Investigating Flame Retardant Applications in Furniture and Impacts on Children's Exposure to Firemaster® 550

by

Xuening Tang

Dr. Heather Stapleton, Advisor

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Executive Summary

Flame retardants are chemicals that have been commonly added to furniture, electronics, and construction materials in order to prevent or reduce the spread of fire. 2-ethylhexyl-2,3,4,5-tetrabromobenzoate(EH-TBB) is one component in a flame retardant mixture known as Firemaster® 550 (FM550), which is a replacement for PentaBDE that was banned in 2004 due to health concerns. In this study, we investigated whether FM550 treatment in furniture contributed to higher levels of exposure in children residing in NC.

This study includes samples collected from participants in the TESIE study. The Toddlers Exposure to SVOCs in the Indoor Environment (TESIE) study sought to investigate exposure of children to SVOCs mixtures and examine their possible effects. Children in this study were recruited between 2014 to 2016. Our project selected 125 participants from the TESIE cohort who had paired samples of furniture foam, house dust, a personal handwipe and a composite urine sample. In this study, we measured tetrabromobenzoic acid (TBBA), the urinary metabolite of EH-TBB, to measure children's exposure to EH-TBB and then compared their exposure to levels in house dust, furniture foam, and in handwipes. After using standard protocols to extract different samples and applying statistical analysis of raw data, our findings demonstrate that children experience exposure to EH-TBB from the application of Firemaster® 550 in residential furniture.

Key findings include:

1) The presence of Firemaster® 550 in furniture was associated with significantly higher average levels of EH-TBB in house dust, in hand wipes, and in the urinary levels of tetrabromobenzoic acid (TBBA), the metabolite of EH-TBB ($p<0.01$).
2) Higher levels of EH-TBB in the home (e.g., in dust) were correlated with higher levels of EH-TBB on children's hands, which is also consistent with higher level of EH-TBB urinary metabolites, and thus higher exposure, in children ($p<0.001$).
3) Higher urinary tetrabromobenzoic acid (TBBA) levels were observed in Non-Hispanic Black children compared to Hispanic or White Children ($p<0.05$).

Key recommendations include:

1) Limited data is available on children's exposure to EH-TBB, and more studies are needed to measure urinary levels in both adults and children.
2) As this was a small study, larger studies are needed to determine if exposure levels are consistent in the broader population and in different regions. Including a larger number of participants with different age ranges and more diversity of participants' race would be valuable to understanding variables contributing to exposure.
3) Additional studies are needed to investigate how stable TBBA is in the body and how variable levels are in urine from day to day.

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1. INTRODUCTION

Flame retardants (FRs) are a group of chemicals that have been commonly added to furnishings, electronics, transportation products and construction materials since the 1970s in order to prevent or reduce the spread of fire (de Wit, 2002). While some of these standards are voluntary, the strict flammability standard implemented by the State of California in 1975, known as Technical Bulletin 117(TB 117), is required for some residential furniture products on the market (State of California BEARHFTI, 2000). Therefore, FR chemicals have been used over the past few decades, especially in polyurethane foam (PUF), which is usually found in upholstered furniture and then purchased by customers from markets (Hammel et. al, 2017). However, due to the constant and frequent use in furniture and electronic devices, concerns have been raised about the exposure risk to human and environmental health, and many flame retardants are gradually being removed from production and from the market. In 2013, a revised regulation called California Technical Bulletin 117-2013(TB 117-2013) was announced to eliminate the open flame test requirement of TB 117. This new standard gives the manufacturers the option of using smolder resistant fabrics or barriers beneath the fabrics in California to pass the flammability standard. In 2019, the CPSC amended the law to require that all residential furniture solid in the US meet TB 117-2013.

