

Supplementary Materials

Metabolic stability of eight airborne OrganoPhosphate Flame Retardants (OPFRs) in human liver and skin microsomes and in human hepatocytes

Stefano Di Bona,^{1*} Emanuele Artino,^{2*} Francesca Buiarelli,³ Patrizia Di Filippo,^{3,4} Roberta Galarini,⁵ Stefano Lorenzetti,⁶ Franco Lucarelli,⁷ Gabriele Cruciani² and Laura Goracci^{2,*}

¹ Molecular Horizon srl, 06084 Bettona (Perugia), Italy; stefano.dibona@molhorizon.it

² Department of Chemistry, Biology and Biotechnology, University of Perugia, 06123 Perugia, Italy, emanuele.artino@studenti.unipg.it, gabriele.cruciani@unipg.it, laura.goracci@unipg.it

³ Department of Chemistry, Sapienza University of Rome, 00185 Rome, Italy, francesca.buiarelli@uniroma1.it

⁴ Italian Workers' Compensation Authority (INAIL) - DIT, 00143 Rome, Italy, p.difilippo@inail.it

⁵ Istituto Zooprofilattico Sperimentale dell'Umbria e delle Marche "Togo Rosati", 06126 Perugia, Italy, r.galarini@izsum.it

⁶ Department of Food Safety, Nutrition and Veterinary Public Health, Istituto Superiore di Sanità, 00161 Rome, Italy, stefano.lorenzetti@iss.it

⁷ Department of Physics and Astronomy and INFN, University of Florence, 50019 Sesto Fiorentino (Florence), Italy; lucarelli@fi.infn.it

* Correspondence: laura.goracci@unipg.it; Tel.: +39 0755855632

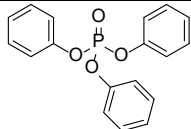
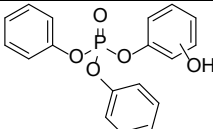
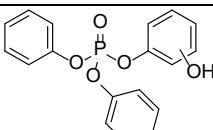
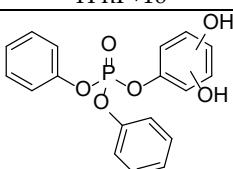
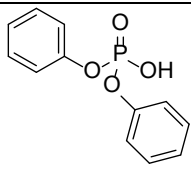
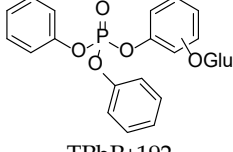
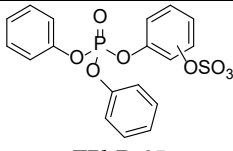
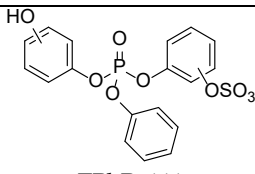
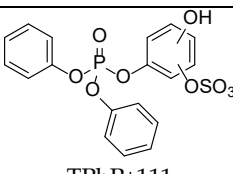
Content:

8 pages

8 tables

The supplementary materials includes the tables for the 8 OPFRs. The table includes the structure of the substrate and metabolites, the retention time expressed in minutes, the formula, the most intense adduct, theoretical and experimental m/z and the matrix in which it was detected.

Table S1: LC-MS data for triphenyl phosphate (TPhP) and its detected metabolites in HLM, HuHep and HSM.

