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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date: April 22, 2003

From: Research Biologist, Cosmetic Toxicology Branch, HFS-128; Division of Science and Applied Technology; Office of Cosmetics and Colors

Subject: Review of Petition CAP7C0208, Carbon Black for Use as a Color Additive in Cosmetics (Including Eye Area Use).

To: Martha Peiperl, Division of Petition Control, HFS-215
Through: Director, DSAT, OCAC, HFS-125 4/25/03

The Cosmetic, Toiletry, and Fragrance Association (CTFA) submitted an amendment dated February 7, 2002 to Color Additive Petition 7C0208, carbon black for use as color additive in cosmetics including eye area use. The amendment includes two Cabot Corporation memoranda/reports dated November 29, 2001. This amendment modifies the proposed identity of the color additive and addresses the issues raised by FDA (FDA letters to CTFA, April 19, 2001 and June 29, 2001). Of particular interest to the Cosmetic Toxicology Branch (CTXB) was the concern regarding extraction of PAHs from carbon black to a cosmetic foundation and bioavailability. A toxicology review of the current amendment is presented below.

I. Identity

In the previous submission, CTFA had identified two grades of carbon black or high purity furnace black (HPFB) as the color additive. The lower-jet grade product had larger particles with a proposed lower surface area (98 to 110 m^2/g), and the higher-jet grade product had smaller particles with a proposed larger surface area (200 to 260 m^2/g). Instead of distinct low and high ranges, FDA suggested a combined range of surface area that would include both the lower jet and the higher jet black.

In the recent submission (CTFA, February 7, 2002), CTFA stated that the lower jet black is no longer of interest from a business perspective and that the petition no longer seeks approval for the lower surface area specification of 98-110 m^2/gram. CTFA proposed revised specifications to conform with the properties of the higher jet black. The proposed specification for surface area by nitrogen BET determination is now 200-260 m^2/gram.

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II. Extractable Polycyclic Aromatic Hydrocarbon (PAH) Content.

The recoveries of PAHs from carbon black appear to be dependent on the identity of the PAH and the grade of the carbon black used. In previous work, Cabot submitted the results for the recoveries of PAHs spiked directly onto low and high jet carbon blacks (Cabot Corp., memo, July 15, 2000, Appendix I, Table 9). The testing was intended to gauge how readily PAHs are extracted from the carbon black. From the low jet black, the recovery of added 0.005 ppm benzo[*a*]pyrene (B[*a*]P) was 40-60% and the recovery of added 0.025 ppm B[*a*]P was 56-96% (Appendix I, Table 9); however, recoveries of added 0.005 ppm and 0.025 ppm B[a]P from the high jet carbon black were consistently 0% (Cabot Corp. memo, July 15, 2000, Appendix I, Table 9)(CTB Review, A. Scher, Color Technology Branch, HFS-126, March 1, 2001). The petitioner stated that "the lack of recovery for spiked B[*a*]P in the high-jet samples reflects the ability of the Carbon Black to strongly adsorb PAHs." The PAHs were extracted under vigorous conditions that do not occur in biological systems. Measuring the extraction or transfer of PAHs from the carbon black to an oil-in-water cosmetic foundation would provide information that is more relevant to the exposure of the consumer to PAHs from carbon black and availability to the body for absorption.

III. Potential Polycyclic Aromatic Hydrocarbon (PAH) Extraction in Cosmetic Formulations.

CTXB had requested that a study be conducted to determine PAH transfer from a low jet carbon black to a commercially available oil-in-water cosmetic formulation. Cabot presented the results of an initial study on the transfer of PAHs from low jet carbon black to a commercial foundation. In this study, Cabot developed a test which used the absorbance level of uv/vis absorption peaks to measure the concentration of three PAHs, benzo(*k*)fluoranthene (BkF), perylene, and anthanthrene in an extract of a commercial foundation (Cabot Corp., memo, July 15, 2000). Cabot reported that the limited test was developed due to a number of interfering peaks from the foundation that prevented determination of the quantities of the usual 22 PAHs by GCMS. However, the petitioner's previous analysis of an unspiked carbon black by toluene extraction and GCMS found none of these three PAHs. Because there was no indication that the three PAHs were present in the unspiked low jet carbon black, this finding of no transfer of PAHs to cosmetic foundation did not yield useful data. In April, 2001, CTXB requested that the low jet carbon black first be fortified with the three PAHs and dispersed at 5% into the commercial foundation. The dispersion was to be left for seven days and then analyzed for the three PAHs. FDA also requested that the petitioner quantitate the extraction of these three PAHs from carbon black by using toluene extraction and GCMS. In this current submission, CTFA and Cabot presented data on the transfer of the three PAHs (BkF, perylene, and anthanthrene) to a cosmetic foundation and on the recoveries of these three PAHs from a fortified low jet carbon black. The same spiked carbon black itself and unspiked carbon black were directly analyzed by 48-hour toluene extraction and GCMS.

