Temporal trends of cumulative risks from six phthalates in biomonitoring data

2018 – 2019 SOT RASS + MixSS Webinar Series

Jeanette M. Reyes¹ and Paul S. Price²

¹Oak Ridge Institute for Science and Education (ORISE) Research Participation Program, hosted at U.S. Environmental Protection Agency, RTP, NC
²Office of Research and Development, National Exposure Research Laboratory, U.S. Environmental Protection Agency, RTP, NC

DISCLAIMER: This work was prepared through the ORISE program. The views expressed in this presentation are those of the authors and do not necessarily reflect the views or policies of the U.S. Environmental Protection Agency.
Acknowledgements

- Paul Price, PhD
- National Exposure Research Laboratory

- DOI: 10.1021/acs.est.8b03338
- Publication Date (Web): October 1, 2018
Phthalates

- Phthalates
  - Esters of phthalic acid used as plasticizers
  - Substances added to increase their flexibility, transparency, durability, and longevity
- They are in a wide variety of goods and everyday products
- Phthalates get into the body by
  - Inhalation – e.g. from dust
  - Dermal penetration – application of products on skin
  - Intravenous injection
  - Ingestion – from food
- Metabolize quickly but exposures are ubiquitous
- Some phthalates are known endocrine disruptors
  - “phthalate syndrome”: Infertility, decreased sperm count, and changes in reproductive organs (male reproductive development)
- Phthalate mixture (DBP, DIBP, BBP, DINP, DEHP, DIDP) (Qian et al., 2015)
  - National Academy of Science 2008 document (NAS, 2008)
  - Most of this group (i.e., DBP, DIBP, BBP, DINP, DEHP) are associated with the “phthalate syndrome”
# Phthalates

<table>
<thead>
<tr>
<th>Phthalate</th>
<th>Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>di-n-butyl phthalate (DBP)</td>
<td>Adhesives, caulk, cosmetics, industrial solvent, medications</td>
</tr>
<tr>
<td>diisobutyl phthalate (DIBP)</td>
<td>Adhesives, caulk, cosmetics, industrial solvent</td>
</tr>
<tr>
<td>butyl benzyl phthalate (BBP)</td>
<td>Vinyl flooring, adhesives, sealants, industrial solvent</td>
</tr>
<tr>
<td>di(2-ethylhexyl) phthalate (DEHP)</td>
<td>Soft plastic, including tubing, toys, home products, food containers, food packaging</td>
</tr>
<tr>
<td>diisononyl phthalate (DINP)</td>
<td>Soft plastics, replacement for DEHP</td>
</tr>
<tr>
<td>diisodecyl phthalate (DIDP)</td>
<td>Adhesives, sealants, lubricants, greases</td>
</tr>
</tbody>
</table>

Table 2-1, NAS 2008
US Federal Phthalate Regulations

• In 2008, the Consumer Product Safety Commission (CPSC) banned DEHP, DBP, and BBP from children’s toys in concentrations greater than 0.1%

• In 2017, CPSC banned five phthalates in children’s toys in concentrations greater than 0.1%, including DINP and DIBP
Phthalates In the News

• From NYT on July 12, 2017: “The chemicals migrate into food from food processing equipment like plastic tubing, conveyor belts and gaskets and other plastic materials used in the manufacturing process, and can also seep in from printed labels or plastic materials in the packaging.”

• “Since they bind with fats, they tend to build up in fatty foods, including not just cheese but baked goods, infant formula, meats, oils and fats, and fast food, studies show.”

• From Slate on July 14, 2017: “It’s a piece about toxicity, but there is one glaring omission: dosage.”

