

Ref. 3

**Memorandum**

Date: September 30, 2003

From: Division of Petition Review (HFS-265)  
Chemistry Review Team

Subject: CAP 7C0208 (MATS#197 M2.3.2): The Cosmetic, Toiletry, and Fragrance Association (CTFA), Carbon black for use as a color additive in cosmetics (including eye area use). Risk assessment for polyaromatic hydrocarbons (PAHs) using conservative approach.

To: Division of Petition Review (HFS-265)  
Regulatory Group I  
Attention: C. Johnston

You requested that we perform a risk assessment for polyaromatic hydrocarbon (PAH) contaminants using a more conservative approach than that used in the 3/23/98 Chemistry Review Team (CRT) memorandum (E. Jensen to R. White). The CRT memorandum presented a risk assessment for PAH contaminants using a toxic equivalency factor (TEF) approach for the 22 PAHs associated with carbon black or high purity furnace black (HPFB). While this approach is valid, and has been used before by FDA<sup>1</sup>, it is less conservative than the approach taken in the most recently regulated HPFB petition (FAP 5B4464, 62 FR 25475, May 9, 1997). Instead of using a TEF approach, which takes into account the differing levels of toxicities of the individual PAHs, FAP 5B4464 employed a more conservative risk assessment in which all PAHs present were assumed to have the same toxicity as the highly toxic PAH, benzo[a]pyrene (B[a]P). In this memorandum, we perform a risk assessment for PAH contaminants in HPFB used as a color additive in cosmetics (including eye area use) which employs similar conservative assumptions to those used in FAP 5B4464.

We performed a more conservative risk assessment for PAHs in HPFB using the following assumptions:

1. The estimated daily intake (EDI) of HPFB from use as a color additive in cosmetics (including eye area use) is 10 mg/p/d.<sup>2</sup>
2. PAHs are present in HPFB at the maximum allowed specification level of 0.5 mg/kg.
3. All PAHs present in HPFB have the same toxicity as B[a]P.
4. B[a]P has a unit risk factor<sup>3</sup> of 1.75 (mg/kg-bw/d)<sup>-1</sup>
5. Only 10% of PAHs present in HPFB are absorbed by the body<sup>4</sup>

<sup>1</sup> See discussion on p. 7 of the 3/23/98 CRT memorandum.

<sup>2</sup> Exposure to HPFB from uses in this petition was determined in the 3/23/98 CRT memorandum from E. Jensen to R. White regarding CAP 7C0208.

<sup>3</sup> See the Quantitative Risk Assessment Committee memorandum of August 9, 1990.

The EDI for HPFB from uses in this petition is 10 mg/p/d. Assuming a PAH concentration of 0.5 mg/kg, and that only 10% of PAH contaminants are absorbed, the EDI for PAHs is:

$$EDI_{PAH} = [(10 \text{ mg/p/d}) \times (0.5 \text{ mg/kg}) \times 10\%] = 5 \times 10^{-7} \text{ mg/p/d}$$

For a 60 kg person, the EDI becomes:

$$EDI_{PAH, 60 \text{ kg person}} = [(5 \times 10^{-7} \text{ mg/p/d}) / (60 \text{ kg-bw/p})] = 8.33 \times 10^{-9} \text{ mg/kg-bw/d}$$

Multiplying the above-calculated EDI for PAHs by the unit risk for the PAH B[a]P yields an upper-bound lifetime risk of:

$$\begin{aligned} \text{Upper-bound lifetime risk} &= \{(8.33 \times 10^{-9} \text{ mg/kg-bw/d}) \times [1.75 (\text{mg/kg-bw/d})^{-1}]\} \\ &= 1.5 \times 10^{-8} \end{aligned}$$

### Summary

In this memorandum, we have performed a risk assessment using the conservative assumption that all PAHs present in HPFB have the same toxicity as B[a]P. This resulted in an upper-bound lifetime risk (UBLR) of  $1.5 \times 10^{-8}$ . We note that this value, as expected, is higher than the UBLR of  $1.25 \times 10^{-9}$  calculated in the 3/23/98 CRT memorandum. Despite being more conservative, however, the UBLR calculated for the single petitioned use in this memorandum is still on the order of 1 in 100 million ( $1 \times 10^{-8}$ ).