FRs are usually categorized into two groups based on their mode of application. These two groups are additive and reactive FRs, among which, we will focus on additive FRs. Additive FRs are not chemically bonded to the material in which they are applied and include halogenated or non-halogenated flame retardants (Talsness et al., 2008). Reactive FRs in contrast are mixtures which can chemically transformed to create a new fire-resistant material (Hull et al., 2014). Then, halogenated FRs can further be classified as brominated or chlorinated FRs. Among them, the dominant type in the past introduced in furniture is a PBDE commercial mixture known as PentaBDE, which has been detected in numerous previous studies with ubiquitous detection in human tissues and the environment (Stapleton et al., 2012a; Stapleton et al., 2012b; Hoffman et al., 2014). Chemical replacements for PBDE's have gradually been developed and introduced to the market over the last 20 years in order to fulfill product flammability standards. One of these replacements is Firemaster® 550 (FM550) (Stapleton et. al, 2012a). Firemaster® 550 is a formerly proprietary FR mixture consisting of triphenyl phosphate (TPP; 19.8±0.1%), 2-ethylhexyl-2,3,4,5-tetrabromo-benzoate (EH-TBB; 29.7%±0.3%), bis(2-ethylhexyl)-2,3,4,5-tetrabromophthalate (TBPH; 13.9%±0.1%) and the mixture of isopropylated triphenyl phosphate isomers (ITPs; ~ 36.6%) (Stapleton et al. 2008a). FM550 is an additive flame retardant like PBDEs, which means it could easily leach into environment from furniture over time due to not chemically bounded to products (Stapleton et al. 2008a).

In this study, we will focus on EH-TBB, the most abundant brominated compound in FM550. EH-TBB has been highly detected in home indoor dust and outdoor air in previous research studies, suggesting it is emitted from products during their use (Ali et. al, 2012; Dodson et. al, 2012). This chemical has a log K_{ow} of 7.47; a log K_{oa} of 11.6 and a vapor pressure of 3.56e-7 mmHg. While the number of toxicity tests conducted are limited, it does have a reported EC_{50} value of 7mg/L and a LOEC (Lowest Observed Effect Concentration) of 2.5mg/L for acute mortality risk in zebrafish (EPA dashboard: 183658-27-7). Previous studies in vivo and in vitro have found that EH-TBB is commonly metabolized in human hepatic tissues to 2,3,4,5-tetrabromobenzoic acid (TBBA), the structure of which is shown in Figure 1; however, there are few studies that have investigated exposure impacts on human health (Roberts et. al, 2012). Based on recent studies in the rat model, FM550 may be an endocrine disruptor and may be an obesogen. Impacts on the following health endpoints were observed in a rodent perinatal study: altered thyroid function in dams, while offspring entered puberty early, demonstrated obesity, and displayed altered behaviors suggestive of anxiety. (Patisaul et. al, 2011). Furthermore, male offspring displayed cardiachypertrophy. These effects were observed at elevated doses; however, it is still not clear whether these effects could happen in humans. But these results provide a rationale for evaluating EH-TBB exposure, especially for children. Only one prior study has investigated exposure. In that study, children were found to assessed with higher urinary levels of TBBA compared with their mothers, suggesting higher exposure due to the frequent hand-month behaviors, which simulates dust-associated contaminants exposure level (Butt et. al, 2014).

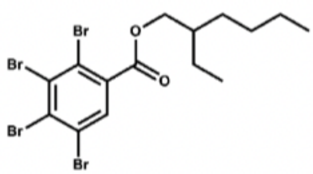
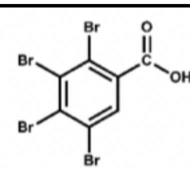
Parent Compound	**Metabolite**
	
2-ethylhexyltetrabromobenzoate (EH-TBB)	tetrabromobenzoic acid (TBBA)

Figure 1. The structure of the parent chemical, EH-TBB (present in Firemaster 550) and its metabolite, TBBA.

The main objective of this research study was to investigate whether FM550 treatment in furniture contributes to higher levels of exposure in residential children in North Carolina (NC). Specific aims of this study were to: 1) measure urinary levels of TBBA in archived pooled urine samples from toddlers; 2) assess the relationships between the detection of FM550 in furniture foam with exposure levels in children, 3) evaluate demographic predictors of urinary TBBA exposure in children residing in North Carolina, and 4) assess the correlations between TBB levels in house dust and hand wipes samples with the TBBA levels in children's urine.

