Message

From: Woodbury, Lynn [woodburyl@cdmsmith.com]
Sent: 12/10/2019 6:37:49 PM
To: Partridge, Charles [Partridge.Charles@epa.gov]
CC: Wall, Dan [wall.dan@epa.gov]; OBrien, Wendy [OBrien.Wendy@epa.gov]; Greene, Nikia [Greene.Nikia@epa.gov]; David Shanight [shanightdt@cdmsmith.com]
Subject: RE: meconium literature

Just for illustration…here are the results for a simple Google Scholar query of the search terms "meconium+metal+infant".
https://scholar.google.com/scholar?hl=en&as_sdt=0%2C44&as_ylo=2000&as_yhi=2020&q=meconium+metal+infant&btnG=
As shown, there are more than 3,300 potentially relevant papers published since 2000 with these keywords.

There are 4 studies cited in the McDermott discussion of their results – Arbuckle et al. (2016), Ettinger et al. (2017), Aziz et al. (2017) and Turker et al. (2013). EPA should have copies of all four studies. Here are the key excerpts from the McDermott discussion regarding these studies:

4. Discussion

The relatively low concentrations in the 17 newborns from Columbia are similar to levels reported in other studies of meconium and in the low μg kg^{-1} range (or less) (Arbuckle et al., 2016; Ettinger et al., 2017; Aziz et al., 2017; Turker et al., 2013). It is noteworthy that the primary metal being monitored by the EPA in Butte, MT on an ongoing

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implicated in the literature as potential neurotoxins, especially when exposure is chronic (Turker et al., 2013; Karri et al., 2016; Lucchini et al., 2017). A study from Turkey compared meconium levels of Pb, Cd, Zn, Fe and Cu in preterm surviving and non-surviving fetuses/stillbirths, and reported statistically significant higher metal levels in the non-survivors (Turker et al., 2013). The concentrations in the live births of that study were comparable to the Columbia data and the stillbirths had levels of metals that were actually lower than the measurements made in Butte. Clearly, this preliminary study warrants further work in integrating data on environmental exposure, other exposures and no-

The results of the two MIREC studies (Arbuckle/Ettinger) and the Aziz study are very clear…all present meconium concentrations as ug/g or ppm.

As I noted in my earlier email, the Turker study does not provide results as metal concentration per mass of meconium, but has also normalized by infant body weight. Thus, their results would need to be converted to make direct comparisons to the McDermott results. There were also a few other inconsistencies with this paper – for example, the units reported for the detection limits are as ug/mL (whereas meconium is a solid and the tabular results are expressed not as ug but as ng). Also, the Turker discussion makes mention of a toxicity threshold in terms of ug/g, which is odd since that is not the basis of their results. I didn't feel comfortable enough with the content of this study to include it in the summary table provided in the presentation. However, if believe the results are indeed ng/g/kg and you adjust the reported values based on the median body weight, they would be closer to the Columbia values, but also inconsistent with the Aziz study.

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From: Partridge, Charles <Partridge.Charles@epa.gov>
Sent: Tuesday, December 10, 2019 10:41 AM
To: Woodbury, Lynn <woodburyl@cdmsmith.com>

Cc: Wall, Dan <wall.dan@epa.gov>; OBrien, Wendy <OBrien.Wendy@epa.gov>; Greene, Nikia <Greene.Nikia@epa.gov>
Subject: RE: meconium literature

Thanks Lynn, please move forward and we realize that it may not be logistically feasible for today. That being said, I believe that the main concern is that we have not missed something and that there are not any studies referenced in that Butte paper in which similar low levels of metals in the meconium appear.

cp

From: Woodbury, Lynn <woodburyl@cdmsmith.com>
Sent: Tuesday, December 10, 2019 10:17 AM
To: Partridge, Charles <Partridge.Charles@epa.gov>; OBrien, Wendy <OBrien.Wendy@epa.gov>
Cc: Wall, Dan <wall.dan@epa.gov>; Greene, Nikia <Greene.Nikia@epa.gov>; David Shanight <shanightdt@cdmsmith.com>
Subject: RE: meconium literature

I think there probably are several other studies that may be available in the literature. I have not sought to do a comprehensive literature search. To date, I was mainly focused on obtaining the primary literature cited in the McDermott study discussion and some of the secondary sources identified in those cited papers.

I can request that our CDM Smith InfoCenter perform a more comprehensive search; however, I'm not sure if it is feasible to have that search completed, literature acquired, and relevant studies reviewed today/tomorrow.

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From: Partridge, Charles <Partridge.Charles@epa.gov>
Sent: Tuesday, December 10, 2019 10:08 AM
To: Woodbury, Lynn <woodburyl@cdmsmith.com>; OBrien, Wendy <OBrien.Wendy@epa.gov>
Cc: Wall, Dan <wall.dan@epa.gov>; Greene, Nikia <Greene.Nikia@epa.gov>
Subject: RE: meconium literature

Lynn,

Can you do a quick literature search to see if we are missing any studies? We need to know that we have a good grasp on the literature before we release a press release today or tomorrow. Of course only with Nikia's agreement and direction.

cp

From: Woodbury, Lynn <woodburyl@cdmsmith.com>
Sent: Tuesday, December 10, 2019 8:48 AM
To: OBrien, Wendy <OBrien.Wendy@epa.gov>
Cc: Partridge, Charles <Partridge.Charles@epa.gov>
Subject: RE: meconium literature

Wendy –

Here is literature I have pulled thus far…see attached. I have added highlights in most documents specific to the meconium results.

A few items of note:

- There are two published MIREC studies with meconium data – Ettinger 2017 (arsenic) and Arbuckle 2016 (cadmium, lead, manganese, mercury). Both are referenced in the McDermott paper in the discussion.

- The Turker et al. (2013) study is also one that is being referenced in the McDermott paper; however, I didn't find this study to be especially helpful because of the way the meconium concentrations are being reported. First, the authors indicated the values are being expressed as ng/g/kg (i.e., as a dose per mass of infant body weight). Because individual body weight values aren't provided, we would need to convert based on an assumption the median reported body weight applies to all samples, which is not ideal. Second, I suspect there may be a typo in the reported units. In other places within the article text, it appears the Greek mu character (μ) was manually added after the fact. Given expected meconium concentrations in other studies, I suspect the 'n' character in ng/g/kg was supposed to replaced by μ. The other oddity about this study is that the detection limits are reported as μg/mL, which is unexpected as meconium is a solid. These are Turkish researchers publishing an English translation in a Japanese journal…I'm thinking something may have gotten lost in translation. I have not included this results of this study in the presentation, but it may be worth reaching out to the researchers to clarify their results as McDermott does rely upon this study in their results interpretation.

- The Friel et al. (1989) study looked promising at first, but it too has limitations due to the way the results were reported. Meconium concentrations were reported as μg/kg, BUT the kg in the denominator is not based on the mass of meconium, but the mass of the infant. I estimated the meconium concentration based on the total metal mass reported and then normalized it based on the average mass of stool passed for full-term infants (8.9 g), which is not ideal, but provides another dataset to support our findings.

Let me know if you need any additional literature,
Lynn

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From: OBrien, Wendy <OBrien.Wendy@epa.gov>
Sent: Tuesday, December 10, 2019 8:11 AM
To: Partridge, Charles <Partridge.Charles@epa.gov>; Woodbury, Lynn <woodburyl@cdmsmith.com>
Subject: meconium literature

Can anyone share the literature cited in the presentation with me? I have the Canadian study and the Aziz study. Thx.

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