The UBLR presented in this memorandum is a worst-case estimate for comparison purposes only. The UBLR of  $1.25 \times 10^{-9}$  calculated in the 3/23/98 CRT memorandum should still be considered the appropriate UBLR for PAHs from the uses of HPFB addressed in this petition.



Daniel E. Folmer, Ph.D.

HFS-245 (Perfetti); 205 (Kuznesof, R/F)  
 HFS-265:DFolmer:208-3148:CAP7C0208\_C\_Memo2.doc  
 Init: SECberry:9/30/03  
 Final: def: 9/30/03

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<sup>4</sup> This determination is presented in detail in the 3/23/98 CRT memorandum. Briefly, the determination resulted in consideration of the extreme measures necessary (e.g., Soxhlet extraction with dichloromethane for 150 hours) to extract PAHs from HPFB during testing. While the assumption that only 10% of PAHs contained in HPFB are absorbed by the body was not used in the risk assessment for FAP 5B4464, we believe it is appropriate to use this assumption in this case since the primary means of PAH absorption is through skin rather than ingestion, as was the case for FAP 5B4464.

**Johnston, Celeste**

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**From:** Folmer, Daniel  
**Sent:** Wednesday, November 12, 2003 11:21 AM  
**To:** Johnston, Celeste  
**Cc:** Carberry, Susan E  
**Subject:** Clarification of 9/30/03 chemistry memorandum regarding CAP 7C0208

Celeste,

This e-mail message is intended to clarify an issue resulting from the exposure calculation and risk assessment performed for polyaromatic hydrocarbon (PAH) contaminants in our 9/30/03 memorandum concerning CAP 7C0208. In this memorandum we performed a more conservative (when compared to the 3/23/98 chemistry memorandum from E. Jenson to R. White) exposure calculation and risk assessment for PAH contaminants resulting from the use of carbon black as a color additive in cosmetics (including eye area use). Our 9/30/03 memorandum generated confusion due to our use of the "term of art" Estimated Daily Intake (EDI) when calculating exposure to PAH contaminants. For the petitioned use of carbon black, PAH exposure could result from ingestion (as with lipstick), or from absorption through the skin (as with blushes or rouge). When we calculated exposure to PAH contaminants from the use of carbon black in cosmetics, we considered exposure from both ingestion and absorption through the skin. However, since we called the PAH exposure an EDI, there could be confusion that the estimate would only cover exposure from ingestion. This is not the case. Our exposure estimate (and hence the risk assessment for PAH contaminants) includes exposure from both ingestion and absorption of PAH contaminants. It may have been more appropriate to call this an estimated daily exposure rather than an estimated daily intake. I hope that this e-mail provides clarification on this issue.

Dan Folmer

A handwritten signature in cursive script that reads "Daniel E. Folmer, Ph.D." The signature is written in black ink and is positioned below the typed name "Dan Folmer".

**Johnston, Celeste**

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**From:** Folmer, Daniel  
**Sent:** Tuesday, November 25, 2003 8:41 AM  
**To:** Biddle, Garfield N  
**Cc:** Zajac, Andrew J; Johnston, Celeste; Carberry, Susan E  
**Subject:** review of 10% extraction "assumption"

Kirk,

You had requested that we justify the use of the assumption that a maximum 10% polycyclic aromatic hydrocarbon (PAHs) would be extracted from carbon black (also known as high purity furnace black (HPFB)) under typical use conditions as a color additive in cosmetics (CAP 7C0208 by the Cosmetic, Toiletry and Fragrance Association (CTFA)). Specifically, we had estimated that no more than 10% of PAHs adsorbed to HPFB would be extracted into cosmetics and thus made available for absorption by the skin (as in foundation), or intake (as in lipstick).

The assumption that a maximum 10% PAHs would be extracted from HPFB originated in the 7/25/90 chemistry memorandum (Kramer to Kashtok regarding CAP 7C0208). This memorandum discussed the high affinity that carbon blacks have for PAHs, and that complete extraction of PAHs typically requires the use of an aromatic solvent (e.g., toluene or benzene) at reflux temperatures for 48 hours. This type of environment is not typical of cosmetic use. Cosmetics typically consist of fatty/oily, aqueous, or alcoholic type media.