2. MATERIALS AND METHODS

2.1 Sample collection

This research includes samples collected from participants in the TESIE study. The Toddlers Exposure to SVOCs in the Indoor Environment (TESIE) study sought to investigate exposure of young children to SVOCs mixtures as well as examine their possible effects on health and development. The cohort included 190 families with total 203 children that previously enrolled in The Newborn Epigenetic Study (NEST). Participants were recruited by phone, mail or email invitation between August 2014 to April 2016. During home visit, detailed environmental assessments were conducted and questionnaires about children's living environment, behavior and health conditions were completed by their parents. For further information of this cohort, it could be found in Hoffman et al., 2018 and Hoyo et al., 2011. This study includes paired samples of indoor dust, furniture foam, children's handwipe and children's urine collected during the TESIE home visit using standard protocols. Details of the sample collection and analysis are provided below.

2.2 Foam sample analyses

Participants were asked if the research team could collect a very small piece (a marble sized sample) of the foam from a resident's sofa or chairs in the main living area. Samples were only collected if a participant agreed, and if the cushions contained a zipper to access the foam. Pre-cleaned scissors were used to cut out a small piece which was then transferred and wrapped with pre-clean foil and stored in an airtight plastic bag. After collection, samples were taken back to the lab and stored at -20°C until being processed and analyzed. All foam samples collected were screened for the presence of 7 specific flame retardant chemicals using GC-MS (gas chromatography mass spectrometry) as reported in Cooper et al. 2016. The 7 flame retardants that were assessed included PentaBDE, Firemaster 550, Firemaster 600, a mixture of isopropylated triaryl phosphates, TCCP, TDCPP and V6. Samples were deemed positive for a flame retardant if there was a match with an authentic standard and the concentration of the FR was >0.1% by weight.

2.3 Handwipe and dust analysis

Dust and hand wipe samples were processed in the laboratory and analyzed for 2-ethylhexyl-2,3,4,5-tetrabromobenzoate (EH-TBB) level based on methods previously reported (Stapleton et al., 2014, Van den Eede et al., 2012, Van den Eede et al., 2011). Briefly, hand wipes samples were first spiked with internal standards and then extracted with 1:1 volume of dichloromethane and hexane by sonication and using a SpeedVac™ Concentrator to concentrate samples to around 1 mL. Florisil solid-phase extraction was applied for cleaning extracts (Supel-clean ENVI-Florisil, 6 mL, 500 mg; Supelco). Final extracts were concentrated down again to around 1ml with a SpeedVac™ Concentrator and then analyzed via GC-MS. For dust samples, they were extracted in a similar protocol as hand wipe samples except for minor difference with splitting extracts. More details on the dust extraction methods can be found in previous publications (Phillips et al., 2018).

2.4 Urine extraction and analysis

The pH and specific gravity (SG) value of each pooled urine sample was measured by a pH meter and a digital handheld refractometer, respectively, prior to analysis. The method used to extract

TBBA from urine is a modified method from a previous publication (Fang et al. 2015). Urine samples (5 mL) were extracted using an Oasis HLB cartridge (6 mL/500 mg). Cartridges were first conditioned with 5 mL 0.12 M HCl-MeOH ("AMeOH") followed by 5 mL 0.12M HCl. Before loading onto cartridges, all samples were acidified to pH ≤1.2 with 6M HCl (~100-300 uL) and spiked with ^{13}C-TBBA (50 µl, 0.5 µg/ml). Then the loaded cartridges were washed with 5 mL 0.12M HCl followed by 5 mL 100% MeOH and 5 ml DI water and finally eluted with 2% NH_4OH in ACN. After concentration to near dryness using an N-EVAP 112 Nitrogen Evaporator (Organomation Associates, Inc, part # 11250), the samples were reconstructed in 400 uL 1:1 LC-grade water: ACN (v/v) and filtered through 0.2 um nylon disc filter. TIBA (110 ng) was added prior to analysis using LC-MS/MS (liquid chromatography tandem mass spectrometry) with an Agilent Eclipse XDB C8 column (3.5 µm, 4.6 mm x 100 mm). Lab processing blanks were included and analyzed alongside samples. Quantification was applied using multiple reaction monitoring (MRM) with negative ion electrospray (ESI-) LC-MS/MS. Agilent Masshunter quantitative analysis software was used to integrate the data files.

