On 9/11/18, 8:38 AM, "NTP Website" <ntpweb-noreply@ntp.niehs.nih.gov> wrote:

The following comments have been submitted to the Office of the Report on Carcinogens.

Our record of the submission is:

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Re: Nomination of Meat-Related Exposures to the National Toxicology Program for the Report on Carcinogens

Dear Dr. Lunn:

In a submission made on October 7, 2016, The Beef Checkoff provided evidence (reference number 13334) to the Office of the Report on Carcinogens (RoC) regarding critical research gaps and barriers to accurate assessment of polycyclic aromatic hydrocarbons (PAH) and heterocyclic amines (HCA) exposure from meat cooked at high temperatures, as identified by the reviews of Alaejos and Afonso (2011), Gibis (2016), and Singh et al. (2016). Since our earlier comment, two new studies (see attached) have been published, one creates meta-regression models to estimate the HCA and PAH content of meat and bread (Pouzou et al., 2018a) and the other uses these models and NHANES intake data to estimate dietary HCA and PAH exposure from meat and bread in the United States (Pouzou et al., 2018b). We would like to take this opportunity to provide your Office with a brief review of these new study citations, and alert you to this newly available exposure data.

Pouzou et al. (2018a) construct random effects meta-regression models to estimate the concentration of 2 HCA, 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP) and 2-amino-3,8-dimethylimidazo[4,5-f]quinoxaline (MeIQx), and 8 PAH [BaP, Chrysene (Chy), Benzo[a]Anthracene (BaA), Benzo[k]Fluoranthene (BkF), Benzo[b]Fluoranthene (BbF), Dibenzo[a,h]Anthracene (DahA), Indeno[1,2,3,c,d]Pyrene (IP) and Benzo[g,h,i] Pyrene (BghiP)], in beef, poultry, pork, seafood and bread using published reports of food concentration analysis. The concentration estimates obtained from this approach represent an improvement over existing estimation tools often used by epidemiologic cohorts. For example, compared to the Computerized Heterocyclic Amines Resource for Research in Epidemiology of Disease (CHARRED), the concentration estimates obtained by Pouzou and co-workers consider relevant cooking covariants (e.g. distance between heat source and food, cooking time, cooking temperature, and cooking instrument, and presence of skin, bone, or added oil), a broader array of foods (e.g. seafood and bread) and cooking methods (e.g. smoking), and include uncertainty estimations. In addition, Pouzou et al. include more analyses, many of which are up to 20 years more recent than those used to populate CHARRED. Continuous updating of food PAH and HCA analyses and databases are required to reflect advancements in detection equipment and methodology and changes in the food supply (Alaejos and Afonso, 2011; Singh et al., 2016).

NTP has previously acknowledged the complexity of evaluating exposure of HCAs from cooked meat (NTP 2002; NTP, 2016). The evidence provided by Pouzou et al. (2018a) affirms NTP's observation. While representing an improvement on estimate compilations such as CHARRED, Pouzou et al (2018a) highlight limitations in the published literature which continue to confound the ability to accurately assess meats cooked at high temperature as potentially carcinogenic exposures. Specifically, many experimental reports lack the methodological detail necessary to fully evaluate the accuracy and relevancy of results obtained. As such Pouzou et al. (2018a) were unable to use data from several publications due to lack of limit of detection reporting. In addition, the authors found limited information regarding relevant meat and cooking characteristics such as the fat and water content of the meat and the surface temperature of the meat during cooking. Often the core temperature of the final product was reported, but the core temperature is not directly related to the surface temperatures necessary to model the formation of surface compounds. The authors also found a trade-off between sample replications and breadth of sample types analyzed with one or the other often limited and most reports limited for both. An example of this comes from the CHARRED database where concentration of three of the 25 identified HCAs are estimated based on a one-time sample of meat collected from a local USA grocery store in the late 1990's (Sinha et al., 1998a; Sinha et al., 1998b). The sample types selected include one fat level of hamburger, 2 beef steak cuts, and one beef roast. Fresh pork was represented by a pork chop and processed pork by one brand of hot dog, a ham slice, and several types of breakfast sausage (Sinha et al., 1998b).

Using the models created by Pouzou et al. (2018a), Pouzou et al. (2018b) estimate dietary exposure to HCA and PHA from meat. The combined results from the two-day dietary component of NHANES for the years 1999–2014 were used to estimate the mean daily consumption of beef, pork, non-game poultry, and seafood of any kind (fish, mollusks, crustaceans, and cephalopods), and wheat-grain breads. The two most common methods of cooking for all types of meat were baking and pan-frying. Smoking was the third most consumed method of preparation for pork. No single meat type was found to dominate the exposure contribution to HCA and PAH. Cooking methods were the greatest drivers of PAH and HCA dietary exposure, even in the high consumption groups. A substitution scenario analysis was used to determine the estimated exposure associated with avoiding certain food preparation methods. Very few significant differences in HCA exposure overall suggests there may be little gain in exposures to those compounds by switching preparation methods or types of food. These data suggest that while high temperature cooking increases HCA exposure, the total consumption of foods prepared in the manner may not be sufficient to make recommendations to avoid foods prepared in this manner meaningful.

Differences in PAH exposures were most common when comparing barbecued foods of any kind against the fried or broiled equivalent, for example, barbecued beef was higher in PAH exposure than fried beef steak. Pork and poultry exposures to PAH8 were significantly lower than seafood, and pork exposures were significantly lower than bread PAH8 exposures. The observation of bread as a greater PAH contributor than pork echoes conclusions made by DeMeyer and coworkers (2016), "Indeed, comparable levels of PAHs are found in cereal products and in grilled poultry and fish, foods not found to be associated with an increased risk for CRC." These data suggest that rather than limiting assessment of exposure to these compounds to meat cooked at high temperature, assessment of all foods cooked at high temperature (i.e. breads, vegetables, etc), may provide a more accurate assessment of dietary HCA and PAH exposure from various cooking methods.

Pouzou et al. (2018a, 2018b) identify critical research gaps that continue to challenge accurate assessment of PAH and HCA exposure from foods cooked at high temperature. Significant evidence limitations call into question the importance and relevance of dietary PAHs and HCAs as a possible mechanism associated with cancer risk for red and processed meat intake (DeMeyer et al, 2016).

REFERENCES:

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Pouzou, J.G., Costard, S., Zagmutt, F.J. (2018a). Probabilistic estimates of heterocyclic amines and polycyclic aromatic hydrocarbons concentrations in meats and breads applicable to exposure assessments. Food Chem Tox. 114:346-360.

Pouzou, J.G., Costard, S., Zagmutt, F.J. (2018b). Probabilistic assessment of dietary exposure to heterocyclic amines and polycyclic aromatic hydrocarbons from consumption of meats and breads in the United States. Food Chem Tox. 114:361-374.

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Sinha, R., Knize M.G, Salmon, C.P., et al. (1998a). Heterocyclic amine content in beef cooked by different methods to varying degrees of doneness and gravy made from meat drippings. Food Chem Tox. 36:279-287.

Sinha, R., Knize, M.G., Salmon, C.P., et al. (1998b). Heterocyclic amine content of pork cooked by different methods and to varying degrees of doneness. Food Chem Tox. 36:289-297.

The files sent as attachments were:

Pouzou et al., 2018a.pdf

Pouzou et al., 2018b.pdf
