Priv.-Doz. Dr. Wolfgang Völkel (PhD)
European Registered Toxicologist (ERT)
Bavarian Health and Food Safety Authority

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Dear Dr. Shane,

I want to send some comments for NTP Draft Brief on Bisphenol A.

In the Appendix 1 NTP cites a lot of literature measuring blood levels (including Völkel et al). Your conclusions are that in some cases the published values of free BPA may not represents the "true" concentration of free BPA. I fully agree to this conclusion and in addition I fully agree to the statement that CDC methods may be considered to be very accurate. This is also discussed in a publication in press of Völkel et al.
http://www.sciencedirect.com/science?_ob=PublicationURL&_tockey=%23TOC%235177%239999%23999999999%2399999%23FLA%23&_cdi=5177&_pubType=J&_auth=y&_acct=C000050221&_version=1&_urlVersion=0&_userid=10&md5=7925f51f51a48fcf9bc5715c2fd4719b
In this paper more than 400 urine samples for free BPA were analysed. All results were compared to CDC's data and to data of Tsukioka et al. and were very similar. Nevertheless some data were provided that these low free BPA levels may occur from contamination and an experiment was performed to confirm such statements administering both BPA and d-$_{16}$-BPA and in good agreement with the results published by Völkel et al. 2002 no free $d_{16}$-BPA was observed in urine.
It's a pity that many researchers do not discuss such small background levels although (to me) it may be normal to get contaminations or background problems if you have to analyse chemicals produced in large quantities like BPA.
Look to the publication of Schönfelder et al 2002 in EHP – in figure 3A a signal for BPA is described at LLOD and in B a signal for BPA "clearly below LOQ" but with a totally different scale and if you zoom in you clearly see a signal similar in height as shown in A. In my mind this shows clearly that there is a background or contamination but this is not discussed in the text and not criticised by the reviewers of the article.
Nevertheless as described in the publication of Völkel et al. Tox Lett. in press (tab. 3) the observed free BPA levels measured by the 3 independent groups are about 800-fold below the TDI of BPA for the maximum value observed. Since the median levels of free BPA are more than 6000-fold below the TDI in my mind it is not so important whether this value is true or a contamination.
In addition in this publication blood levels calculated from the measured urine levels are discussed and an assessment for the uptake of babies using BPA containing PC-bottles is given.
A comment to page 13 paragraph 2 starting with "Taken together these data indicate that…" and the statement that the data of Taylor show that first pass metabolism is reduced in fetal or infant animals. In my mind the data of Taylor didn't show that there is no metabolism to conjugates of BPA. The authors didn't provide any data of total BPA of BPA conjugates and so on. Why did they not show a chromatogram of the water sample where they expect conjugates (if present) or a separation with and without enzymatic treatment (as CDC and others did) to show there is an increase or not. In addition the Peaks given in figure 1 are really broad especially for the

analytical parameters described. Therefore in my mind the results presented did not really confirm that higher levels of free BPA occur in infants.
Furthermore it is clearly shown that rodents and humans provide different kinetics for BPA and so a transfer of results observed in rodents to humans would be difficult. Therefore I suggest as already done in the manuscript (in Press Tox. Lett.) to analyse urine samples from human infants for free and total BPA. Using these data a valuable risk assessment is possible.
I did really not understand why so much animal treatments in rodents were performed if it is clear that they are a weak model for humans in case of BPA.
At the end I would say that we have really a lot of data especially in humans to perform a valid risk assessment for BPA and in my eyes the chemical is safe for adults and with a high feasibility also for infants. Therefore I don’t understand why BPA should be banned and a new surrogate with probably not so well known data sets regarding exposure, kinetics and adverse effects especially in humans should replace BPA. I would say with such an action we will get a higher risk compared to BPA exposure due to unknown features of new compounds.