2.5 Statistical Analysis

This test evaluated 125 urine samples from children including samples from their siblings who live in the same home. Prior data on EH-TBB levels in paired samples of handwipes, dust and foam were also included, which were analyzed with SAS statistical software (version 9.4; SAS Institute Inc., Cary, NC). For dust and urine samples, method detection limits (MDLs) were calculated by three times the standard deviation of the average lab blanks, and for handwipes, the MDL was calculated by three times the standard deviation of the average field blanks (Phillips et al., 2018).

Based on the specific gravity adjusted TBBA concentrations in urine, the distribution of data was heavily skewed and the detection frequency was 43%. For statistical analyses, all TBBA level below MDL were imputed with a value equal to ½ MDL. Spearman correlations were applied to evaluate correlations between paired samples of urine, handwipes and dust. The detections of EH-TBB in foam samples were modeled as a dichotomized variable (EH-TBB presence or absence in foam) and used in a Mann-Whitney test to determine whether it was related to levels in urine, handwipes or dust. Positive detections of FM550 or FM600 in each foam sample were considered positive for the presence of EH-TBB.

A logistic regression model was performed to assess the probability of urinary TBBA detection (above MDL) based on race and the absence or presence of EH-TBB in foam as independent variables. Exponentiated beta coefficients were applied in the results interpretation part and represent the change in odds to the outcomes related to the reference category. In all cases, statistically significant was considered as a p-value smaller than 0.05 .

3. RESULTS AND DISCUSSION

3.1 Study population

Data included in this study were collected from 125 participants who had paired urine and foam samples available for analysis. Of those 125 children, 42.4% were female and 56.8% were male (only one sample was reported as unknown). Children's age ranged from 38 to 73 months and most families identified as Non-Hispanic Black (41.6%), while 39.2% identified as White and 17.6% identified as Hispanic. A majority of the mothers (52.8%) reported receiving less than a college degree while 44.8% reported receiving a college degree. Further demographic characteristics information can be found in Table 1.

Table 1. Demographic Information of Participants in TESIE Cohort (N = 125)

Characteristics	N or mean	% or range
Child gender		
Male	71	56.8%
Female	53	42.4%
Child age		
Months (average)	54	
38 months-51 months	39	31.2%
52 months-56 months	39	31.2%
57 months-73 months	45	36.0%
Maternal race/ Ethnicity		
Non-Hispanic white	49	39.2%
Non-Hispanic black	52	41.6%
Hispanic white	22	17.6%
Other	2	1.6%
Maternal educational		
Less than college graduate	66	52.8%
College graduate or more	56	44.8%
Weight of children (kg)	18.5	13.0~35.5

3.2 EH-TBB measurements in induvial matrices

3.2.1 Urine

The detection frequency for urinary TBBA was 43.20% (Table 2). Although the detection frequency was low, the maximum value measured was approximately 23 times higher than the MDL, which reflects a wide range in exposure to EH-TBB among the population. Values reported here are similar to the range of values reported in an adult cohort in NC (Hoffman et al., 2014).

Table 2. Descriptive Statistics of Testing Samples (N=125)

	MDL	Detection Frequency (%)	Median	75th Percentile	95th Percentile
TBBA in Urine (pg./ml)	7.11	43.20%	<MDL	21.28	118.2
EH-TBB In Handwipes (ng)	0.29	100%	10.36	35.76	145.6
EH-TBB in dust (ng/g)	1.53	100%	298.2	769.1	8206

3.2.2 Dust and Handwipes

The detection frequencies for EH-TBB in both hand wipes and dust were 100% (Table 2). Median EH-TBB levels in dust were 298.2 ng/g while the 95th percentile reached 8206 ng/g. In handwipes the median mass of EH-TBB measured was 10.36 ng with a 95th percentile of 145.6 ng. This wide range of measured EH-TBB in dust and in handwipes indicate that there is wide variability in the levels of exposure in different living conditions. These levels include data ranges and median values in dust and handwipes that are similar to levels reported in adult and children's studies from NC (Hoffman et al., 2014; Hammel et al. 2017).

