Supplemental Material

Exposure to Free and Conjugated Forms of Bisphenol A and Triclosan among Pregnant Women in the MIREC Cohort

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Table S1. Characteristics of participants in the MIREC Study (n = 1890 women) and their urine collection during the 1st trimester.

| Characteristic                                      | N   | Percent |
|-----------------------------------------------------|-----|---------|
| **Time of urine collection (n = 2 missing)**        |     |         |
| 6:00 – 9:00                                         | 28  | 1.48    |
| 9:00 – 12:00                                        | 814 | 43.11   |
| 12:00 – 15:00                                       | 643 | 34.06   |
| 15:00 – 18:00                                       | 367 | 19.44   |
| 18:00 – 24:00                                       | 36  | 1.91    |
| **Season of collection**                            |     |         |
| Fall                                                 | 547 | 28.94   |
| Winter                                               | 456 | 24.13   |
| Spring                                               | 442 | 23.39   |
| Summer                                               | 445 | 23.54   |
| **Time since last urine void (min.) (n = 93 missing)** |     |         |
| ≤ 75                                                 | 488 | 27.16   |
| 76 - 120                                             | 597 | 33.22   |
| 121 – 170                                            | 266 | 14.80   |
| > 170                                                | 446 | 24.82   |
| **Fasting at collection (n = 25 missing)**          |     |         |
| No                                                   | 1828| 98.02   |
| Yes                                                  | 37  | 1.98    |
| **Maternal age (yr.) (n = 1 missing)**               |     |         |
| < 25                                                 | 125 | 6.62    |
| 25 – 29                                              | 441 | 23.34   |
| 30 – 34                                              | 682 | 36.10   |
| ≥ 35                                                 | 641 | 33.93   |
| **Education (n = 3 missing)**                       |     |         |
| High school or less                                  | 168 | 8.90    |
| College courses or diploma                           | 540 | 28.62   |
| University degree                                    | 1179| 62.48   |
| **Household income (n = 84 missing)**                |     |         |
| ≤ $50,000                                            | 326 | 18.05   |
| $50,001 – 100,000                                   | 754 | 41.75   |
| > $100,000                                          | 726 | 40.20   |
| **Country of birth**                                 |     |         |
| Canada                                               | 1537| 81.32   |
| Elsewhere                                            | 353 | 18.68   |
| **Smoking status at 1st visit (n = 2 missing)**      |     |         |
| Current or quit during pregnancy                     | 225 | 11.92   |
| Former                                               | 521 | 27.59   |
| Never                                                | 1142| 60.49   |
| **Pre-pregnancy BMI (kg/m²) (n = 136 missing)**      |     |         |
| < 25 (underweight-normal)                            | 1108| 63.17   |
| 25 – 29 (overweight)                                | 385 | 21.95   |
| ≥ 30 (obese)                                        | 261 | 14.88   |
| **Parity (n = 2 missing)**                           |     |         |
| 0                                                    | 835 | 44.23   |
| 1                                                    | 765 | 40.52   |
| ≥ 2                                                  | 288 | 15.25   |
Table S2. Summary of first trimester urinary concentrations of free and conjugated forms of bisphenol A (BPA) and triclosan (TCS), volumetric and specific gravity (SG) adjusted (µg equivalents/L) – Censored methods [Kaplan-Meier and Maximum Likelihood Estimation (MLE)] (n = 3 missing SG).