| Compound | RT (min) | Formula | Adduct | Theoretical m/z | Experimental m/z | Δ ppm | Matrix |
|---|----------|---|--------------------|-----------------|------------------|--------------|---------------------|
|  TPhP | 12.04 | C ₁₈ H ₁₅ O ₄ P | [M+H] ⁺ | 327.0781 | 327.0783 | 0.61 | HLM HuHep HSM |
|  TPhP+16 | 10.36 | C ₁₈ H ₁₅ O ₅ P | [M+H] ⁺ | 343.0730 | 343.0734 | 1.07 | HLM HuHep |
|  TPhP+16 | 11.28 | C ₁₈ H ₁₅ O ₅ P | [M+H] ⁺ | 343.0730 | 343.0729 | -0.29 | HLM HuHep |
|  TPhP+32 | 10.85 | C ₁₈ H ₁₅ O ₆ P | [M+H] ⁺ | 359.0679 | 359.0682 | 0.83 | HLM |
|  TPhP-76 | 7.32 | C ₁₂ H ₁₁ O ₄ P | [M-H] ⁻ | 249.0322 | 249.0324 | 0.80 | HLM HuHep HSM |
|  TPhP+192 | 9.19 | C ₂₄ H ₂₃ O ₁₁ P | [M-H] ⁻ | 517.0905 | 517.0903 | -0.38 | HuHep |
|  TPhP+95 | 9.62 | C ₁₈ H ₁₅ O ₈ PS | [M-H] ⁻ | 421.0152 | 421.0153 | 0.24 | HuHep |
|  TPhP+111 | 8.90 | C ₁₈ H ₁₅ O ₉ PS | [M-H] ⁻ | 437.0102 | 437.0102 | 0 | HuHep |
|  TPhP+111 | 9.45 | C ₁₈ H ₁₅ O ₉ PS | [M-H] ⁻ | 437.0102 | 437.0101 | -0.23 | HuHep |

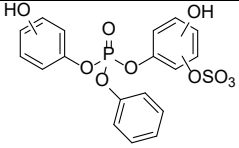
| | | | | | | | |
|---|------|--|--------------------|----------|----------|------|-------|
|  <p>TPhP+128</p> | 8.73 | C ₁₈ H ₁₅ O ₁₀ PS | [M-H] ⁻ | 453.0051 | 453.0052 | 0.22 | HuHep |
|---|------|--|--------------------|----------|----------|------|-------|

Table S2: LC-MS data for [diphenyl phosphate \(DPhP\)](#) and its detected metabolites in HLM, HuHep and HSM.

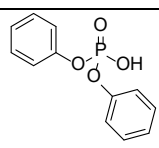
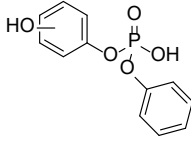
| Compound | RT (min) | Formula | Adduct | Theoretical m/z | Experimental m/z | Δppm | Matrix |
|--|----------|--|--------------------|-----------------|------------------|-------|---------------------|
|  <p>DPhP</p> | 7.26 | C ₁₂ H ₁₁ O ₄ P | [M-H] ⁻ | 249.0322 | 249.0318 | -1.61 | HLM HuHep HSM |
|  <p>DPhP+16</p> | 4.93 | C ₁₂ H ₁₁ O ₅ P | [M+H] ⁺ | 265.0271 | 265.0270 | -0.37 | HLM |

Table S3: LC-MS data for [bisphenol A bis\(diphenyl phosphate\) \(BDP\)](#) and its detected metabolites in HLM, HuHep and HSM.