In this study, each PAH (BkF, perylene and anthanthrene) was spiked onto the low jet carbon black at a concentration of 0.3 μg/g (0.3 ppm) carbon black, for a total PAH amount of 0.9 ppm (0.9 μg/g). This total PAH amount is higher than the proposed specification for total PAHs of

0.5 ppm and higher than the greatest total PAHs found (0.38 ppm) in ten production batches of low and high jet carbon black analyzed (CTB Review, A. Scher, Color Technology Branch, HFS-126, February 20, 2003). The individual PAH level of 0.3 ppm is higher than the greatest amount of an individual PAH (0.19 ppm naphthalene) found in ten production batches analyzed.

A five percent mixture of the spiked carbon black in foundation was prepared. The dispersion was allowed to stand for more than seven days and analyzed in duplicate. Three samples of foundation spiked with the PAHs (no carbon black) were also analyzed for comparison. One sample of the foundation itself (no carbon black) was spiked at 0.15 μg of each of the 3 PAHs/g of foundation. A second sample of the foundation itself (no carbon black) was spiked only with 0.0056 μg BkF/g foundation and 0.0041 μg perylene/g foundation.

Cabot reported (Cabot memo, November 29, 2001) that the mean percent recoveries of the three PAHs extracted from spiked low jet carbon black by 48 h toluene extraction followed by GCMS analysis were 74% BkF, 47% perylene, and <9 to 11% anthanthrene. The foundation was analyzed for the PAHs using spectrophotometry. Cabot reported that none of the three PAHs were detected migrating from fortified carbon black to the foundation. The mean recovery of PAH in spiked foundation (no carbon black) was 23% (Cabot memo, November 29, 2001, Tables 3 and 6d). Based on the limit of detection (as described in the Cabot memo, November 29, 2001; Reviewed by CTB, A. Scher, Color Technology Branch, HFS-126, February 20, 2003), Cabot estimated that migration would be detected if PAH migration were greater than 10-27% for BkF, 4-12% for perylene, and 5% for anthanthrene. Cabot concluded that the amounts of BkF and perylene that might have migrated to the foundation at the limit of detection were not greater than the amounts of BkF and perylene that could be recovered from the fortified carbon black by toluene extraction. The limit of detection of migration of anthanthrene was low (<5%), however, the recovery of anthanthrene from carbon black by toluene extraction was also low. The possibilities are that no PAHs migrated to the foundation or that up to 27% BkF (4 ppb), 12% perylene (2 ppb), and 5% anthanthrene (1 ppb) actually migrated to the matrix but were not seen because of difficulties with the method and the matrix (Appendix I, Table 3, Cabot, November, 29, 2001; CTB Review, A. Scher, Color Technology Branch, HFS-126, February 20, 2003). It appears that no more PAHs could migrate to the foundation from the fortified carbon black than the amount of PAHs extracted from the fortified carbon black by toluene extraction.

IV. Bioavailability.

The primary concern in evaluating the safety of carbon black is the bioavailability of the PAHs from the carbon black. In a previous toxicology review (M. Kraeling, July 15, 1999), CTXB discussed the limited bioavailability of PAHs, specifically benzo[*a*]pyrene (B[*a*]P), and that exposure to carbon blacks containing PAHs does not result in adverse effects by subcutaneous, oral, or intraperitoneal routes of administration except where a high PAH load is placed on carbon black in excess of the ability of the pigment to adsorb the PAHs on the carbon black surface. The recoveries of PAHs from carbon black by extraction appear to be dependent on the identity of the PAH and the grade of the carbon black used. Carbon black with a larger surface

area has lower extractable PAH fractions[1]. It is not known whether the lower amount of extractable PAHs is strictly due to tighter binding between carbon blacks, or due to higher binding capacity. The low jet carbon black is no longer under consideration for approval in this petition. However, PAH extraction from low jet carbon black is greater than from high jet carbon black. Therefore, PAH bioavailability data from the low jet carbon black can be considered for this review of the high jet HPFB.