PAH extraction is strongly dependent on solvent choice and extraction conditions. The 7/25/90 memorandum pointed to an article (D. Rivin and R.G. Smith, *Rubber Chemistry and Technology*, **55**, 707-761 (1982)) which reported the qualitative degree of extraction of the PAH benzo[a]pyrene (B[a]P) from carbon black using various solvents relative to toluene (i.e. toluene extraction = 100%). The article indicated that ethanol extracted only 3% of the B[a]P present in a carbon black sample, relative to toluene. The 7/25/90 chemistry memorandum argued that the 3% ethanol extraction value could be extrapolated to the scenario of carbon black in cosmetic formulations by conservatively saying that no more than 10% of PAHs adsorbed to the carbon black would be extracted into the cosmetic matrix. This argument is based on discussions in a 1/4/85 chemistry memorandum (Kramer to Ho, FMF 277) regarding the extraction of PAHs from carbon black in food-contact polymers. The 1/4/85 memorandum discusses the Food Additive Chemistry Evaluation Branch's use of ethanol as a fatty food simulant for migration from polymers into fatty foods. Taking into consideration the likely matrices for cosmetics (aqueous, fatty/oily, alcoholic) and that ethanol can be considered an effective fatty food simulant, the 7/25/90 memorandum concluded that the use of a 10% factor for extraction of PAHs from carbon black into a cosmetic formulation would be suitably conservative.

At the time of the 7/25/90 memorandum, CTFA requested the use of both low jet and high jet HPFB in cosmetics. In the 2/7/02 amendment to CAP 7C0208, CTFA stated that they no longer wished to pursue the use of low jet HPFB, but rather wished to focus on high jet HPFB. High jet HPFB has a smaller particle size than low jet, and thus a larger surface area per gram of HPFB. The larger surface area of high jet HPFB essentially means that PAHs would be less likely to extract into the cosmetic matrix compared with low jet HPFB. This is supported by actual testing performed by CTFA (see CAP 7C0208 pp. 001662-3), in which low and high jet HPFB spiked with 0.005 mg/kg B[a]P and extracted with toluene yielded recoveries of 40 to 96% for low jet and 0% for high jet (limit of detection likely to be 0.001 mg/kg). Thus, even under the extreme conditions of Soxhlet extraction with toluene, high jet

HPFB spiked with B[a]P at a level of 0.005 mg/kg did not yield any B[a]P.

CTFA reported further tests in the 11/29/01 amendment regarding the extraction of PAHs from HPFB in a simulated cosmetic matrix. CTFA generated a test cosmetic foundation consisting of a commercially available foundation mixed with 5% low jet HPFB (mimicking the petitioned level). (Although CTFA no longer seeks approval for low jet HPFB, the substance will yield greater extractables than the petitioned substance, high jet HPFB, as noted above.) The HPFB had been spiked with the following 3 PAHs at a level of 0.3 mg/kg each: benzo(k)fluoranthrene (B(k)F), perylene, and anthanthrene. Samples of the foundation were also prepared without carbon black, but spiked with varying amounts of the 3 PAHs for comparison.

A new method was developed to extract and analyze the cosmetic foundation samples since the typical Soxhlet extraction with toluene followed by analysis with gas chromatography/mass spectrometry (GC/MS) was unacceptable due to the interference of toluene-soluble compounds from the foundation. CTFA employed a method involving a complicated solvent extraction step, followed by separation on a silica gel column, which yielded two fractions (from 10% toluene in hexane solution, and from 40% toluene in hexane solution). The fractions were analyzed by UV-Vis spectrophotometry at 403 nm and 433 nm. The method is not very robust, as it results in PAH spike recoveries averaging 23% for a single fraction of the spiked formulation (no HPFB). However, the method is useful for providing PAH extract data from a matrix that more closely simulates the intended use.