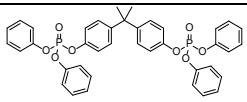
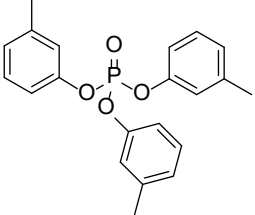
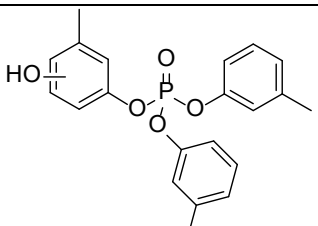
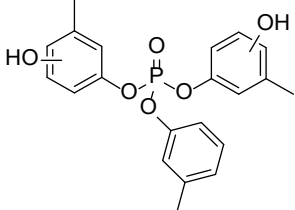
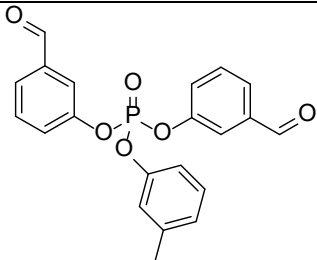
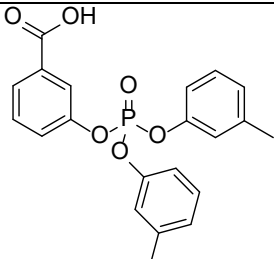
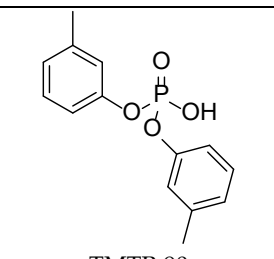
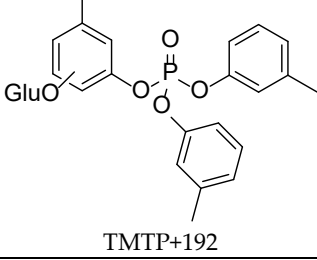
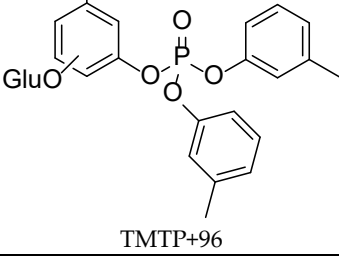
| Compound | RT (min) | Formula | Adduct | Theoretical m/z | Experimental m/z | Δppm | Matrix |
|--|----------|---|---------------------|-----------------|------------------|------|---------------------|
|  <p>BDP</p> | 13.87 | C ₃₉ H ₃₄ O ₈ P ₂ | [M+Na] ⁺ | 715.1621 | 715.1632 | 1.54 | HLM HuHep HSM |

Table S4: LC-MS data for [tri-m-tolyl phosphate \(TMTP\)](#) and its detected metabolites in HLM, HuHep and HSM.

| Compound | RT (min) | Formula | Adduct | Theoretical m/z | Experimental m/z | Δppm | Matrix |
|---|----------|--|--------------------|-----------------|------------------|------|---------------------|
|  <p>TMTP</p> | 13.14 | C ₂₁ H ₂₁ O ₄ P | [M+H] ⁺ | 369.1250 | 369.1261 | 2.98 | HLM HuHep HSM |
|  | 12.11 | C ₂₁ H ₂₁ O ₅ P | [M+H] ⁺ | 385.1199 | 385.1202 | 0.78 | HLM HuHep |

| | | | | | | | |
|---|-------|---|--------------------|----------|----------|-------|--------------|
| TMTP+16 | | | | | | | |
|  TMTP+16 | 10.97 | C ₂₁ H ₂₁ O ₆ P | [M+H] ⁺ | 401.1149 | 401.1152 | 0.75 | HLM |
|  TMTP+32 | 11.21 | C ₂₁ H ₁₇ O ₆ P | [M+H] ⁺ | 397.0836 | 397.0839 | 0.76 | HLM HuHep |
|  TMTP+28 | 10.73 | C ₂₁ H ₁₉ O ₆ P | [M-H] ⁻ | 397.0846 | 397.0851 | 1.26 | HLM HuHep |
|  TMTP+30 | 9.16 | C ₁₄ H ₁₅ O ₄ P | [M-H] ⁻ | 277.0635 | 277.0640 | 1.33 | HLM HuHep |
|  TMTP-90 | 10.55 | C ₂₇ H ₂₉ O ₁₁ P | [M-H] ⁻ | 559.1375 | 559.1374 | -1.79 | HuHep |
|  TMTP+192 | 10.93 | C ₂₁ H ₂₁ O ₈ PS | [M-H] ⁻ | 463.0622 | 463.0619 | -0.65 | HuHep |