Previously, Cabot reported the recoveries of added 0.07 ppm naphthalene, added 0.053 ppm pyrene, and added 0.005 ppm chrysene to high jet carbon black were 80-107%, but the recovery of added 0.005 ppm B[*a*]P was 0% (Cabot Corp., memo, July 15, 2000, Appendix I, Table 9). Recoveries of added 0.35 ppm naphthalene, added 0.265 ppm pyrene, and added 0.025 ppm chrysene were 75-104%, but the recovery of added 0.025 ppm B[*a*]P was again 0%. The inability to extract added B[*a*]P under these vigorous conditions (toluene Soxhlet extraction) indicates that the B[*a*]P probably remains bound to the high jet carbon black, and is not available to the body for absorption. From the low jet carbon black, recoveries of added 0.17 ppm naphthalene, added 0.07 ppm pyrene, and added 0.005 ppm chrysene were 96-101% (with the exception of one anomalous sample that yielded 100% recovery of naphthalene but only 20% recovery of pyrene and 0% recovery of chrysene)(CTB Review, A. Scher, Color Technology Branch, HFS-126, March 1, 2001). For higher level fortification of the low jet carbon black, recoveries of added 0.86 ppm napthalene, added 0.35 ppm pyrene, and added 0.025 ppm chrysene were 57-104%. Similar recoveries were obtained from the low and high jet carbon black for napthalene, pyrene and chrysene.

In this current study, PAHs were spiked onto the low jet carbon black at a higher load than what was found in the production batches of carbon black. PAH migration into the foundation was estimated to be 10-27% for BkF, 4-12% for perylene, and 5% for anthanthrene. The data did not indicate that more PAHs migrated to the foundation from the fortified carbon black than the amount of PAHs extracted from the fortified carbon black by toluene extraction (CTB Review, A. Scher, Color Technology Branch, HFS-126, February 20, 2003) Extrapolation of these results to a high jet carbon black incubation with the cosmetic foundation suggest that B[*a*]P would not be extracted by the foundation. B[*a*]P has previously been found to remain bound to the high jet carbon black and was not extracted by toluene.

Other toxicological studies support the position of limited PAH bioavailability (Toxicology review, M. Kraeling, CTXB, HFS-128, July 15, 1999). In one study, swine lung, swine serum, and human plasma were used to evaluate the bioavailability of B[*a*]P from three rubber-grade oil furnace blacks (ASTM N-351;N2 surface area 70m^2/g, N-375; N2 surface area 101 m^2/g, and N-

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[1] Falk, H.L. and Stein, P.E. Cancer Research 12:30-39, 40-43 (1952); Hase, A, Lin, P.H. and Hites, R.A., Carcinogenesis-Comprehensive Survey 1:435-442 (1976); Lakowicz, J.R., and Bevan, D.RR., Biochemistry 18(23):5170-5176 (1979); Pylev, L.N. and Yenkova, G.D. Gigienda Trudal Professional/nye Zabolevaniya 17(4):52 (1974).

234; N2 surface area 128 m^2/g) as compared to their extractability with toluene[2]. It was determined that less than 0.005% of the toluene-extractable B[*a*]P was extracted by the serum, plasma, or tissue homogenate.

In the Federal Register notice of final rule, [62 FR 25475, May 9, 1997, § 178.3297, (FAP 5B4464)] FDA concluded that the polymer colorant HPFB is insoluble in common solvents, including aqueous and fatty foods. As a consequence, there was no potential for significant levels of migration of the carbon black from food contact surfaces to food. FDA concluded that there was reasonable certainty of no harm from exposure to PAHs from the petitioned uses of the indirect colorant.

V. Exposure Assessment and Lifetime Cancer Risk.

Because some PAHs were able to be extracted from the high jet HPFB by toluene extraction, an exposure assessment would be supportive in evaluating the safety of these PAHs under the conditions of use requested in this color additive petition. Again, these PAHs were extracted under vigorous conditions (toluene extraction) that do not occur in biological systems. In a previous toxicology review (M. Kraeling, CTXB, HFS-128, July 15, 1999) of carbon black, a summary of PAH exposure and cancer risk assessments were discussed.

A. CTFA Exposure Estimate

CTFA estimated the worst-case potential lifetime cancer risk due to exposure to PAHs present in carbon black by assuming that all of the PAHs present on the carbon black would desorb from the pigment. For total expected daily exposure to carbon black, CTFA used the exposure value of 1.0 mg/kg body weight/day (December 18, 1997 amendment to Color Additive Petition 7C0208, submitted by CTFA). If carbon black routinely contains the maximum proposed PAH specification level of 0.5 ppm (5×10^{-7} mg/mg), the maximum potential exposure to PAHs resulting from exposure to1.0 mg/kg body weight/day of carbon black would be 5×10^{-7} mg/kg body weight/day.