• “But does boxed mac and cheese offer a uniquely high and risky exposure to these chemicals? The New York Times story doesn’t make that clear. The closest it comes to specificity on this point is to say the groups ‘found high levels in all of them,’ though it does not specify how it decided that the levels are ‘high.’"
Screening Tools for Mixtures

• Hazard Quotient (HQ)
  • Screening tool for hazard
  • Chemical specific
  • \( HQ_{i,j} = DI_{i,j}/RfV_j \) (participant \( i \) and phthalate \( j \))

• Hazard Index (HI)
  • Screening tool for hazard over a group of similar chemicals
  • Assumes dose addition
  • \( HI_i = \sum_{j=1}^{N} HQ_{i,j} \) (participant \( i \) and phthalate \( j \) for \( N \) phthalates)
  • \( HI_i > 1 \) warrants further action
  • \( HQ_{M,i} = \max_{j \in \{1,\ldots,N\}} HQ_{i,j} \)

• Tolerable Daily Intake (TDI)
  • “... An estimate of the amount of contaminant, expressed on a body weight basis that can be ingested daily over a lifetime without appreciable health risk.” (IGHRC, 2009)
  • \( HQ_{i,j} = DI_{i,j}/RfV_j = DI_{i,j}/TDI_j \)
National Health and Nutrition Examination Survey

- Design
  - Since 1999, once every 2 years (i.e. a “cycle”) – NOT longitudinal; 100+ chemicals/metabolites
  - Phthalate data: 2005 – 2014 NHANES Cycle Urinary Metabolite data (CDC, 2016)
  - Daily Intake \( DI = \frac{100 \times Ph_{CI} \times CE}{F_{UE} \times 1000 \text{ mg/g}} \times \frac{MW_p}{MW_m} \) (Christensen et al., 2014)

<table>
<thead>
<tr>
<th>Phthalate</th>
<th>Tolerable Daily Intake (ug/kg-d)</th>
<th>Metabolite</th>
</tr>
</thead>
<tbody>
<tr>
<td>di-n-butyl phthalate (DBP)</td>
<td>10(^a)</td>
<td>monobutyl phthalate (MBP)</td>
</tr>
<tr>
<td>diisobutyl phthalate (DIBP)</td>
<td>1250(^b)</td>
<td>monoisobutyl phthalate (MIBP)</td>
</tr>
<tr>
<td>butyl benzyl phthalate (BBP)</td>
<td>500(^c)</td>
<td>monobenzyl phthalate (MBZP)</td>
</tr>
<tr>
<td>di(2-ethylhexyl) phthalate (DEHP)</td>
<td>50(^d)</td>
<td>mono(2-ethyl-5-carboxypentyl) phthalate (MECPP)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>mono(2-ethyl-5-oxohexyl) phthalate (MEOHP)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>mono(2-ethylhexyl) phthalate (MEHP)</td>
</tr>
<tr>
<td>diisononyl phthalate (DINP)</td>
<td>150(^e)</td>
<td>monoisononyl phthalate (MINP)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>mono(carboxyoctyl) phthalate (MCOP)</td>
</tr>
<tr>
<td>diisodecyl phthalate (DIDP)</td>
<td>130(^f)</td>
<td>mono(carboxyynonyl) phthalate (MCNP)</td>
</tr>
</tbody>
</table>

\(^a\)(EFSA 2005c); \(^b\)(Saillenfait et al. 2008); \(^c\)(EFSA 2005a); \(^d\)(EFSA 2005d); \(^e\)(EFSA 2005b); \(^f\)(CPSC 2010)

- Background
- Methods
- Hazard Index
- Mixtures
- Discussion
Hazard Index and Hazard Quotients Across Cycles

- Hazard Index has **decreased** over the past 10 years
- Decrease in HI mostly attributed to decreases in **DEHP** (and DBP)
- **DINP** is the only phthalate whose HQ increased over the past 10 years

