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October 7, 2016

National Toxicology Program  
P.O. Box 12233, MD K2-03  
Research Triangle Park, NC 27709

Dear Dr. Lunn:

As an academic researcher specializing in meat science, I appreciate the opportunity to respond to the National Toxicology Program's request for information regarding the nomination of meat cooked at high temperatures for possible review in their Report on Cancer. I am specifically commenting regarding the request for important scientific issues that will likely preclude efforts to accurately determine human exposure to the compounds formed during high temperature cooking, namely, heterocyclic amines (HCA) and polycyclic aromatic hydrocarbons (PAH). I'm available for further consultation, should the NTP wish to discuss the issues I've outlined below.

**Despite the availability in the past decade of numerous quantitative reports of HCA and PAH in various foods, the two most readily available HCA estimation databases have not been updated since at least 2003.**

Continuous updating of food HCA analyses and databases linked to these analyses are required to reflect changes in the food supply. The CHARRED database (NCI, 2015) is used to estimate exposure to HCA in a multitude of epidemiologic observational studies of human diet and cancer risk. Unfortunately, the CHARRED database reports only three of the 25 HCA identified in the food supply and then only in a one-time sample of meat collected from a local grocery in the USA in the late 1990's (Sinha et al., 1998a; Sinha et al., 1998b) and analyzed by a single laboratory. In addition, the meat selected for quantitation of HCA was limited, for beef – one fat level of ground beef, 2 steak cuts, and one roast were considered (Sinha et al., 1998a). Fresh pork was represented solely by a pork chop. Processed pork was represented by one brand of hot dog, a ham slice, and several types of breakfast sausage (Sinha et al., 1998b).

Jakszyn and co-workers (2004) created a database of HCA, PAH, and nitrosamines based on quantitative reports in the literature. While this database expands on values available from CHARRED, the methodology for HCA measurement is not uniformly reported or standardized across studies. In addition, no additional food data has been included since 2003. Despite availability of newer data, the CHARRED database also appears to have had no data updates but rather has only corrected errors and fixed database glitches (NCI, 2015). The limited scope of HCA compounds and representative foods used in the available HCA estimation databases calls into question the reliability of any estimates of human exposure to HCA reported since 2003.

Of the two, the Jakszyn database covers a wider variety of foods compared to CHARRED but both contain data that is at least 10 years old and not reflective of current detection methodologies and equipment.

The CHARRED database almost exclusively contains HCA data, with only a very limited amount of BaP data contributed to reflect PAH. Granted, the CHARRED database is most typically used to estimate HCA exposure, but the evaluation of meat cooked at high temperatures requires reliable estimation of both PAH and HCA. Unfortunately, the CHARRED database is not reliable tool for estimating either group of compounds.

**Standardization of cooking methods and terminology are needed in order to make comparisons between studies and across regions.** Failure to specify cooking conditions in experimental reports and variations in terminology for cooking methods used around the world has been recognized as a critical issue limiting comparison of the literature regarding HCA (Alaejos and Afonso, 2011). The same is apparent in the PAH/BaP literature. For example, in some countries “grilling” may or may not expose foods to direct flame, but limited or unspecified cooking conditions reported in research publications prohibits the ability to discern these differences. Limited methodologic details regarding cooking temperature, cooking duration, internal temperature reached at end of cooking, procurement procedures for food products, etc. limit the ability to replicate and compare results. Sound advice regarding preferred cooking methodologies designed to limit human exposure to PAH and HCA depends on complete and detailed reporting of experimental methodologies and replication of findings.

Marinating meat has been suggested as a practical method to decrease intake of HCA. However, there is also limited consistency with regard to the types of and ingredients in various marinades reported in the literature making it difficult to standardize a marinating strategy beneficial for all meats prepared via all methods and degrees of doneness.

**Experimental cooking methods may not represent typical preparation.** In an effort to maximize the production of cooking-derived compounds, many experiments are performed under extremes of cooking time or temperature that have little relevance to the cooking methods used by the general population (Alaejos and Afonso, 2011).

**CONCLUSIONS** - Critical research gaps indicate significant shortfalls and barriers to accurate assessment of HCA and PAH exposure from all foods. Consequently, there is a critical need to update existing databases, through an assessment of the current food supply and typical in-home preparation methods, using recent methodology, in order to better evaluate exposure to HCA and PAH from red and processed meat, as well as from other foods, including white meats.

Sincerely,

Signature redacted

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## References:

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