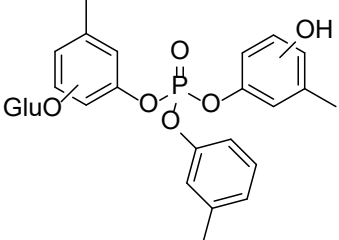
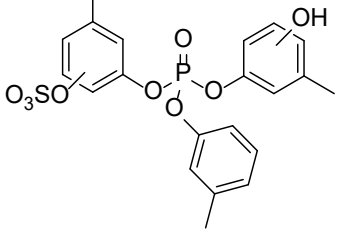
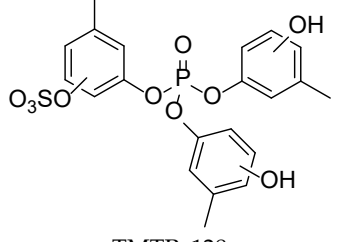
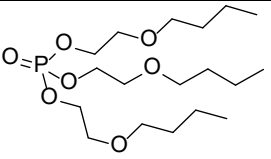
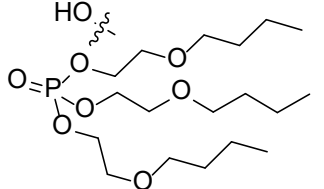
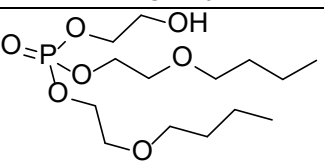
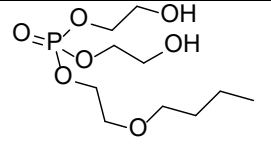
| | | | | | | | |
|--|------|--|--------------------|----------|----------|------|-------|
|  <p>TMTP+208</p> | 9.42 | C ₂₇ H ₂₉ O ₁₂ P | [M-H] ⁻ | 575.1324 | 575.1328 | 0.70 | HuHep |
|  <p>TMTP+111</p> | 9.63 | C ₂₁ H ₂₁ O ₉ PS | [M-H] ⁻ | 479.0571 | 479.0571 | 0 | HuHep |
|  <p>TMTP+128</p> | 8.62 | C ₂₁ H ₂₁ O ₁₀ PS | [M-H] ⁻ | 495.0520 | 495.0521 | 0.20 | HuHep |

Table S5: LC-MS data for **tributoxyethyl phosphate (TBEOP)** and its detected metabolites in HLM, HuHep and HSM.

| Compound | RT (min) | Formula | Adduct | Theoretical m/z | Experimental m/z | Δppm | Matrix |
|--|----------|--|--------------------|-----------------|------------------|-------|---------------------|
|  <p>TBEOP</p> | 12.79 | C ₁₈ H ₃₉ O ₇ P | [M+H] ⁺ | 399.2506 | 399.2503 | -0.75 | HLM HuHep HSM |
|  <p>TBEOP+16</p> | 11.39 | C ₁₈ H ₃₉ O ₈ P | [M+H] ⁺ | 415.2455 | 415.2457 | 0.48 | HLM HuHep |
|  <p>TBEOP-56</p> | 10.67 | C ₁₄ H ₃₁ O ₇ P | [M+H] ⁺ | 343.1880 | 343.1880 | 0 | HLM HuHep |
|  <p>TBEOP-112</p> | 6.77 | C ₁₀ H ₂₃ O ₇ P | [M+H] ⁺ | 287.1254 | 287.1253 | -0.35 | HLM HuHep |