<table>
<thead>
<tr>
<th>Cycle</th>
<th>Mean HI</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005-2006</td>
<td>0.34</td>
</tr>
<tr>
<td>2007-2008</td>
<td>0.41</td>
</tr>
<tr>
<td>2009-2010</td>
<td>0.26</td>
</tr>
<tr>
<td>2011-2012</td>
<td>0.19</td>
</tr>
<tr>
<td>2013-2014</td>
<td>0.15</td>
</tr>
</tbody>
</table>
Hazard Index Across Cycles by Demographics

- Least Squares Geometric Mean (LSGM) of the HI (with 95% CI) from Zota et al., 2014
- Hazard Index has greatly **decreased** over the past 10 years
- After covariate adjustments, **children** have **larger** hazards for every cycle
Differences in Hazard Index Stratified by Group


- Consistent, sizable significant differences in children compared with adolescents and adults

- Difference in the LSGM of the HI

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Male - Female</td>
<td>0.034</td>
<td>-0.107b</td>
<td>0.069</td>
<td>0.048</td>
<td>-0.049</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td>Mexican American - Non-Hispanic White</td>
<td>-0.151a</td>
<td>-0.027</td>
<td>-0.042</td>
<td>-0.086</td>
<td>-0.061</td>
</tr>
<tr>
<td></td>
<td>Mexican American - Non-Hispanic Black</td>
<td>-0.232b</td>
<td>-0.077</td>
<td>0.001</td>
<td>-0.154</td>
<td>-0.039</td>
</tr>
<tr>
<td></td>
<td>Non-Hispanic White - Non-Hispanic Black</td>
<td>-0.081</td>
<td>-0.049</td>
<td>0.042</td>
<td>-0.068</td>
<td>0.021</td>
</tr>
<tr>
<td>Age</td>
<td>6-11 years - 12-19 years</td>
<td>0.298b</td>
<td>0.356c</td>
<td>0.357c</td>
<td>0.271b</td>
<td>0.433c</td>
</tr>
<tr>
<td></td>
<td>6-11 years - 20+ years</td>
<td>0.430c</td>
<td>0.490c</td>
<td>0.466c</td>
<td>0.357c</td>
<td>0.585c</td>
</tr>
<tr>
<td></td>
<td>12-19 years - 20+ years</td>
<td>0.132</td>
<td>0.134</td>
<td>0.109</td>
<td>0.086</td>
<td>0.152a</td>
</tr>
</tbody>
</table>

*\( p \leq 0.05 \), \( b p \leq 0.01 \), \( c p \leq 0.001 \)
Mixtures

• Under what circumstance is a chemical-by-chemical assessment a sufficient substitute for a cumulative assessment?

• When/how often is a mixture being dominated by one particular chemical?

(EPA, 2007)
Frequency of Maximum HQ ($HQ_M$) Across Cycles

- Which phthalate in the mixture is contributing most to hazard?
- Count of which phthalate produced $HQ_M$ in every participant
- Over time, less participants have $HQ_M$ produced by DEHP and more participants have $HQ_M$ produced by DINP
- Across cycles, frequency of $HI > 1$ dropped sizably
Maximum Cumulative Ratio (MCR)

- MCR measures the dominance of a single chemical within a mixture
- Applications: surface water (Price and Han, 2011; Price et al., 2012; Vallotton and Price, 2016), ground water (Han and Price, 2011), residential indoor air (Brouwere et al., 2014), dioxin biomonitoring (Han and Price, 2013)

