Comment on “Identifying and Prioritizing Chemicals with Uncertain Burden of Exposure: Opportunities for Biomonitoring and Health-Related Research” and “Beyond the Light under the Lamppost: New Chemical Candidates for Biomonitoring in Young Children”

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In their exhaustive attempt to identify priority chemicals to evaluate in the Environmental Influences on Child Health Outcomes (ECHO) trial, Pellizzari et al. (2019) consulted no fewer than 21 databases and eventually identified 155 likely candidates. However, the authors were unable to identify the chemicals U.S. children are exposed to, instead stating that “Tens of thousands of chemicals have been approved for use in the United States” (Pellizzari et al. 2019). This indicates the lack of information about the number of synthetic chemicals Americans are exposed to.

The Science Selection summary of the paper by Pellizzari et al. (2019) refers to “40,000 chemicals approved for commercial use in the United States” (Seltenrich 2020). This is incorrect. Chemicals do not undergo an approval process by the U.S. Environmental Protection Agency (EPA). They are entered into the U.S. EPA’s Toxic Substances Control Act (TSCA) Inventory upon 90 d notice (“Premanufacture Notice”) of the intent to manufacture or import, with numerous exemptions (Table 1). Accordingly, only a fraction of the commercially available chemicals in the United States are in the TSCA Inventory.

Testing data are not required, nor are they usually provided, for the TSCA Inventory. If the chemical is for a “significant new use,” the company must submit “information” (substituted for “test data” in 2016) (Control of Toxic Substances—Definitions 2018). The U.S. EPA has adopted predictive models to assess risk based on structural similarity (U.S. EPA 2017) even though structure alone is not predictive of toxicity (Padberg et al. 2019; Preciados et al. 2016). If the agency finds that a chemical poses an “unreasonable risk,” it may implement a phase-out up to 5 y after it publishes a final rule unless it finds an exemption (Control of Toxic Substances—Prioritization, Risk Evaluation, and Regulation of Chemical Substances and Mixtures 2018). The U.S. EPA is currently conducting risk evaluations on 33 chemicals, including chemicals that were grandfathered in when the inventory was established in 1976 (U.S. EPA 2021). The 40,000 figure referenced in the Science Selection is from a U.S. EPA press release announcing that approximately half the chemicals on the inventory have been deleted because they are no longer active in U.S. commerce (U.S. EPA 2019). According to a U.S. EPA representative, use information was provided by manufacturers, and nothing other than the press release and the database are publicly available (personal communication, Tracy Williamson). The number of chemicals formerly listed in the inventory—87,000—is often misinterpreted as the number of chemicals in use in the United States (Colborn 2004) and misconstrued as the number of synthetic chemicals Americans are exposed to. The American Chemical Society currently lists more than 167 million chemical substances worldwide in its Chemical Abstract Service Registry (https://www.cas.org/support/documentation/chemical-substances). This registry can potentially yield the best estimate of chemical exposure in the United States.

Table 1. Exemptions to the Toxic Substances Control Act Inventory.

| Category                | Example                                                                 |
|-------------------------|-------------------------------------------------------------------------|
| Mixtures                | Chemicals that do not pose an unreasonable risk to health or the environment |
| Impurities              | Chemical reaction products created during storage, disposal, or end use   |
| Nonisolated intermediates | Chemical reaction products with other chemicals                           |
| Mixture products        | Byproducts not used commercially                                         |
| Nuclear materials       | Tobacco and tobacco products                                             |
| Munitions               | Nuclear materials                                                       |
| Certain types of polymers | Nanomaterials except for “discrete forms”                               |
| Petroleum products      | Microorganisms                                                          |
| Naturally occurring chemicals | Chemicals used in hydraulic fracturing (“fracking”)                        |

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