3.2.3 Polyurethane foam

In some cases, participants provided more than one furniture sample for testing of flame retardants, and thus ultimately there were 169 PUF samples tested from the 125 participants. Of the 169 foam samples collected from participants' sofas and chairs, the most frequently detected flame retardant mixture was FM550, which appeared in 31 samples. The next most commonly detected flame retardants were TDCPP, found in 25 samples, FM600, found in 10 samples, and PentaBDE detected in 10 samples (Table 3).

Table 3. Flame retardants detected in residential foam samples (N=169)

Flame Retardant Mixture	Detection Number in Samples
FM550	31
TDCPP	25
FM600	10
PENTA	10
TCPP	6
TBPP	6
MPP	2
TPP	2
V6	1
DEG-BCPP	1
ITPP	1
Thermolin101	0

3.3 Spearman rank correlations

To assess whether the chemical concentrations were similar among the children and homes, spearman correlations were calculated with the urine, handwipe and dust data. Figure 2 presents the scatter plots and highlights the positive and significant correlations observed among the various matrices. The Spearman rank correlation coefficients (*rho, Rs*) for dust and handwipes resulted in the highest correlation coefficient of 0.53, which was statistically significant ($p<0.001$). The fact that these two matrices are correlated suggests that if higher levels of EH-TBB are detected in dust, higher EH-TBB will be detected on handwipes. Furthermore, both dust and hand wipes were significantly correlated with urinary TBBA levels, despite the low detection frequency for TBBA. Although the magnitude of the correlation coefficient in for dust and urine is lower than the coefficient for handwipes and urine, it still suggests that as EH-TBB levels in dust increase, higher urinary TBBA level are more likely to be observed (p<0.001). These results suggest higher level of EH-TBB in the home (e.g., in dust) leads to higher levels of EH-TBB on children's hands, which is also consistent with higher level of EH-TBB urinary metabolites, and thus higher exposure, in children.

