Preliminary Screening Information on Possible Classes of Chemicals used in UV Applications

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Presentation to the Scientific Guidance Panel
November 3, 2016
Purpose of agenda item

- Discuss two possible classes of chemicals used in UV applications*
  - Benzophenones
  - Phenolic benzotriazoles
- Obtain Panel and public input on next steps

*“UV applications” includes uses as UV stabilizers, UV absorbers, or photoinitiators, for example.
Why classes?

Evaluating chemical classes or groups, rather than individual chemicals:

- Is resource-efficient for SGP chemical selection
- Allows the Program to quickly respond to shifts in chemical use and target emerging chemicals of concern
- Facilitates development of broad lab panels for related chemicals
- Allows for non-targeted screening within a class of chemicals
Background: Criteria for recommending designated chemicals

- **Exposure or potential exposure** to the public or specific subgroups

- The *known or suspected health effects* resulting from some level of exposure based on peer reviewed scientific studies

- The *need to assess the efficacy of public health actions* to reduce exposure to a chemical

- The *availability of a biomonitoring analytical method* with adequate accuracy, precision, sensitivity, specificity, and speed

- The *availability of adequate biospecimen samples*

- The *incremental analytical cost* to perform the biomonitoring analysis for the chemical
Preliminary screen of compounds used in UV applications

Broad research on a variety of topics, including:

- Chemical identity and structure
- Use and production
- Detections in humans, biota, and the environment
- Bioaccumulation and persistence
- Toxicity information
Some other compounds used in UV applications

- \( p \)-Aminobenzoates
- Avobenzone
- Cinnamates
- Salicylates
Benzophenones: Example chemicals

Benzophenone-3 (BP-3)

Benzophenone (BP)

Benzophenone-4 (BP-4)

Benzophenone-12 (BP-12)
## US production/import volume

<table>
<thead>
<tr>
<th>Chemical</th>
<th>2012 volume (lbs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzophenone-3 (BP-3)</td>
<td>100K – 500K</td>
</tr>
<tr>
<td>Benzophenone</td>
<td>3.9M</td>
</tr>
<tr>
<td>4-Methylbenzophenone</td>
<td>Withheld</td>
</tr>
<tr>
<td>Benzophenone-1 (BP-1)</td>
<td>32K</td>
</tr>
<tr>
<td>Benzophenone-4 (BP-4)</td>
<td>Withheld</td>
</tr>
<tr>
<td>Benzophenone-12 (BP-12)</td>
<td>2M</td>
</tr>
</tbody>
</table>
Biomonitoring studies

- Detections of parent compounds and/or biomarkers in urine:
  - BP-3, BP, BP-1, BP-2, BP-4, BP-8

- Detections in other biospecimens:
  - Placental tissue: BP-4
  - Serum, breast milk, adipose tissue: BP-3
Some toxicity information

- BP listed under Proposition 65 as known to the state to cause cancer
- Several benzophenones, including BP-3, show indications of endocrine activity (estrogenic, anti-estrogenic, anti-androgenic)
- Selected ToxCast™ bioactivity for benzophenones tested included effects on:
  - Endocrine activity
  - Cell viability
  - Cellular metabolism
  - Immune- and inflammation-related endpoints
Phenolic benzotriazoles: Example chemicals

UV P

UV 234

UV 328
## US production/import volume

<table>
<thead>
<tr>
<th>Chemical</th>
<th>2012 volume (lbs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UV P</td>
<td>605K</td>
</tr>
<tr>
<td>UV 234</td>
<td>1M - 10M</td>
</tr>
<tr>
<td>UV 326</td>
<td>394K</td>
</tr>
<tr>
<td>UV 327</td>
<td>Withheld</td>
</tr>
<tr>
<td>UV 328</td>
<td>2.2M</td>
</tr>
<tr>
<td>UV 329</td>
<td>500K - 1M</td>
</tr>
</tbody>
</table>
### LogK\textsubscript{ow} and bioconcentration factor (BCF)

<table>
<thead>
<tr>
<th>Chemical</th>
<th>LogK\textsubscript{ow}</th>
<th>BCF (L/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UV P</td>
<td>4.31 (exp)</td>
<td>324.1</td>
</tr>
<tr>
<td>UV 234</td>
<td>7.67</td>
<td>3,741</td>
</tr>
<tr>
<td>UV 326</td>
<td>5.55</td>
<td>1,283</td>
</tr>
<tr>
<td>UV 327</td>
<td>6.91</td>
<td>10,160</td>
</tr>
<tr>
<td>UV 328</td>
<td>7.25</td>
<td>6,006</td>
</tr>
<tr>
<td>UV 329</td>
<td>6.21</td>
<td>5,843</td>
</tr>
</tbody>
</table>

Evidence for persistence: LogK\textsubscript{ow} ≥ 4  
Evidence for bioaccumulation: BCF > 1,000
### Biomonitoring study: Breast milk

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Detection Frequency (%)</th>
<th>Average ± SD (ng/g)</th>
<th>Maximum (ng/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UV P</td>
<td>13</td>
<td>19.2 ± 60.1</td>
<td>374</td>
</tr>
<tr>
<td>UV 326</td>
<td>9.1</td>
<td>1.77 ± 7.09</td>
<td>53.1</td>
</tr>
<tr>
<td>UV 327</td>
<td>29</td>
<td>10.0 ± 19.0</td>
<td>95.5</td>
</tr>
<tr>
<td>UV 328</td>
<td>98</td>
<td>64.3 ± 66.4</td>
<td>334</td>
</tr>
<tr>
<td>UV 329</td>
<td>8.7</td>
<td>4.54 ± 19.5</td>
<td>178</td>
</tr>
</tbody>
</table>

For comparison:

| Tonalide (synthetic musk) | 54 | 65.1 ± 84.9 | 350 |

Lee et al. 2015
Detections in biota

- Dolphin plasma
- Porpoise blubber
- Aquatic organisms (fish, mussels, and other)
Some toxicity information

- NTP studies underway on several chemicals in this class
- A few phenolic benzotriazoles show indications of:
  - Anti-androgenic activity
  - Aryl hydrocarbon receptor (AhR) pathway activation
- Selected ToxCast results for phenolic benzotriazoles tested included effects on:
  - Endocrine activity
  - AhR pathway activation
  - Xenobiotic metabolism
  - Cell proliferation
  - Immune- and inflammation-related endpoints
Options for the Panel

The SGP could:

- Request that OEHHA prepare a potential designated chemical document on one or both of these classes
- Propose further screening or continued tracking of the classes
- Advise no further action on either classes
- Suggest other classes for possible consideration