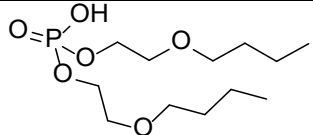
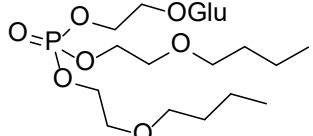
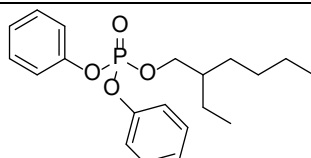
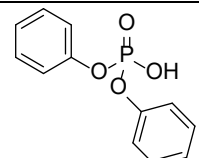
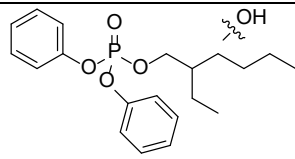
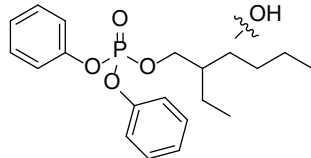
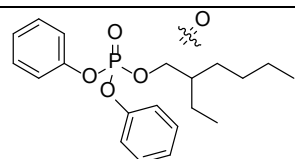
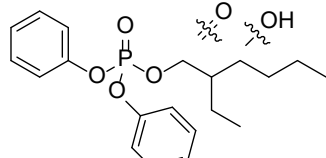
| | | | | | | | |
|--|------|---|--------------------|----------|----------|-------|--------------|
|  <p>TBEOP-100</p> | 9.13 | C ₁₂ H ₂₇ O ₆ P | [M-H] ⁻ | 297.1472 | 297.1472 | 0 | HLM HuHep |
|  <p>TBEOP+120</p> | 9.01 | C ₂₀ H ₃₉ O ₁₃ P | [M-H] ⁻ | 517.2056 | 517.2053 | -0.58 | HuHep |

Table S6: LC-MS data for ethylhexyl diphenyl phosphate (EHDPPhP) and its detected metabolites in HLM, HuHep and HSM.

| Compound | RT (min) | Formula | Adduct | Theoretical m/z | Experimental m/z | Δ ppm | Matrix |
|--|----------|--|---------------------|-----------------|------------------|--------------|--------------|
|  <p>EHDPPhP</p> | 13.38 | C ₂₀ H ₂₇ O ₄ P | [M+Na] ⁺ | 385.1539 | 385.1549 | 2.60 | HLM HSM |
|  <p>EHDPPhP-112</p> | 7.28 | C ₁₂ H ₁₁ O ₄ P | [M-H] ⁻ | 249.0322 | 249.0328 | 2.43 | HLM HuHep |
|  <p>EHDPPhP+16</p> | 11.97 | C ₂₀ H ₂₇ O ₅ P | [M+Na] ⁺ | 401.1488 | 401.1485 | -0.75 | HLM HuHep |
|  <p>EHDPPhP+16</p> | 12.17 | C ₂₀ H ₂₇ O ₅ P | [M+Na] ⁺ | 401.1488 | 401.1496 | 2.00 | HLM HuHep |
|  <p>EHDPPhP+14</p> | 11.80 | C ₂₀ H ₂₅ O ₅ P | [M+Na] ⁺ | 399.1332 | 399.1336 | 1.00 | HLM HuHep |
|  <p>EHDPPhP+30</p> | 11.34 | C ₂₀ H ₂₅ O ₆ P | [M+Na] ⁺ | 415.1281 | 415.1285 | 0.96 | HLM |

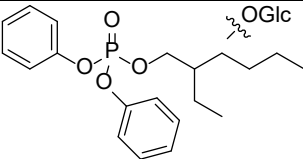
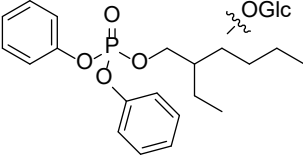
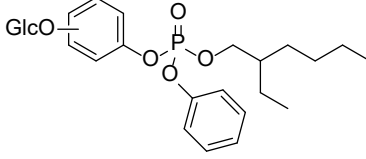
| | | | | | | | |
|--|-------|-----------------------|-----------|----------|----------|------|-------|
|  EHDPPhP+192 | 10.21 | $C_{26}H_{35}O_{11}P$ | $[M-H]^-$ | 553.1844 | 553.1847 | 0.54 | HuHep |
|  EHDPPhP+192 | 10.59 | $C_{26}H_{35}O_{11}P$ | $[M-H]^-$ | 553.1844 | 553.1846 | 0.36 | HuHep |
|  EHDPPhP+192 | 11.02 | $C_{26}H_{35}O_{11}P$ | $[M-H]^-$ | 553.1844 | 553.1846 | 0.36 | HuHep |

Table S7: LC-MS data for [trichloroethyl phosphate \(TCEP\)](#) and its detected metabolites in HLM, HuHep and HSM.