<table>
<thead>
<tr>
<th>Metric</th>
<th>Description</th>
<th>Equation</th>
</tr>
</thead>
<tbody>
<tr>
<td>HQ</td>
<td>Hazard Quotient</td>
<td>$HQ_{i,j} = DI_{i,j}/TDI_j$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$HQ_{M,i} = \max_{j=1,...,N} HQ_{i,j}$</td>
</tr>
<tr>
<td>HI</td>
<td>Hazard Index</td>
<td>$HI_i = \sum_{j=1}^{N} HQ_{i,j}$</td>
</tr>
<tr>
<td>MCR</td>
<td>Maximum Cumulative Ratio</td>
<td>$MCR_i = HI_i/HQ_{M,i} \in [1, N]$</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>Total Hazard</th>
<th>Individual Chemical Hazard</th>
<th>MCR</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>$HI &gt; 1$</td>
<td>$HQ_M &gt; 1$</td>
<td>---</td>
<td>The mixture presents a potential risk already based on individual components</td>
</tr>
<tr>
<td>II</td>
<td>$HI \leq 1$</td>
<td>$HQ_M \leq 1$</td>
<td>---</td>
<td>The assessment does not identify a concern</td>
</tr>
<tr>
<td>IIIA</td>
<td>$HI &gt; 1$</td>
<td>$HQ_M \leq 1$</td>
<td>$MCR &lt; 2$</td>
<td>The majority of the risk offered by the mixture is driven by one substance</td>
</tr>
<tr>
<td>IIIB</td>
<td>$HI &gt; 1$</td>
<td>$HQ_M \leq 1$</td>
<td>$MCR \geq 2$</td>
<td>The potential risk is driven by multiple components</td>
</tr>
</tbody>
</table>
Hazard Index and MCR Across Cycles

- As HI ↑, MCR ↓: higher hazards are dominated by one chemical within a mixture
- Slope decreases in magnitude: across cycles, highest hazards are less dominated by one chemical (across cycles, MCR ↑ among highest HIs)
- Overall, only a few participants have potentially problematic hazards

<table>
<thead>
<tr>
<th>Cycle</th>
<th>Intercept</th>
<th>Slope</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005-2006</td>
<td>-0.671</td>
<td>-0.594</td>
</tr>
<tr>
<td>2007-2008</td>
<td>-0.596</td>
<td>-0.526</td>
</tr>
<tr>
<td>2009-2010</td>
<td>-0.476</td>
<td>-0.457</td>
</tr>
<tr>
<td>2011-2012</td>
<td>-0.435</td>
<td>-0.397</td>
</tr>
<tr>
<td>2013-2014</td>
<td>-0.421</td>
<td>-0.395</td>
</tr>
</tbody>
</table>

Background  Methods  Hazard Index  Mixtures  Discussion
Maximum Cumulative Ratio Across Cycles

- Across cycles, mean MCR ↑: a mixture is more driven by multiple chemicals
- An investigation of mixtures becomes increasingly more important across cycles

<table>
<thead>
<tr>
<th>Cycle</th>
<th>Mean MCR</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005-2006</td>
<td>1.71</td>
</tr>
<tr>
<td>2007-2008</td>
<td>1.77</td>
</tr>
<tr>
<td>2009-2010</td>
<td>1.96</td>
</tr>
<tr>
<td>2011-2012</td>
<td>2.00</td>
</tr>
<tr>
<td>2013-2014</td>
<td>2.01</td>
</tr>
</tbody>
</table>

![Box plot showing adjusted MCR across cycles from 2005-2014]
Discussion

• Trends in hazard index of six phthalates
  • Over **two fold decrease** in mean hazard index from 2005 – 2014 (*0.34 to 0.15*)
  • **Children have higher hazards compared with adolescents and adults**
• Drivers of decreasing hazard index
  • Decreases in DEHP HQ (and to a lesser extent DBP HQ) with increases in DINP HQ
• Potentially problematic hazards (i.e., $HI > 1$)
  • Most participants have $HI \leq 1$ across cycles (ranging from *94% to 99%*)
  • Substantial decrease in the number of surveyed individuals with $HI > 1$ from 2005-2014 (*5.7% to 0.79%*)
• Changes in chemical mixtures
  • Inverse relationship between HI and MCR across all cycles
  • There was a **1.2-fold increase** in mean MCR (*1.7 to 2.1*) and the slope between MCR and HI decreased in magnitude indicating that largest combined exposures are becoming less dominated by one chemical during this time period
Limitations and Considerations, Strengths

