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Review article

# Health risks of chemicals in consumer products: A review

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ABSTRACT

Increasingly diverse chemicals are used in consumer products, while our understanding of their exposure pathways and associated human health risks still lags behind. This paper aims to identify the dominant patterns of exposure pathways and associated health risks of chemicals used in consumer products reported in the peer-reviewed literature. We analyzed 342 articles covering 202 unique chemicals, and distilled the information on the functional uses, product applications, exposure routes, exposure pathways, toxicity endpoints and their combinations. We found that the volume of the literature addressing human health risks of chemicals in consumer products is increasing. Among others, phthalates, bisphenol-A, and polybrominated diphenyl ethers were the most frequently discussed chemical groups in the literature reviewed. Emerged from our review were a number of frequently reported functional use/product application combinations, including plasticizers, polymers/monomers, and flame retardants used in food contact products, personal care products, cosmetics, furniture, flooring, and electronics. We also observed a strong tendency that the number of publications on a chemical surges following major regulatory changes or exposure incidents associated with the chemical. We highlight the need to develop the capacity and the mechanism through which human health risks of chemicals in consumer products can be identified prior to their releases.

## 1. Introduction

Over 140 million chemicals are registered under the Chemical Abstract Service (CAS, 2015), and as the number grows rapidly, understanding their human health implications is increasingly becoming a challenge. One of the areas in which such a challenge has recently been manifested into a public health crisis is in consumer products: a group of humidifier disinfectants were recently identified as the cause of the pulmonary fibrosis outbreak in South Korea that resulted in about a thousand victims to-date (Park et al., 2016; Reckitt Benckiser, 2016; The Independent, 2017).

Chemicals used in consumer products pose a number of unique challenges as compared to the pollutants from industrial sources. First, chemicals in consumer products can reach out to a large population in a short period of time. For example, one of the humidifier disinfectants associated with the pulmonary fibrosis outbreak in South Korea, polyhexamethylene guanidine (PHMG) reached out to an estimated 8 million people (Lung Injury Investigation Committee, 2014). In comparison, the total number of people evacuated or relocated in response to the historically worst nuclear accident, Chernobyl accident of 1986, was about 336,000.

Second, the chemicals in consumer products are subject to close contact with consumers on a daily basis (Csiszar et al., 2016; Jolliet et al., 2015). These chemicals can be transferred to human body as shown in the cases of benzophenone-3 (Calafat et al., 2008; Krause et al., 2012), bisphenol-A (Bemrah et al., 2014; Halden, 2010), phthalates (Berman et al., 2009; Halden, 2010; Philippat et al., 2015), and polybrominated diphenyl ethers (Gump et al., 2014; Kalantzi and Siskos, 2011). Due to the diversity of chemicals in consumer products, there is also the issue of co-exposure to many chemicals in various consumer products, which could lead to combined effects even if individual chemicals are present at safe levels (Kortenkamp and Faust, 2018).

Third, once commercialized, taking those chemicals out of use has proven to be very difficult, even if adverse health effects of the chemicals become known. For example, lead-containing paint in buildings is still a major source of lead exposure worldwide, despite its ban took place in many countries in the 1970s (Etchevers et al., 2014; Gottesfeld et al., 2014; Hore et al., 2014; Mathee, 2014). Products containing banned chemicals may also be passed down through generations or circulate in second-hand markets leading to a source of continued human exposure (Stapleton et al., 2011; Stapleton et al., 2012; Sharmer et al., 2007).

Fourth, the same chemical may pose very different levels of risks depending on how the chemical is used by the product and how humans interact with the product (Phillips et al., 2017; Tao et al., 2018). For example, phthalates are found in cellphones, food containers, and shampoos, while the exposure pathways of phthalates and

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corresponding human health risks greatly vary among these products (Bao et al., 2015; Hartle et al., 2016). Recycling could also lead to the occurrence of chemicals in recycled products, which might have completely different properties in retaining chemicals and different exposure patterns to human (Geueke et al., 2018).

Therefore, central to the understanding and potentially mitigating the human exposure and health risks of chemicals in consumer products is the relationship between the chemicals in consumer products and the patterns of product use by consumers, which determines the characteristic exposure pathways and corresponding risks of the chemical in consumer products. In this review, we are aiming at identifying the patterns of relationship among chemicals, and their functional uses (e.g. flame retardant, plasticizer, solvent, etc.), product applications (e.g. cleaning agent, cosmetics, furniture, etc.), exposure routes (inhalation, dermal absorption, dietary ingestion, and unintentional ingestion), and exposure pathways (food & beverage, dust, aerosol, etc.) reflected in the literature. Understanding such patterns in the literature would provide an insight into the dominant exposure scenarios that the research community has been concerned about the most, which may also offer a perspective on the future research directions and needs.