| Contaminant               | N     | Kaplan-Meier Median (95% CI)a | MLE GM (95% CI)b |
|---------------------------|-------|------------------------------|-----------------|
| BPA disulfate             | 1890  | ND (ND, ND)                  | ND (ND, ND)     |
| SG-adjusted               | 1887  | ND (ND, ND)                  | ND (ND, ND)     |
| BPA glucuronide           | 1889  | 0.84 (0.78, 0.91)            | 0.82 (0.78, 0.87) |
| SG-adjusted               | 1886  | 0.87 (0.83, 0.91)            | 0.93 (0.89, 0.97) |
| BPA free                  | 1885  | NA                           | ND (ND, ND)     |
| SG-adjusted               | 1882  | ND (ND, ND)                  | ND (ND, ND)     |
| BPA mono-sulfate          | 1885  | NA                           | ND (ND, ND)     |
| SG-adjusted               | 1882  | NA                           | ND (ND, ND)     |
| Total BPA                 | 1879  | 0.89 (0.83, 0.96)            | 0.86 (0.81, 0.92) |
| SG-adjusted               | 1876  | 0.94 (0.90, 0.98)            | 0.97 (0.93, 1.02) |
| Total TCS                 | 1861  | 8.74 (7.62, 9.86)            | 12.61 (11.36, 14.00) |
| SG-adjusted               | 1858  | 9.17 (7.90, 10.48)           | 14.34 (12.99, 15.84) |
| TCS glucuronide           | 1868  | 8.42 (7.29, 9.56)            | 12.29 (11.07, 13.64) |
| SG-adjusted               | 1865  | 9.03 (7.79, 10.27)           | 13.94 (12.63, 15.40) |
| TCS free                  | 1882  | 0.06 (0.05, 0.07)            | 0.07 (0.06, 0.08) |
| SG-adjusted               | 1879  | 0.06 (0.05, 0.07)            | 0.08 (0.07, 0.09) |
| TCS sulfate               | 1890  | NA                           | ND (ND, ND)     |
| SG-adjusted               | 1887  | NA                           | ND (ND, ND)     |
| % free/total BPA          | 1879  | 0.83 (0.78, 0.89)            | 0.73 (0.66, 0.81) |
| % free/total TCS          | 1861  | 0.57 (0.54, 0.61)            | 0.61 (0.58, 0.65) |

ND – Estimate below the limit of detection.
NA – Kaplan-Meier could not be produced due to high percent of censoring.

aConfidence Intervals computed using Greenwood’s estimate of the standard error. bGeometric Mean and Confidence Intervals computed using the maximum likelihood method.
Table S3. Predictors of maternal urinary concentrations of total BPA (reported as µg BPA equivalents/L) including specific gravity as a covariate and based on machine readings.

| Characteristic                              | N   | % <LOD | p-valuea | Pairwiseb | GM (95% CI)c |
|---------------------------------------------|-----|--------|----------|-----------|--------------|
| Maternal Age                                |     |        |          |           |              |
| <25                                         | 125 | 12.10  | 0.0012   | A         | 1.14 (0.97, 1.34) |
| 25-29                                       | 441 | 30.30  |          | AB        | 0.91 (0.83, 0.99) |
| 30-34                                       | 682 | 31.12  |          | AB        | 0.90 (0.84, 0.97) |
| >=35                                        | 641 | 34.33  |          | B         | 0.81 (0.75, 0.87) |
| Parity                                      |     |        |          |           |              |
| 0                                           | 834 | 30.41  | 0.0505d  |           | 0.93 (0.87, 0.99) |
| 1                                           | 765 | 31.05  |          |           | 0.86 (0.80, 0.92) |
| 2+                                          | 288 | 31.23  |          |           | 0.82 (0.74, 0.92) |
| Maternal Smoking Status                     |     |        |          |           |              |
| Current/quit during pregnancy               | 225 | 19.64  | 0.0004   | A         | 1.09 (0.97, 1.24) |
| Former                                      | 521 | 32.30  |          | B         | 0.90 (0.83, 0.97) |
| Never                                       | 1141| 32.31  |          | B         | 0.84 (0.79, 0.88) |
| Maternal Education                          |     |        |          |           |              |
| High school or less                         | 168 | 12.65  | 0.0057d  | A         | 1.01 (0.87, 1.16) |
| College courses or diploma                 | 540 | 29.00  |          | AB        | 0.91 (0.84, 0.98) |
| University degree                           | 1179| 34.19  |          | B         | 0.85 (0.81, 0.90) |
| Place of Birth                              |     |        |          |           |              |
| Elsewhere                                   | 353 | 34.94  | 0.0064d  | A         | 0.79 (0.72, 0.88) |
| Canada                                      | 1536| 29.80  |          | B         | 0.90 (0.86, 0.95) |
| Pre-pregnancy BMI (kg/m²)                   |     |        |          |           |              |
| < 25 (underweight-normal)                  | 1108| 33.24  | 0.2206   |           | 0.85 (0.80, 0.90) |
| 25 – 29 (overweight)                       | 384 | 29.84  |          |           | 0.91 (0.82, 1.00) |
| ≥ 30 (obese)                               | 261 | 23.37  |          |           | 0.94 (0.84, 1.05) |
| Household Income                            |     |        |          |           |              |
| ≤ $50,000                                   | 326 | 24.69  | 0.0013d  | A         | 1.00 (0.90, 1.11) |
| > $50,000 – 100,000                         | 754 | 29.56  |          | AB        | 0.90 (0.84, 0.96) |
| > $100,000                                 | 726 | 34.90  |          | B         | 0.83 (0.78, 0.89) |
| Season Urine Collected                      |     |        |          |           |              |
| Fall                                        | 547 | 30.83  | 0.0741d  |           | 0.86 (0.80, 0.93) |
| Winter                                      | 456 | 28.16  |          |           | 0.91 (0.84, 1.00) |
| Spring                                      | 442 | 33.64  |          |           | 0.83 (0.76, 0.90) |
| Summer                                      | 444 | 30.47  |          |           | 0.93 (0.85, 1.02) |
| Fasting Status                              |     |        |          |           |              |
| No                                          | 1827| 30.99  | 0.7304   |           | 0.88 (0.84, 0.92) |
| Yes                                         | 37  | 18.92  |          |           | 0.93 (0.69, 1.25) |
| Time Since Last Urination (min.)            |     |        |          |           |              |
| ≤ 75                                        | 488 | 38.22  | 0.0045   | A         | 0.84 (0.77, 0.91) |
| 76 - 120                                    | 596 | 33.73  |          | A         | 0.83 (0.77, 0.89) |
| 121 - 170                                   | 266 | 27.17  |          | B         | 1.03 (0.92, 1.16) |
| > 170                                       | 446 | 20.90  |          | AB        | 0.93 (0.85, 1.02) |