For their risk assessment, CTFA used a toxic equivalency factor (TEF)-based method that scales the relative carcinogenicity of each PAH in relation to the most potent carcinogen, B[*a*]P, to estimate exposure from the PAHs contained in the carbon black (CTFA, December 18, 1997 amendment to Color Additive Petition 7C0208, Appendix, Table 2). Using the TEF method, CTFA estimated the total B[*a*]P equivalent PAH content is about 43 ppb. Using this approach, the estimated toxicity-weighted PAH content of the carbon black (43 ppb) is ten-fold lower than the maximum total PAH content of 0.5 ppm (500 ppb) specified in the current petition.

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[2]Budding, F., Baiely, M.J. Wells, B., and Haesemeyer, J. American Industrial Hygienist Journal 42:503-509 (1981)

Using the worst-case assumption of 100% desorption of the PAHs from the carbon black with 100% bioavailability, the exposure to PAHs was calculated by CTFA to be 4.3×10^{-8} mg B[*a*]P PAH/kg body weight/day. Multiplying this exposure by the FDA derived unit risk factor (URF)[3] for B[*a*]P of 1.75 (mg/kg body weight/d)$^{-1}$ resulted in a lifetime cancer risk of 7.5×10^{-8}.

B. CRT Review of CTFA Exposure Estimate

The Chemistry Review Team (CRT) evaluated CTFA's exposure estimates to carbon black from cosmetic products (CRT Review memorandum, March 23, 1998). An exposure estimate was developed using product information from the cosmetic industry and color exposure scenarios developed by the Hart Panel. Although CRT's assumptions differed somewhat from CTFA's, CRT estimated a total B[*a*]P-weighted concentration of 44 ppb. Using the FDA derived unit risk factor, and an assumption that 10% of the total PAHs can be absorbed into the body from carbon black, CRT estimated a lifetime cancer risk of 1.25×10^{-9}.

C. Colorant in Polymer Final Rule

In the Federal Register notice of final rule, 62 FR 25475, May 9, 1997, § 178.3297, in assessing the upper bound limit of lifetime human risk, FDA used the worst -case assumption for the risk estimate that all PAHs in the colorant have the same carcinogenic potency as B[*a*]P. Assuming PAHs were present in carbon black at the limit of 0.5 ppm (the specification proposed in the current color additive petition amendment) and all the PAHs present were B[*a*]P, then this worst-case would have B[*a*]P available at 500 ppb (10-fold higher than CTFA and CRT B[*a*]P concentrations). Using this assumption, the risk determined by both the CTFA and CRT risk assessments would each be increased approximately 10-fold. However, the risk calculated by both approaches would still be less than 1×10^{-6}.

VI. Summary

1. CTFA now identifies only the high jet carbon black as the petitioned color additive, with a proposed surface area specification of 200-260 m^2/g.

2. The recoveries of PAHs from carbon black appear to be dependent on the identity of the PAH and the grade of the carbon black used. From previous studies, Cabot reported the recoveries of added 0.005 ppm and added 0.025 ppm B[*a*]P from the low jet black were 40-60% and 56-96%, respectively. The recoveries of added 0.005 ppm and added 0.025 ppm B[*a*]P from the high jet carbon black were consistently 0% (Cabot Corp., memo, July 15, 2000, Appendix I, Table 9). CTB found the recoveries by toluene extraction and GCMS of benzo(*k*)fluoranthrene, perylene, and anthranthene from fortified low jet carbon black were 45-101% for 0.30 ppm of benzo(*k*)fluoranthrene, 18-70% for 0.30 ppm of perylene, and <9-12% for 0.30 ppm of anthranthene (CTB Review, A. Scher, Color Technology Branch, HFS-126, February 20, 2003). The inability to extract added B[*a*]P under these vigorous conditions (toluene Soxhlet extraction) indicates that the

[3]QRAC memorandum of August 9, 1990.

B[*a*]P probably remains bound to the high jet carbon black, and is not available to the body for absorption.