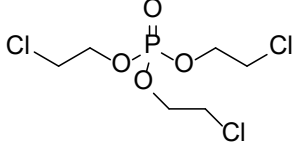
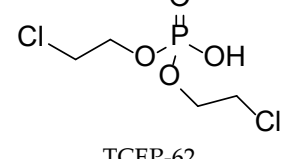
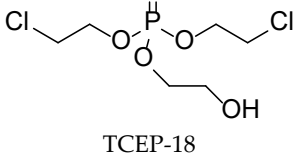
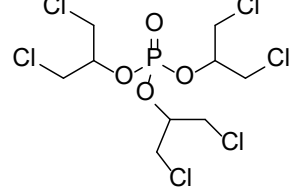
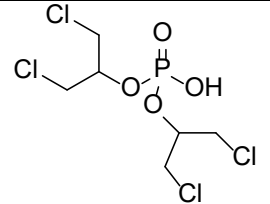
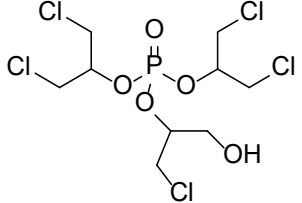
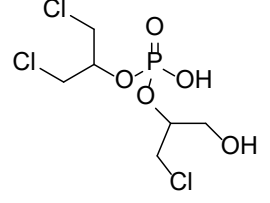
| Compound | RT (min) | Formula | Adduct | Theoretical m/z | Experimental m/z | Δ ppm | Matrix |
|--|----------|---------------------|-----------|-----------------|------------------|--------------|---------------------|
|  TCEP | 8.66 | $C_6H_{12}Cl_3O_4P$ | $[M+H]^+$ | 284.9612 | 284.9612 | 0 | HLM HuHep HSM |
|  TCEP-62 | 6.93 | $C_4H_9Cl_2O_4P$ | $[M+H]^+$ | 222.9688 | 222.9689 | 0.45 | HLM HuHep |
|  TCEP-18 | 5.95 | $C_6H_{13}Cl_2O_5P$ | $[M+H]^+$ | 266.9950 | 266.9955 | 1.87 | HLM HuHep |

Table S8: LC-MS data for [tris\(1,3-dichloropropan-2-yl\) phosphate \(TDCIPP\)](#) and its detected metabolites in HLM, HuHep and HSM.

| Compound | RT (min) | Formula | Adduct | Theoretical m/z | Experimental m/z | Δ ppm | Matrix |
|---|----------|---------------------|-----------|-----------------|------------------|--------------|---------------------|
|  TDCIPP | 11.84 | $C_9H_{15}Cl_6O_4P$ | $[M-H]^-$ | 426.8765 | 426.8766 | 0.23 | HLM HuHep HSM |

| | | | | | | | |
|---|------|---|--------------------|----------|----------|-------|-----|
|  <p>TDCIPP-110</p> | 8.05 | C ₆ H ₁₁ Cl ₄ O ₄ P | [M-H] ⁻ | 316.9077 | 316.9076 | -0.32 | HLM |
|  <p>TDCIPP-18</p> | 9.89 | C ₉ H ₁₆ Cl ₅ O ₅ P | [M-H] ⁻ | 408.9107 | 408.9105 | -0.49 | HLM |
|  <p>TDCIPP-128</p> | 4.90 | C ₆ H ₁₂ Cl ₃ O ₅ P | [M-H] ⁻ | 298.9416 | 298.9415 | -0.33 | HLM |