Administration  
1451 Rockville Pike  
Room 6027  
Rockville, MD 20852

Dear Dr. Woodcock:

Back on October 5, 2000, when my family and I went public with our belief that Accutane was the cause of our son's death, I was joined by seven Members of Congress in making recommendations to the FDA on what course of action FDA should undertake with respect to protecting and informing the American people as to the dangers associated with Accutane.

The recommended MedGuide and Informed Consent outlining the possible psychiatric events with Accutane have been implemented. However, I still believe that Roche continues to use direct-to-consumer advertising through the internet and magazine advertisements.

The eight Members of Congress further recommended that **"Roche should commit to underwriting all necessary independent controlled studies on Accutane's risks of depression, suicidal ideation, suicide and other psychiatric disorders. Such studies should be designed in collaboration with the Food and Drug Administration (FDA) and be conducted by independent investigators."**

With the passing of each day and reports of additional suicides, the American people have become more aware of a connection between Accutane and suicide. I question how or if the FDA has the desire or the capability to explore the connection between Accutane and these reported suicides.

FDA's Medical Review Officer Kathryn O'Connor submitted a memo on January 29, 1998 which stated "Given all the pieces of evidence available, it is difficult for me to avoid the conclusion that Accutane can adversely affect the adult human brain in clinically significant ways and that Accutane use is associated with severe psychiatric disease in some patients. The reported effects on the CNS are not surprising given the profound effects of the drug on the integument, and the common origin of the brain and skin from the neural crest."

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Shortly thereafter, Dr. Jonathan Wilkin of the FDA stated in a (believed to be 1998) *Newark Star-Ledger* article by Edward Silverman that discussed Dr. Middlekoop's study "...the FDA won't take further action. Right now, we don't have a good feeling for what would be a good way to evaluate the hypothesis." The FDA's Wilkin said, "But if someone had a way of pursuing possible causality, we'd be interested in knowing what kind of research to conduct."

A Memorandum dated August 17, 2000, to Dr. Jonathan Wilkin from Diane K. Wysowski and Marilyn Pitts regarding "Consult: Descriptive Analysis of Suicides and Serious Cases of Depression, Suicide Ideation, and Suicide Attempts in U.S. Isotretinoin (Accutane) Users" concludes by asking for further studies to be conducted. In particular this memo states, "The possibility of measuring adrenocorticotrophic hormone (ACTH) and cortisol levels in individuals before, during and after isotretinoin and antibiotic use for acne and cystic acne should be considered. These central nervous system corticotropin releasing factor systems have been implicated in the pathophysiology of both depression and anxiety disorders."

At the December 5, 2000 Government Reform Hearing on Accutane, Dr. James T. O'Donnell specifically testified that, "The mechanism of action as to how Accutane improves or cures acne, from my reading, is unknown. We also don't know why Accutane and Vitamin A substances cause psychiatric conditions." Yet, we know from published reports and this congressional hearing that neurotoxicities, toxic psychosis, schizophrenia-like symptoms and other psychiatric toxicity of Vitamin A are likely to be associated with Accutane. Further, we know that Vitamin A causes toxicities but we are lacking scientific studies providing the cause. To prove the cause there would have to be a neurobiological study. Reports of individuals who commit spontaneous suicide, when there is no indication that a person would do such a thing, leads one to logically conclude that an individual's neurotransmitters are affected with the use of Accutane. Accutane is Vitamin A, which causes toxicity and is "associated with genes that transcribe the neurotransmitters in the brain."

The FDA's November 14, 2000 letter to me states that the "...FDA has initiated discussions with the National Institute of Mental Health to address further research needs. We will work with Hoffman-LaRoche as well as the National Institute of Mental Health on recommendations to help ensure that independent studies proposed will be conducted in a scientifically valid manner."

In a letter to me from Roche dated April 4, 2001, it appears that Roche has "convened its panel of scientific experts" to determine how a study should be conducted and that the FDA and National Institute of Mental Health would be allowed to comment and participate "in the design of this research."

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As the FDA is involved in the "design of this research" of the Accutane study with Roche, I remind you that the study must be truly independent as directed by Members of Congress. It does not appear that FDA has undertaken the research which was suggested by its own personnel, and it does not appear that the FDA is interested in examining a neurobiological connection to the central nervous system and the brain or metabolism, deposition and elimination kinetics of Accutane.

I believe Dr. O'Donnell said it best when he stated. "The condition of vitamin A toxicity causes a change in the brain chemistry. The condition that brings vitamin A toxic patients to the hospital is a swelling in the brain. When we talk about mental health, we have to convert that to chemical actions in the brain." Let us not just talk about mental health of these young victims but look at the pharmacology, neurobiology, and how the body breaks down, stores and releases Accutane throughout the human body and the resulting effects on the human brain.

I hope you will keep these thoughts and the statements of FDA personnel, Dr. James O'Donnell and other health care professionals in mind as FDA designs a truly independent scientific study that answers the questions of how Accutane "can adversely affect the adult human brain in clinically significant ways" and why "Accutane use is associated with severe psychiatric disease in some patients."

Sincerely,

A handwritten signature in black ink that reads "Bart Stupak". The signature is written in a cursive, flowing style.

Bart Stupak  
Member of Congress  
Michigan's First Congressional District

cc: Rep. Thomas Barrett  
Rep. Sherrod Brown  
Rep. Ed Bryant  
Rep. Marge Roukema  
Rep. Zach Wamp  
Rep. Henry A. Waxman