CTFA did not detect any of the 3 PAHs (within the limits of detection of the method) in the cosmetic formulation spiked with 5% PAH-spiked HPFB. It should be noted that, in terms of the percent recovery from the cosmetic formulation, the limits of detection were large: <10 to <27% of carbon black extracted into the cosmetic formulation for B(k)F, <4 to <12 % for perylene, and <5% for anthanthrene. However, the actual amounts detected in all cases correspond to <0.004 mg/kg PAH in the cosmetic formulation (as seen in Table 3 of the 11/29/01 amendment: <0.00143 to <0.00404 mg/kg for B(k)F, <0.00057 to <0.00187 mg/kg for perylene, and <0.00078 mg/kg for anthanthrene). Thus, as pointed out in a 2/20/03 Office of Cosmetics and Colors (OCAC) Chemistry memorandum (A. Scher to M. Peiperl), one could argue that PAHs are either not present, or, at worst, present at a level up to the limit of detection (but not seen by the method).

While it is true that one can not completely rule out that PAHs were extracted by the cosmetic formulation at a level up to the limit of detection, the actual UV-Vis spectra generated from the analysis provide strong evidence that no PAHs were extracted. For example, Figure 2B of the 11/29/01 amendment allows one to compare the lowest absorbance signal which was used to set the limit of detection (0.005 a.u. for the 433 nm absorbance of the cosmetic formulation (no HPFB) spiked with 0.0056 mg/kg B(k)F and 0.0041 mg/kg perylene) with the absorbance signals at 433 nm for the cosmetic formulations with PAH-spiked HPFB (listed in Table 2 of the 11/29/01 amendment as <0.005 a.u.). Whereas the spectrum for the spiked cosmetic formulation (no HPFB) with an actual absorbance of 0.005 a.u. at 433 nm clearly shows structure, the spectra for the cosmetic formulation spiked with PAH-spiked HPFB listed in Table 2 as <0.005 a.u. show no structure discernable from noise. It is also worth noting that the 2 spectra in Figure 2B for the cosmetic formulation with PAH-spiked HPFB are essentially indistinguishable from the 2 spectra for the cosmetic formulation with "unspiked" HPFB (i.e., HPFB not spiked with PAHs).

It should be recalled that the formulation study was performed with low jet HPFB, not high jet HPFB. As noted earlier, the larger surface area of high jet HPFB particles typically result in lower PAH extractables than low jet HPFB. Thus, it can be conservatively concluded that the maximum amount of PAHs present in low jet HPFB extracted into the cosmetic formulation is at the limit of detection, and that, under the same conditions, the amount of PAHs in high jet HPFB extracted into the cosmetic

formulation would be lower than the limit of detection.

Based on the evidence presented above, it is our conclusion that the use of an extraction factor of 10% for PAHs from HPFB into cosmetics is conservative.

We propose changing the text in the draft final rule from:

"It was also assumed that no more than 10 percent of the total PAHs present were extractable from the additive under typical use conditions, and thus available for absorption by the body."

To something on the order of:

"Based on evidence presented in the petition, it was also concluded that no more than 10 percent of the total PAHs present were likely to be extractable from the additive under typical use conditions, and thus available for absorption by the body."

Hopefully our analysis was useful. Please contact me if you have any questions or comments. Thanks.

Dan Folmer

A handwritten signature in cursive script that reads "Dan G. Folmer, Ph.D." The signature is written in black ink and is positioned below the typed name.

**Johnston, Celeste**


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**From:** Folmer, Daniel  
**Sent:** Wednesday, December 10, 2003 3:38 PM  
**To:** Sheu, Chingju W  
**Cc:** Biddle, Garfield N; Varner, Sandra L; Zajac, Andrew J; Carberry, Susan E; Johnston, Celeste  
**Subject:** Description of Dr. Jensen's 3/23/98 PAH risk assessment calculation

Chingju,

Celeste Johnston requested that I supply you with a description of the risk assessment for polycyclic aromatic hydrocarbons (PAHs) in high purity furnace black (HPFB), or carbon black, performed by Dr. Jensen in her 3/23/98 chemistry memorandum (Jensen to White, CAP 7C0208). This information should help you to satisfy Dr. Biddle's request to perform a review of the PAH risk assessment calculations as requested in Margaret Kraeling's 7/15/99 Color Toxicology Branch memorandum. As you recall, Kraeling's memorandum requested that the Quantitative Risk Assessment Committee review the approaches to PAH risk assessment calculations performed by the Chemistry Review Team (in Dr. Jensen's 3/23/98 memorandum) and the Cosmetic, Toiletry, and Fragrance Association (pp. 000840-842 of CAP 7C0208).