a p-value for overall group effect based on machine readings. b Group levels with the same letter indicate no significant difference using Scheffé multiple comparisons. Groups with different letters indicate significant differences in contaminant levels. c GM: geometric mean; 95% CI: the 95% confidence intervals for the GM were corrected for multiple comparisons using Scheffé correction. d ANCOVA model based on the ranks of the data (non-parametric ANCOVA). Each group is assumed to have the same slope with respect to the covariate [i.e., the interaction between the potential predictor (characteristic) and specific gravity was not significant (p>0.05)].
Table S4. Comparisons of maternal urinary concentrations of total bisphenol A (BPA)a (reported as µg BPA equivalents/L) at the various times of urine collection, with respect to different levels of specific gravityb.

| Time of Urine Collection | P25 of SG Differenced | P25 of SG Adjusted Geometric Mean (95% CI) | P50 of SG Differenced | P50 of SG Adjusted Geometric Mean (95% CI) | P75 of SG Differenced | P75 of SG Adjusted Geometric Mean (95% CI) |
|--------------------------|------------------------|------------------------------------------|-----------------------|------------------------------------------|-----------------------|------------------------------------------|
| 6:00 - 9:00              | AB                     | 0.31 (0.19, 0.51)                        | AB                    | 0.68 (0.48, 0.97)                        | 1.70 (1.14, 2.55)     |
| 9:00 - 12:00             | A                      | 0.39 (0.36, 0.42)                        | A                     | 0.74 (0.69, 0.79)                        | 1.55 (1.42, 1.70)     |
| 12:00 - 15:00            | A                      | 0.40 (0.36, 0.44)                        | AB                    | 0.77 (0.72, 0.83)                        | 1.68 (1.54, 1.84)     |
| 15:00 - 18:00            | B                      | 0.61 (0.53, 0.70)                        | C                     | 1.01 (0.92, 1.12)                        | 1.83 (1.64, 2.04)     |
| 18:00 - 24:00            | AB                     | 0.77 (0.47, 1.27)                        | BC                    | 1.26 (0.89, 1.79)                        | 2.24 (1.63, 3.08)     |

aANCOVA model based on the ranks of the data (non-parametric) model, assuming separate slopes for each of the groups of the characteristic, since the interaction between time of urine collection and SG was significant p<0.05. Pairwise comparisons were made at each level of SG only when the overall difference between the characteristic was significant at that level of SG. Therefore where no pairwise comparisons are made there was no significant difference between the groups of the characteristic. bP25 of SG is the 25th percentile of specific gravity = 1.007; P50 of SG is the 50th percentile of specific gravity = 1.013; P75 of SG is the 75th percentile of specific gravity = 1.020.
Table S5. Predictors of maternal urinary concentrations of total triclosan (reported as µg TCS equivalents/L) with specific gravity as a covariate, based on machine readings.