• Limitations and Considerations
  • NHANES: cross-sectional, population-wide trends, ages 6+
  • Phthalates: short-lived (non-persistent), limitation in measuring daily intake
  • Different potential reference values (e.g. TDI versus RfD)
  • Only considered six phthalates (results may change with a different group)
  • Understanding the utility of the hazard quotient/hazard index

• Strengths
  • First study to examine the hazard index of this groups of phthalates in the general US population over time.
  • First study to explore MCR values of phthalates in the general US population over time.
Conclusions

• Future work
  • Simulations of hazards to further explore relationship between HI and MCR

• Parting thoughts
  • If decreasing HI trend continues, $HI > 1$ will most likely only be identified through mixtures
  • With strong temporal trends, tracking new phthalates and plasticizers entering the market and collecting biomonitoring data will remain important tasks
Thank You

• Acknowledgements
  • Dr. Paul Price
  • Funding
• Contact
  • Jeanette Reyes, PhD
  • reyes.jeanette@epa.gov
  • orcid.org/0000-0003-4068-3996
  • https://www.linkedin.com/in/jeanette-reyes/
References

- CPSC. Overview of Phthalates Toxicity. 2010.
- EFSA. Opinion of the Scientific Panel on food additives, flavourings, processing aids and materials in contact with food (AFC) on a request from the Commission related to Di-isonylphthalate (DINP) for use in food contact materials. Eur. Food Saf. Auth. J. 2005, No. 244, 1–18.
References (continued)


- Price, Paul, et al. "An application of a decision tree for assessing effects from exposures to multiple substances to the assessment of human and ecological effects from combined exposures to chemicals observed in surface waters and waste water effluents." Environmental Sciences Europe 24.1 (2012): 34.


Extra Slides
# Urinary Flow Rate

<table>
<thead>
<tr>
<th>Creatinine</th>
<th>UFR</th>
<th>2009-2010</th>
<th>2011-2012</th>
<th>2013-2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>HI&gt;1</td>
<td>HI&gt;1</td>
<td>37</td>
<td>21</td>
<td>13</td>
</tr>
<tr>
<td>HI&gt;1</td>
<td>HI&lt;1</td>
<td>25</td>
<td>14</td>
<td>6</td>
</tr>
<tr>
<td>HI&lt;1</td>
<td>HI&gt;1</td>
<td>24</td>
<td>34</td>
<td>22</td>
</tr>
<tr>
<td>HI&lt;1</td>
<td>HI&lt;1</td>
<td>2414</td>
<td>2241</td>
<td>2355</td>
</tr>
</tbody>
</table>

![Box plot showing adjusted log(HI) values for Creatinine and Urinary Flow Rate (UFR) over different time periods.]
Additional Zota Comparisons: PIR
Equations

• UFR Equation
  \[ DI_{i,j,k} = \left( \frac{[60 \times 24 \times Met_{i,k} \times UFR_i]}{[BW_i \times F_{UE,i,k} \times 1000]} \right) \times \left( MW_{i,j} / MW_{i,j,k} \right) \]

• Creatinine Equation
  \[ DI_{i,j,k} = \left( \frac{[100 \times (Met_{i,k} / Cr_i) \times CE_i]}{[F_{UE,i,k} \times 1000]} \right) \times \left( MW_{i,j} / MW_{i,j,k} \right) \]

• Zota Regressions
  • OVERALL: \( \log(HI) \sim \text{Cycle} \)
  • AGE: \( \log(HI) \sim \text{Cycle} + + \text{Gender} + \text{Race} + \text{PIR} + \text{Cycle*Age} \)
  • GENDER: \( \log(HI) \sim \text{Cycle} + \text{ridageyr} + \text{Race} + \text{PIR} + \text{Cycle*Gender} \)
  • RACE/ETHNICITY: \( \log(HI) \sim \text{Cycle} + \text{ridageyr} + \text{Gender} + \text{PIR} + \text{Race} + \text{Cycle*Race} \)
  • PIR: \( \log(HI) \sim \text{Cycle} + \text{ridageyr} + \text{Gender} + \text{Race} + \text{PIR} + \text{Cycle*PIR} \)
## Limit of Detection (LOD) Over Time