The descriptions of Dr. Jensen's and CTFA's calculations are included below. Please contact me if you have any further questions. Thank you.

Dan Folmer

**Description of the PAH Risk Assessment Calculations for carbon black (high purity furnace black) in the 3/23/98 memorandum (E. Jensen to R. White) regarding CAP 7C0208**

Dr. Jensen determined that the exposure to high purity furnace black (HPFB) from use as a color additive in cosmetics (including eye are use) is 10 mg/p/d. She then estimated the benzo[a]pyrene (B[a]P)-equivalent PAH concentration in HPFB using the toxicological equivalency factors (TEFs) provided in Table 2 of the petition (p. 000846) and concentrations for the individual 22 PAHs identified by the petitioner using the arguments presented below.

The maximum allowable PAH level in HPFB is 0.5 ppm (mg/kg). In addition to this specification limit, there are further specifications that no more than 0.005 ppm B[a]P and 0.005 ppm dibenz[a,h]anthracene (DB[a,h]A) are present in HPFB. Assuming that B[a]P and DB[a,h]A are present at their respective specification limits, and that each of the other 20 PAHs identified by the petitioner are present at equal levels, the following concentration for the other 20 PAHs is obtained:

$$\begin{aligned} \text{Conc. for PAHs without separate specs} &= \{(\text{Total PAH conc.}) - (\text{B[a]P} + \text{DB[ah]A} \\ &\quad \text{conc)}) / (\# \text{ PAHs without separate specs}) \\ &= \{(0.5 \text{ ppm}) - (0.005 \text{ ppm} + 0.005 \text{ ppm})\} / 20 \\ &= 0.0245 \text{ ppm or } 24.5 \text{ } \mu\text{g/kg (ppb)} \end{aligned}$$

Using these concentrations and the toxic equivalency factors (TEFs) listed in Table 2 of the petition (p.

000846), Dr. Jensen was able to calculate a total B[a]P-equivalent PAH concentration in HPFB:

PAH	TEF	Concentration (µg/kg)	B[a]P-weighted concentration (µg/kg)
acenaphthene	0.001	24.5	0.0245
acenaphthylene	0.001	24.5	0.0245
anthanthrene	0.32	24.5	7.84
anthracene	0.01	24.5	0.245
benz[a]anthracene	0.014	24.5	0.343
benzo[b]fluoranthene	0.11	24.5	2.70
benzo[k]fluoranthene	0.07	24.5	1.72
benzo[ghi]fluoranthene	0.01	24.5	0.245
benzo[ghi]perylene	0.03	24.5	0.735
benzo[a]pyrene	1	5	5
benzo[e]pyrene	0.007	24.5	0.172
chrysene	0.013	24.5	0.319
coronene	0.01	24.5	0.245
cyclopenta[cd]pyrene	0.1	24.5	2.45
dibenz[a,h]anthracene	1.05	5	5.25
fluoranthene	0.02	24.5	0.49
fluorene	0.001	24.5	0.0245
indeno[1,2,3-cd]pyrene	0.25	24.5	6.13
naphthalene	0.28	24.5	6.86
perylene	0.01	24.5	0.245
phenanthrene	0.01	24.5	0.245
pyrene	0.13	24.5	3.19
<b>Total B[a]P-equivalent</b>			<b>44.4</b>

Thus, the total B[a]P-equivalent concentration in HPFB is 44 µg/kg (ppb). We observe that although a B[a]P-equivalent concentration of 44 ppb was calculated, Dr. Jensen used a value of 43 ppb in the calculation. The value of 43 ppb was derived by CTFA using a similar approach for calculating the B[a]P-equivalent concentration as that outlined in the table above. Dr. Jensen noted that her value of 44 ppb (calculated above) “is essentially the same as that presented by CTFA” (43 ppb). Therefore, Dr. Jensen chose to use a B[a]P-equivalent concentration of 43 ppb in her subsequent calculations. We shall continue to use the value of 43 ppb in the elaboration of Dr. Jensen’s calculation.

