



Synthetic Food, Drug & Cosmetic Colors Safety, Allergenicity and Hypersensitivity Concerns

Ongoing toxicology studies have been routinely conducted worldwide by organizations such as the World Health Organization (WHO), the U.S. Food and Drug Administration (FDA), and the European Commission (EC) to assess the safety of synthetic food, drug and cosmetic colorants in various applications. Many articles have been written on assessing the safety of these colorants [1-6]. Scientific and public opinion vary on the true interpretation of safety and these views have impacted the development of food and drug regulations around the world.

Though these colors have a good safety record, consumers have voiced certain concerns about hyperactivity and allergic sensitivity regarding some of the synthetic colors.

Although this theory was popularized in the 1970s, well-controlled studies conducted since then have produced no evidence that food and drug color additives such as azo dyes (FD&C Yellow #5, FD&C Yellow #6, etc.) cause hyperactivity or learning disabilities in children. A Consensus Development Panel of the National Institutes of Health concluded in 1982 that there was no scientific evidence to support the claim that colorings or other food additives cause hyperactivity. The panel said that elimination diets should not be used universally to treat childhood hyperactivity, since there is no scientific evidence to predict which children may benefit [7].

The FDA's Advisory Committee on Hypersensitivity to Food Constituents concluded in 1986 that FD&C Yellow #5 (tartrazine) might cause hives in fewer than one out of 10,000 people. The committee found that there was no evidence the color additive in foods provokes asthma attacks or that aspirin-intolerant individuals may have a cross-sensitivity to the color [7]. As with other color additives certifiable for food and drug use, whenever FD&C Yellow #5 is added to a food or drug, it is listed on the product label. This allows the small portion of people who may be sensitive to the color to avoid it. (As of May 8, 1993, labels must list all certified colors as part of the requirements of the Nutrition Labeling and Education Act of 1990 [8])

During the early 1980s, before some of these reports were available, a regulation was included in 21CFR regarding additional label requirements for FD&C Yellow #5 concerning allergenicity. This regulation (201.20) required that for prescription drugs only, in addition to the label declaration showing that the product contains FD&C Yellow #5, the label must also bear this warning statement:

“This product contains FD&C Yellow #5 (tartrazine) which may cause allergic-type reactions (including bronchial asthma) in certain susceptible persons. Although the overall incidence of FD&C Yellow #5 (tartrazine) sensitivity in the general population is low, it is frequently seen in patients who also have aspirin hypersensitivity” [9].

When considering the very small potential for this type of a reaction, when compared to other products on the market with higher allergenic potential, and the conclusions of the FDA's Advisory Committee on Hypersensitivity to Food Constituents and the Consensus Development Panel of the National Institutes of Health, it appears that this statement may be overly cautious and that, once these conclusions were reached, the requirement for this warning statement should have been deleted by the FDA.. However, this statement is still required for prescription drugs based on current U.S. regulations.

No similar type of warning statement is required for non-prescription drugs or foods. In reality, the potential exposure to FD&C Yellow #5 is much greater from these products than from prescription drugs. Therefore, this regulation does not seem to make sense, given the current information.

Although the industry has requested that this regulation on FD&C Yellow #5 be eliminated, the FDA has not taken any action on this as of this time. It is uncertain why the FDA has not reacted to these requests. This situation has created much confusion concerning the actual data regarding hypersensitivity and allergenicity of FD&C Yellow #5. Due to this confusion in the marketplace, most pharmaceutical companies have eliminated the use of this colorant in their prescription drug formulations to prevent the need for this misleading label requirement, which could create consumer concern.

Due to questions people had about azo dyes during the 70's and early 80's, FDA had also proposed to require a label declaration showing the presence of FD&C Yellow #6 in 21CFR 201.20(c), but suspended this initiative in 1988 when they realized that there were no credible studies to support the need for such a requirement [9]. Unfortunately, they did not go back in a similar manner and rectify the existing regulation they had already implemented for FD&C Yellow #5 labeling once their own committees had indicated that there really was not a significant allergenicity or hypersensitivity problem with the color.

There is also a European requirement which was recently instituted to place allergen labeling on drug labels for a number of synthetic azo colors [10]. Sound scientific data showing a need for this labeling is not apparent, and this requirement seems to be based more on non-scientific consumer concerns based on the precautionary principle than on any real need. Considering the lack of evidence that FD&C Yellow #5 (tartrazine) and other azo dyes such as FD&C Yellow #6 (Sunset Yellow FCF) cause any significant hypersensitivity or allergenicity problems, except in very rare cases, it appears that all that should be required is to make sure that the colorants are listed as a component on drug labels. This would allow consumers to make up their own decisions about acceptability for use based on their specific personal experiences. These types of label requirements already apply in most industrialized countries and provide appropriate controls to allow those few people who are affected by these colors to manage their intake.

It is unfortunate that some of the regulations established in the past do not reflect the best science relative to this issue. This has created much consumer confusion about the facts related to color allergenicity and hypersensitivity. Although companies who use these colors in their products must meet all the current regulatory requirements on their labels for particular target markets, an effort is needed to further discuss these situations with regulators to take advantage of the current science and adjust the regulations accordingly down the road.

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