<table>
<thead>
<tr>
<th>Metabolite</th>
<th>Limit of detection (ng/mL)</th>
<th>Number of samples (%) below the limit of detection</th>
</tr>
</thead>
<tbody>
<tr>
<td>MBZP (BBP)</td>
<td>0.216 0.216 0.216 0.3 0.3</td>
<td>29 (1.14) 46 (1.78) 13 (0.47) 44 (1.79) 63 (2.36)</td>
</tr>
<tr>
<td>MBP (DBP)</td>
<td>0.6 0.6 0.4 0.4 0.4</td>
<td>7 (0.27) 19 (0.73) 12 (0.44) 136 (5.54) 43 (1.61)</td>
</tr>
<tr>
<td>MEHP (DEHP)</td>
<td>1.2 1.1 0.5 0.5 0.8</td>
<td>789 (31.1) 850 (32.9) 615 (22.5) 568 (23.1) 1003 (37.6)</td>
</tr>
<tr>
<td>MEOHP (DEHP)</td>
<td>0.7 0.6 0.2 0.2 0.2</td>
<td>26 (1.02) 44 (1.70) 8 (0.29) 9 (0.36) 13 (0.48)</td>
</tr>
<tr>
<td>MECPP (DEHP)</td>
<td>0.6 0.5 0.2 0.2 0.4</td>
<td>1 (0.03) 2 (0.07) 1 (0.03) 7 (0.28) 6 (0.22)</td>
</tr>
<tr>
<td>MEHHP (DEHP)</td>
<td>0.7 0.7 0.2 0.2 0.4</td>
<td>10 (0.39) 20 (0.77) 2 (0.07) 6 (0.24) 19 (0.71)</td>
</tr>
<tr>
<td>MIBP (DIBP)</td>
<td>0.3 0.3 0.2 0.2 0.8</td>
<td>52 (2.05) 47 (1.82) 4 (0.14) 23 (0.93) 72 (2.70)</td>
</tr>
<tr>
<td>MCNP (DIDP)</td>
<td>0.6 0.5 0.2 0.2 0.2</td>
<td>225 (8.89) 247 (9.57) 30 (1.10) 18 (0.73) 32 (1.20)</td>
</tr>
<tr>
<td>MINP (DINP)</td>
<td>1.323 1.232 0.77 0.5 0.9</td>
<td>2181 (86.2) 2297 (89.0) 1672 (61.3) 1013 (41.2) 1586 (59.5)</td>
</tr>
<tr>
<td>MCOP (DINP)</td>
<td>0.7 0.7 0.2 0.2 0.3</td>
<td>101 (3.99) 94 (3.64) 5 (0.18) 0 (0) 3 (0.11)</td>
</tr>
</tbody>
</table>
### Available Metabolites Over Time

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>urxcnp</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>urxcop</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>urxda</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>urdxma</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>urxcp</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>urxequ</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>urxetd</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>urxet</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>urngs</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>urnhbp</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>urnhbp</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>urnhc1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>urnhcp</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>urnhcp</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>urnhhp</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>urnhhh</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>urnhhc</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>urnhhp</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>urnhmb</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>urnhmn</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>urnhmp</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>urnhmph</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>urnhmp</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>urnhnh</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>urnhnp</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>urnhnp</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>urnhnp</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>urnhnp</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>urnhnp</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>urnhnp</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>urnhnp</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>urnhnp</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>urnhnp</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>urnhnp</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>urnhnp</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>urnhnp</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>8</td>
</tr>
</tbody>
</table>