Using the B[a]P-equivalent concentration of 43 ppb, the assumption that no more than 10% of PAHs present in HPFB are likely to be extracted into the cosmetic formulation<sup>[1]</sup>, and the unit risk factor for B[a]P<sup>[2]</sup> of 1.75 (mg/kg-bw/d)<sup>-1</sup>, Dr. Jensen was able to perform the following risk assessment for PAHs in HPFB:

$$\begin{aligned} \text{Exposure to B[a]P-equivalent PAHs} &= [(10 \text{ mg/p/d}) \times (0.043 \text{ mg/kg}) \times 10\%] \\ &= 4.3 \times 10^{-8} \text{ mg/p/d} \end{aligned}$$

For a 60 kg person, the exposure becomes:

$$\text{Exposure}_{\text{PAH, 60 kg person}} = [(4.3 \times 10^{-8} \text{ mg/p/d}) / (60 \text{ kg-bw/p})] = 7.2 \times 10^{-10} \text{ mg/kg-bw/d}$$

Multiplying the above-calculated exposure for B[a]P-equivalent PAHs by the unit risk for the PAH B[a]P yields an upper-bound lifetime risk of:

$$\begin{aligned} \text{Upper-bound lifetime risk} &= \{(7.2 \times 10^{-10} \text{ mg/kg-bw/d}) \times [1.75 \text{ (mg/kg-bw/d)}^{-1}]\} \\ &= \mathbf{1.25 \times 10^{-9}} \end{aligned}$$

In this way, Dr. Jensen calculated a lifetime cancer risk for PAHs contained in HPFB for use in cosmetics (including eye area use) of  $1.25 \times 10^{-9}$ .

By way of clarification, we note a calculation error on p. 7 of Dr. Jensen's 3/23/98 memorandum for the risk assessment derived by CTFA. We have reproduced the calculation from the information in Dr. Jensen's memorandum, below. Corrections are noted in **bold** font.

CTFA estimated the exposure to HPFB to be 50 mg/p/d and determined a B[a]P-equivalent concentration of 43 ppb. CTFA conservatively assumed that all PAHs present in HPFB were available for absorption by the body. Thus, CTFA calculated the exposure to B[a]P-equivalent PAHs to be:

$$(50 \text{ mg/p/d} \times 0.043 \text{ mg/kg}) = 2.15 \text{ ng/p/d} = 2.15 \times 10^{-6} \text{ mg/p/d} \text{ (Dr. Jensen's memorandum states 2.12 ng)}$$

for a 50-kg person this becomes:

$$[(2.15 \times 10^{-6} \text{ mg/p/d}) / (50 \text{ kg-bw/p})] = 4.3 \times 10^{-8} \text{ mg/kg-bw/d}$$

Multiplying by the unit risk factor of  $1.75 \text{ (mg/kg-bw/d)}^{-1}$  for B[a]P yields the upper-bound lifetime risk of:

$$\begin{aligned} \text{Upper-bound lifetime risk} &= \{(4.3 \times 10^{-8} \text{ mg/kg-bw/d}) \times [1.75 \text{ (mg/kg-bw/d)}^{-1}]\} \\ &= \mathbf{7.5 \times 10^{-8}} \text{ (not } 4.3 \times 10^{-8}, \text{ as in Dr. Jensen's memorandum)} \end{aligned}$$

Finally, we note that the risk assessment calculated in the memorandum dated 9/30/2003 (Folmer to Johnston; upper-bound lifetime risk of  $1.5 \times 10^{-8}$ ) represents a worst-case scenario in which the TEFs were not used (i.e., all PAHs present have the same toxicity as B[a]P). As this calculation was performed to reflect a different scenario from that presented by CTFA and Dr. Jensen, it cannot be directly compared.

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[1] See the 11/25/03 e-mail from D. Folmer to K. Biddle for a detailed discussion of the 10% assumption.

[2] See the Quantitative Risk Assessment Committee memorandum of August 9, 1990.

**Johnston, Celeste**

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**From:** Sheu, Chingju W  
**Sent:** Thursday, December 11, 2003 11:07 AM  
**To:** Johnston, Celeste  
**Subject:** Dr. Folmer's risk calculations

Celeste:

Dan provides a clear description of all the assumptions and calculations in arriving at the final cancer risk estimations. It was very easy to follow his memo and I fully concur with his risk assessment calculation.

Chingju

*Chingju W. Sheu*