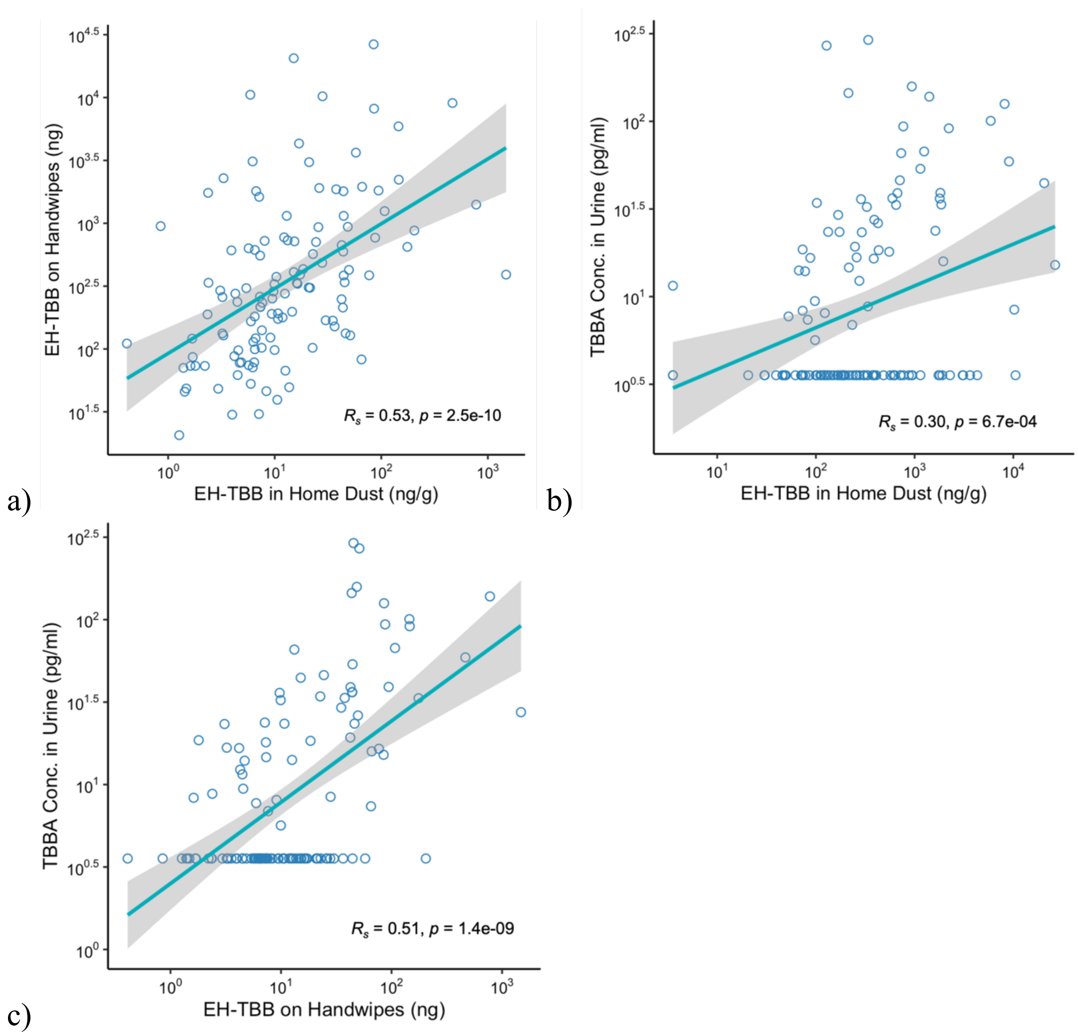


Figure 2. Scatter plots showing paired EH-TBB data in hand wipes and in house dust and TBBA in urine samples. Spearman correlation coefficients (R_s) and associated p-value are displayed in bottom-right corner (N=125).

3.4 Associations between EH-TBB in foam and TBBA in urine

Using a Wilcoxon rank sum test, we found that the presence of EH-TBB in foam (from use of either FM550 or FM600) was significantly associated with higher levels of TBBA in children's urine. As shown in Figure 3, if EH-TBB was detected in the foam from furniture in the children's home, the average urinary levels of TBBA were about 4.9 times higher compared to children living in homes without EH-TBB in their furniture ($p<0.01$). The median urinary TBBA level in the 98 urine samples from children living in homes without EH-TBB detection in foam (3.56 pg./ml) is really close to the MDL. The TBBA detection frequency in the group of children that have EH-TBB in the foam was 57.14% compared to the detection frequency in children that did not have EH-TBB in their foam (39.58%). Some children had elevated levels of TBBA detected in their urine even if FM550/600 was not detected in their sofa, suggesting that the sofa may not be the only source of their EH-TBB exposure. It's possible that other furniture items in the house, or even baby and children's products, such as nursing pillows or changing-table pads, could contain FM550/600 and be additional sources of exposure in children (Stapleton et al., 2011). Regardless, this association indicates furniture containing FM550 and FM600 likely serves as a primary source of EH-TBB exposure.

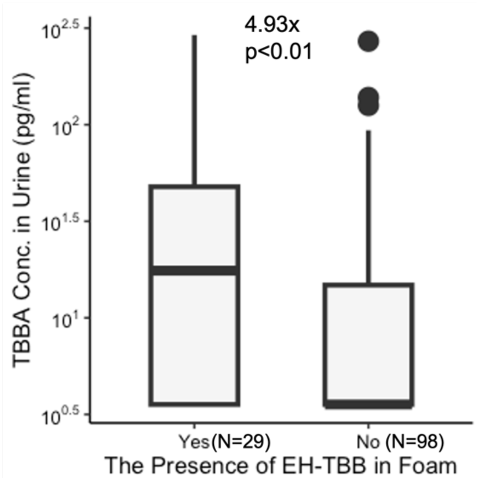
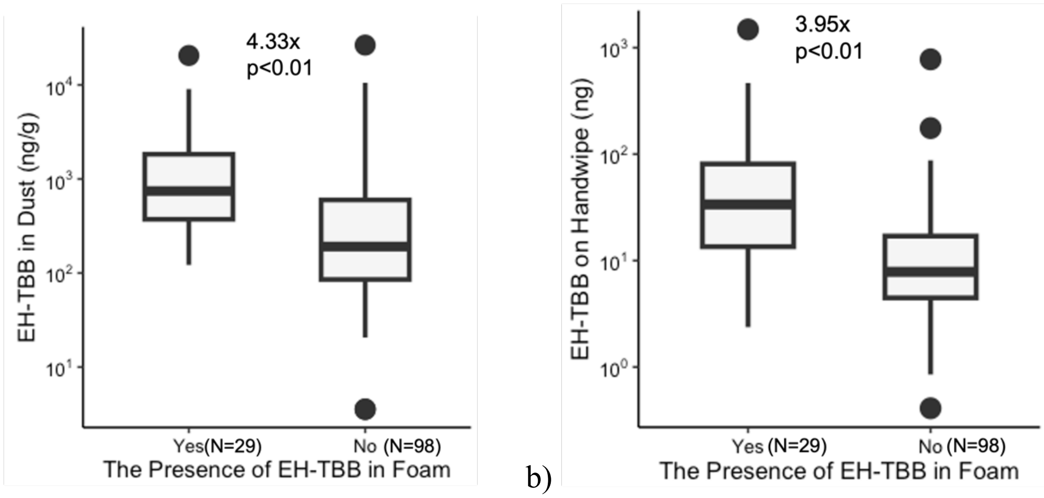