| Characteristic                              | N    | % <LOD | p-value | Pairwise | GM (95% CI) |
|---------------------------------------------|------|--------|---------|----------|-------------|
| **Maternal Age**                            |      |        |         |          |             |
| <25                                         | 122  | 0.82   | 0.0001  | A        | 5.38 (3.65, 7.92) |
| 25-29                                       | 437  | 0.23   |         | B        | 13.58 (11.07, 16.65) |
| 30-34                                       | 672  | 0.89   |         | B        | 13.39 (11.36, 15.78) |
| >=35                                        | 630  | 0.48   |         | B        | 13.31 (11.23, 15.77) |
| **Maternal Smoking Status**                 |      |        |         |          |             |
| Current/quit during pregnancy                | 220  | 0.45   | 0.0022  | A        | 8.78 (6.57, 11.71) |
| Former                                      | 515  | 0.97   |         | AB       | 11.03 (9.14, 13.32) |
| Never                                       | 1124 | 0.44   |         | B        | 14.42 (12.69, 16.37) |
| **Maternal Education**                      |      |        |         |          |             |
| High school or less                         | 163  | 0.61   | 0.0003  | A        | 7.78 (5.55, 10.90) |
| College courses or diploma                  | 530  | 0.38   |         | A        | 10.63 (8.83, 12.79) |
| University degree                           | 1166 | 0.69   |         | B        | 14.62 (12.90, 16.57) |
| **Place of Birth**                          |      |        |         |          |             |
| Elsewhere                                   | 347  | 0.86   | 0.3030  |          | 11.32 (9.00, 14.25) |
| Canada                                      | 1514 | 0.53   |         |          | 12.94 (11.60, 14.45) |
| **Pre-pregnancy BMI (kg/m²)**               |      |        |         |          |             |
| < 25 (underweight-normal)                   | 1089 | 0.55   | 0.7080  | A        | 12.07 (10.61, 13.74) |
| 25 – 29 (overweight)                        | 383  | 0.26   |         | A        | 12.55 (10.10, 15.60) |
| ≥ 30 (obese)                                | 258  | 0.39   |         | A        | 13.09 (10.02, 17.11) |
| **Household Income**                        |      |        |         |          |             |
| $≤$50,000                                   | 318  | 0.31   | 0.0001  | A        | 9.68 (7.62, 12.30) |
| $50,001 – 100,000                           | 743  | 0.40   |         | A        | 10.96 (9.38, 12.81) |
| > $100,000                                  | 717  | 0.84   |         | B        | 16.36 (13.95, 19.19) |
| **Season Urine Collected**                  |      |        |         |          |             |
| Fall                                        | 540  | 0.19   | 0.3462  |          | 14.42 (12.00, 17.34) |
| Winter                                      | 448  | 0.45   |         |          | 12.67 (10.35, 15.51) |
| Spring                                      | 436  | 0.92   |         |          | 11.62 (9.47, 14.27) |
| Summer                                      | 437  | 0.92   |         |          | 11.59 (9.44, 14.22) |
| **Fasting Status**                          |      |        |         |          |             |
| No                                          | 1799 | 0.61   | 0.2511  |          | 12.60 (11.39, 13.94) |
| Yes                                         | 37   | 0.00   |         |          | 8.31 (4.11, 16.80) |
| **Time of Urine Collection**                |      |        |         |          |             |
| 6:00 – 9:00                                 | 28   | 3.57   | 0.3722  |          | 13.86 (6.18, 31.10) |
| 9:00 – 12:00                                | 797  | 0.63   |         |          | 14.15 (12.15, 16.48) |
| 12:00 – 15:00                               | 635  | 0.63   |         |          | 11.94 (10.08, 14.16) |
| 15:00 – 18:00                               | 364  | 0.27   |         |          | 11.00 (8.78, 13.78) |
| 18:00 – 24:00                               | 35   | 0.00   |         |          | 10.38 (5.03, 21.41) |
| **Time Since Last Urination (min.)**        |      |        |         |          |             |
| ≤ 75                                        | 480  | 1.04   | 0.1168  |          | 10.47 (8.61, 12.73) |
| 76 – 120                                     | 593  | 0.67   |         |          | 13.62 (11.43, 16.23) |
| 121 – 170                                    | 262  | 0.38   |         |          | 14.56 (11.18, 18.96) |
| > 170                                       | 438  | 0.00   |         |          | 13.73 (11.19, 16.85) |
a p-value for overall group effect using machine readings. b Group levels with the same letter indicate no significant difference using Scheffé multiple comparisons. Groups with different letters indicate significant differences in contaminant levels. c GM: geometric mean; 95% CI: the 95% confidence intervals for the GM was corrected for multiple comparisons using Scheffé correction. d ANCOVA model based on the ranks of the data (non-parametric ANCOVA). Each group is assumed to have the same slope with respect to the covariate [i.e., the interaction between the potential predictor (characteristic) and specific gravity is not significant (p>0.05)].
Table S6. Comparisons of maternal urinary concentrations of total triclosan (TCS)\(^a\) (reported as µg TCS equivalents/L) at the various parity groups, with respect to different levels of specific gravity\(^b\).