3. Since the low jet carbon black is no longer under consideration for approval in this petition, PAH bioavailability should be considered only from the high jet carbon black. However, studies on the possible transfer of PAHs from carbon black to a cosmetic foundation were conducted only on low jet carbon black. Data in the petition show that the PAH extraction from low jet carbon black is greater than or equal to their extraction from high jet carbon black. Therefore, PAH bioavailability data from low jet carbon black can be used to estimate what might occur in the high jet black. The total PAH amount (0.9) ppm loaded on the low jet carbon black was higher than the proposed specification for total PAHs (0.5 ppm) and the individual PAH level (0.3 ppm) was higher than the individual PAH level (0.19 ppm naphthalene) found in ten production batches analyzed. Although there are some uncertainties about the interpretation of the data, the worst-case scenario is that, due to the limit of determination, up to 27% benzo(*k*)fluoranthene, 12% perylene, and 5% anthanthrene actually migrated to the cosmetic foundation but was not seen because of difficulties with the method and the cosmetic foundation. The data indicate that the migration of PAHs to the cosmetic foundation from the fortified carbon black was no larger than the amount of PAHs extracted from the fortified carbon black by toluene extraction (CTB Review, A. Scher, Color Technology Branch, HFS-126, February 20, 2003). The PAHs were extracted by toluene under vigorous conditions that do not occur in biological systems and no B[*a*]P was extracted. Therefore, no extraction of B[*a*]P would likely occur from high jet carbon black into the cosmetic foundation.

4. Additional information to support the safety of high jet carbon black is given in a summary of risk assessments for exposure to carbon black and PAH bioavailability, that was previously presented (M. Kraeling, CTXB, HFS-128, July 15, 1999) and is given below. CTFA listed the following uses for high jet carbon black in cosmetics formulations: eyeliner, brush-on-brow, eye shadow, mascara, lipstick, blushes and rouge, makeup and foundation, and nail enamel. Uses of these products cover three principal routes of administration for exposure: dermal, ocular, and oral. A regulation based on FAP 5B4464 limited the total PAH content to 0.5 ppm and the B[*a*]P and dibenz[*a,h*]anthracene (the most potent carcinogens) content to 5 ppb (0.005 ppm) for indirect food contact uses of carbon black. By using a toxicity-equivalency based approach, CRT estimated the total B[*a*]P equivalent PAH content of the carbon black to be 44 ppb and CTFA estimated the total B[*a*]P equivalent PAH content of carbon black to be 43 ppb. Assuming that 10% of the total PAHs can be absorbed into the body from the carbon black from all product types, CRT estimated a lifetime cancer risk of 1.25×10^{-9}. With a more conservative approach, and assuming a worst-case scenario of 100% desorption of the PAHs from the carbon black from all product types with 100% bioavailability, CTFA estimated a lifetime cancer risk of approximately 7.5×10^{-8}. In the Federal Register notice of final rule, 62 FR 25475, May 9, 1997, § 178.3297, (FAP 5B4464), FDA used the worst-case assumption in assessing the upper bound limit of

lifetime human cancer risk, that all PAHs in the colorant had the same carcinogenic potency as B[*a*]P. With this precedent, assuming PAHs were present in the carbon black at the limit of 0.5 ppm (the specification proposed in the current color additive petition amendment) and that all the PAHs present on the carbon black were B[*a*]P, then this worst-case assumption would have B[*a*]P available at 500 ppb (10-fold higher than CTFA and CRT B[*a*]P concentrations). Using this assumption, the risk determined by both the CTFA and CRT risk assessments would each be increased approximately 10-fold. However, the risk calculated by both approaches would still be less than 1×10^{-6}.

5. The acceptable safety margin for this color additive is dependent upon the proposed specifications for PAHs. Therefore, CTXB concludes that the proposed specifications for PAHs as presented in the Chemistry Review of CAP7C0208 (CTB Review, A. Scher, Color Technology Branch, HFS-126, February 20, 2003) must be incorporated in any final regulation to list carbon black as a color additive for cosmetic uses. The specifications for PAHs are defined as extractable B[*a*]P and Dibenz[*a,h*]anthracene PAHs not to exceed 0.005 ppm, and total extractable PAHs not to exceed 0.5 ppm, as determined by 48- hour toluene Soxhlet extraction (Cabot's Determination of PAH Content for Low PAH Carbon Blacks with revision date April 1, 2000).

Margaret E. K. Kraeling

cc:

HFS-100 (LKatz)
HFS-125 (DADennis)
HFS-126 (SBell, AScher)
HFS-128 (RBronaugh, JYourick)
HFS-215 (ALipman)
HFS-225 (CJohnson)
HFS-265 (SCarberry)

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RBronaugh:HFS-128:04/21/03