Figure 3. Box whisker plots of urinary TBBA levels based on absence or presence of EH-TBB in paired foam samples. The relative difference in the median urinary levels based on category (yes or no) is shown in the top center, which was performed by Wilcoxon rank sum exact test.

3.5 EH-TBB in foam and dust/ on hand wipes

The presence of EH-TBB in foam was also associated with higher levels of this chemical in both the home dust and in children's hand wipe levels (Figure 4). EH-TBB levels in dust and in handwipes from homes with FM550/600 were 4.33 and 3.95 times higher than in children living in homes without FM550/600, respectively ($p<0.01$). These results lend further evidence to suggest that the furniture in the home is a significant source of EH-TBB to the ambient environment and leading to higher concentrations in both house dust and in chemical residues on our skin.



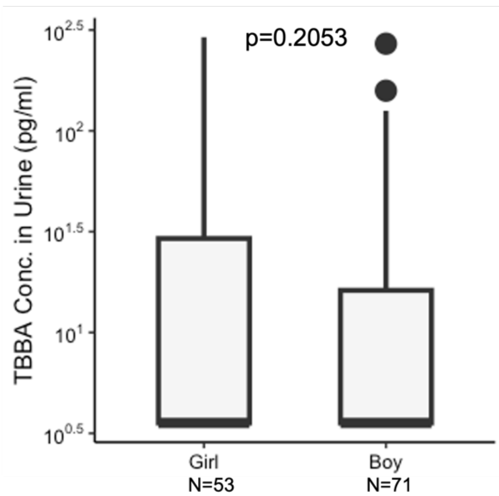
a) b)

Figure 4. Boxplots displaying the EH-TBB levels in dust (a) and hand wipes (b) based on presence or absence of EH-TBB in paired foam samples. The relative difference in the median dust and hand wipe levels based on category (yes or no) are shown in the top center of each plot, which were performed by Wilcoxon rank sum exact test.

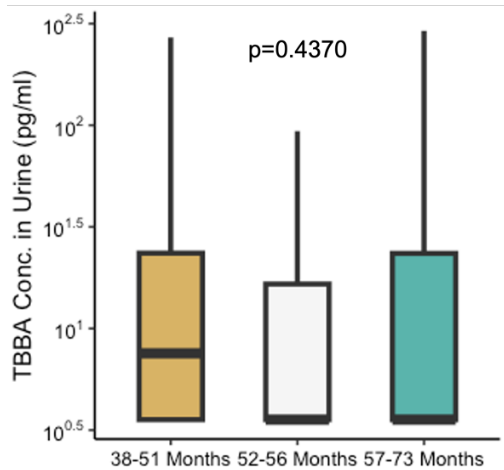
3.6 Urinary TBBA in different categories