| Parity | P25 of SG Differences | P25 of SG Adjusted Geometric Mean (95% CI) | P25 of SG Differences | P25 of SG Adjusted Geometric Mean (95% CI) | P25 of SG Differences | P25 of SG Adjusted Geometric Mean (95% CI) |
|--------|------------------------|---------------------------------------------|------------------------|---------------------------------------------|------------------------|---------------------------------------------|
| 0      | 6.33 (5.20, 7.70)      | 12.58 (10.84, 14.59)                        | A                      | 28.03 (22.95, 34.23)                        |
| 1      | 7.12 (6.76, 8.80)      | 11.33 (9.67, 13.27)                        | B                      | 19.50 (16.09, 23.62)                        |
| 2+     | 5.18 (3.64, 7.39)      | 9.69 (7.47, 12.56)                         | AB                     | 20.10 (14.71, 27.45)                        |

\(^a\)ANCOVA model, assuming separate slopes for each of the groups of the characteristic since the interaction between parity and SG was significant (p<0.05). Pairwise comparisons were made at each level of SG only when the overall difference between the groups of the characteristic was significant at that level of SG. Therefore, where no pairwise comparisons were made, there was no significant difference between the groups of the characteristic. 
\(^b\)P25 of SG is the 25th percentile of specific gravity = 1.007; P50 of SG is the 50th percentile of specific gravity = 1.013; P75 of SG is the 75th percentile of specific gravity = 1.020.
### Table S7. Comparison of international studies that have measured total triclosan (unadjusted) in the urine of pregnant women and in women of reproductive age.

| Study Population                                      | Sample Size | Gestational Age at Collection | Triclosan Geometric Mean | Triclosan Median | Triclosan Maximum Value | Reference                          |
|--------------------------------------------------------|-------------|-------------------------------|--------------------------|------------------|--------------------------|------------------------------------|
| California MIEEP project                               | 77          | 3rd trimester                 | 17.2 (95% CI: 10.5, 28.2) µg/L | 11.1 µg/L        | 90th %ile: 445 µg/L        | California 2013                    |
| US NHANES 2003-2004 pregnant women                    | 86          | 1st – 3rd trimester           | 17.00 µg/L               | 8.2 µg/L         | 95th %ile: 283.0 µg/L      | Woodruff et al. 2011               |
| Case-control study of male malformations in France     | 191         | 6 – 30 wks                    | 24.1 µg/L                |                  | 95th %ile: 634 µg/L        | Philippat et al. 2012              |
| Multiethnic cohort in New York City                   | 367         | 3rd trimester                 | 11.0 µg/L                |                  | 1790 µg/L                 | Wolff et al. 2008                  |
| INMA cohort study in Spain                             | 120         | 3rd trimester                 | 6.1 ng/mL                |                  |                          | Casas et al. 2011                  |
| PROTECT project, Puerto Rico                           | 105         | 18, 22 & 26 wks               | 29.9 (95% CI: 23.6, 37.9) ng/ml | 26.2 ng/ml       | 2000 µg/L                 | Meeker et al. 2013                 |
| Women undergoing amniocentesis in New York City        | 71          | 18, 23 and 33 wks             | 6.5 µg/L at 18 wks; 15.4 at 23 wks; 16.2 at 33 wks | 8.74 µg/L        | Maximum 95th %ile: 789 µg/L | Philippat et al. 2013              |
| MIREC Study of Canadian women                          | 1861        | 1st trimester                 | 12.6 (95% CI: 11.4, 14.0) µg/L | 8.74 µg/L        | 6784.3 µg/L               | Our study                          |
| CHMS Cycle 2 (2009-2011) females 20-39 years of age   | 188         |                               | 19.0 (95% CI: 11, 35) µg/L | 16.0 (95% CI: 6, 27) µg/L |                          | Health Canada 2013                 |
Figure S1. Plots of maternal urinary concentrations of (a) Log(free BPA) vs Log(total BPA) ($r = 0.42$, $p<0.0001$) and (b) Log(%free BPA) vs Log(total BPA) ($r = -0.22$, $p<0.0001$).
S1b

Log(\% Free BPA) vs Log(Total BPA)
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