To further examine predictors of urinary TBBA levels in children, additional analyses were conducted with the demographic information. Differences in exposure levels by gender (boy & girl), age (three age groups) and race (Black & White & Hispanic) were assessed (Figure 5). For gender and age categories, no significant differences in the average urinary TBBA levels were detected. However, based on the results from Kruskal-Wallis rank sum test, the average urinary TBBA levels were significantly different based on race and ethnicity ($p<0.05$, Figure 5c). A Pairwise Wilcox test was conducted to further assess differences, revealing that exposure was significantly higher in Non-Hispanic Black children compared to Hispanic children ($p<0.05$). However, there was no difference between detected urinary levels in Non-Hispanic White children compared with the Hispanic group ($p=0.105$). On average, urinary levels of TBBA were 2.12

times higher in Non-Hispanic Black children compared to Hispanic children. The reasons for this difference are unclear but may be attributed to the age of the furniture or differences in behaviors that influence exposure (e.g. time spent indoors).



a)



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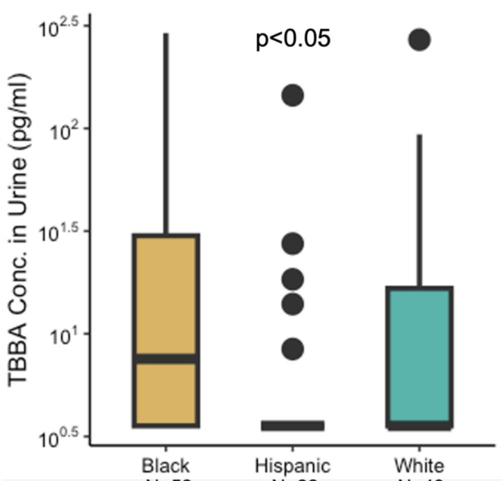

c)

Figure 5. The difference of TBBA level in urine based on: a) gender, b) age, and c) race categories.

3.7 Logistic regression model

Based on the results of the urinary analyses, a logistic regression model was developed to estimate the combined influence of race and FR treatment in foam on the urinary TBBA levels in children. Due to the low detection limits, the outcome variable was dichotomized (i.e. detected above MDL in urine is set as 1, below MDL is set as 0). While not quite statistically significant, the modeling results suggest that both foam and race contribute to urinary TBBA levels. For example, the presence of FM550/600 in foam leads to a 2.06 increased Odds of having a detectable TBBA level ($e^{0.724}$; 95% CI: 0.88, 4.94; p=0.097). If the child was non-Hispanic black, there was a 2.04 increased Odds of having detectable TBBA levels in urine ($e^{0.715}$; 95% CI: 0.99, 4.27; p=0.054). Therefore, these results suggest that other factors outside of chemical treatments in foam may be contributing to exposure.

3.8 Limitations

There are some important limitations to this research that should be mentioned. Although we did identify significant associations between the levels of EH-TBB in the home and urinary TBBA, it is important to note that the detection frequency was quite low overall. New analytical methods may be able to improve the sensitivity to detect TBBA in the future. This is also a relatively small study, including only 125 children from North Carolina. Larger studies are needed to determine if exposure levels are consistent in the broader population and in different regions. While these data do suggest that the chemical treatment of FM550/600 contributes to exposure, there are likely other variables that could be playing a role in overall exposure. Detailed information such as hand-mouth behaviors frequency and the time spent in the room with the treated sofa could provide additional insights about the relationship between personal measurements (i.e., internal dose) and exposure levels. It’s also unclear how stable TBBA is in the body and if levels would change significantly in urine samples from day to day.

4. CONCLUSION

Our results indicate that the presence of Firemaster® 550/600 in furniture was associated with significantly higher levels of EH-TBB in house dust, in personal measures of exposure (e.g. hand wipes) and higher urinary levels of TBBA ($p<0.01$). Moderate positive correlations were found between dust, handwipes and urine . And while gender or age was not a significant predictor of urinary TBBA levels, race was a significant predictor. These finding suggest foam in upholstered furniture serves as a primary source of EH-TBB exposure for young children in the home environment and may be contributing to the high levels of EH-TBB in house dust or on personal measurements. Given the increasing concern about neurodevelopmental effects of FM550, and due to its common use in the United States, more studies should be designed with larger populations to investigate the long-term effects of FM550 exposure in young children.

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