The objectives of this review are (1) to identify the combinations of functional uses, product applications, exposure routes, exposure pathways, and toxicity endpoints that are frequently reported in the literature in the context of chemicals in consumer products and associated human health risks; and (2) to identify research needs to close knowledge gaps, if any, in examining the human health risks of chemicals in consumer products. In this paper, we are focusing on the chemicals reported in the literature, which may not represent the full spectrum of chemicals in consumer products relevant to human health.

## 2. Methods

### 2.1. Scope

We searched Web of Science (webofknowledge.com) and PubMed (ncbi.nlm.nih.gov/pubmed) for peer-reviewed research or review papers ever published in English up until end of 2017. The search was completed in February 2018. The keywords were "consumer products", "use", "human", "health", and "exposure" and combined with the logic operator AND, searched in the "Topic" field of Web of Science and "All Fields" in PubMed. We did not include "toxicity" or "risk" in the searched keywords because we found including either of them would substantially decrease the returned results from the databases and compromise the comprehensiveness of the literature search. To ensure comprehensive coverage, "products" in the keyword "consumer products" was substituted with 84 specific products identified from the dictionary of the U.S. Environmental Protection Agency (U.S. EPA)'s Chemical and Product Categories database (CPCat) (Dionisio et al., 2015) (see Supplemental material part 1, Table S1 for complete list and Supplemental material part 2.1 for the criterion used). Ingestion of food contaminated by chemicals found in consumer products via bioaccumulation through the food web, albeit an important issue and showed up frequently in our initial literature search, is not included within the scope of this study.

We compared the year of publication against significant events worldwide such as product recalls, governmental regulations, manufacturer phase-outs in relation to the chemical(s) that these papers deal with. We distilled the following information from the literature: (1) functional use of chemicals, (2) products applications, (3) exposure routes, (4) exposure pathways, (5) the toxicity of the chemicals, and (6) whether the authors indicated that the chemicals pose risks to human health. Review papers were directly included to extract information, not used to identify original research papers.

### 2.2. Extraction of information

Whenever possible, the CAS numbers for the chemicals were recorded for disambiguation. If several chemicals within the same group (e.g. phthalates) were often discussed together, we used the chemical group rather than distinguishing each within the group.

We assigned the functional uses to chemicals from a list of 11 functional uses based primarily on the U.S. EPA's Safer Chemical Ingredients List (US EPA, 2013b) with the addition of plasticizers (used in packaging or within the formulation), flame retardants, and ultraviolet (UV) absorbents given their frequencies of occurrence in the literature. For the chemicals that have multiple functional uses, we used the most commonly mentioned in the original papers collected in this review. A total of 46 consumer products types classified in CPCat (Dionisio et al., 2015) were aggregated into 15 product applications (see Supplemental material part 1, Table S2). Product applications mentioned in the papers were matched with the product applications list. Both the functional uses and product applications lists include an "other" category reserved for less common functional uses or product applications.

Exposure routes found in the papers were grouped into four categories: (1) dermal absorption, (2) dietary ingestion, (3) inhalation and (4) unintentional ingestion. Exposure pathways described in the collected papers were grouped into five categories: (1) aerosol, (2) direct contact, (3) dust, (4) food & beverage, and (5) fugitive emission to air. These exposure pathways represent the interface between the products where the chemicals are used in and the exposure routes for humans.

Toxicity endpoints extracted from the literature were classified to: (1) carcinogenicity, (2) cardiovascular toxicity, (3) developmental toxicity, (4) endocrine disruption, (5) irritation, (6) neurotoxicity, (7) pulmonary toxicity, and (8) reproductive toxicity. We referred to the National Institutes of Health Hazardous Substances Data Bank (HSDB) (NIH, 2018) for toxicity endpoints except carcinogenicity, for which we referred to the International Agency for Research on Cancer (IARC) classifications (IARC, 2018). The chemicals that are reported to pose human health impacts by epidemiological studies or those with human cell line testing results in HSDB were considered to have the corresponding toxicity endpoint. Chemicals with group 1 ("Carcinogenic to humans"), 2A ("Probably carcinogenic to humans"), or 2B ("Possibly carcinogenic to humans") classifications in IARC are considered to have carcinogenicity in this review.

All full names and abbreviations of functional uses, product applications, exposure routes, exposure pathways, and toxicity endpoints used in this review are listed in Table 1. Descriptions of the exposure routes and exposure pathways can be found in Supplemental material part 2.2.

### 2.3. Methods for analyzing trends and patterns

We tallied the number of papers on each chemical based on their functional uses, production applications, exposure routes, exposure pathways, toxicity endpoints, and various combinations of these factors. Many papers discussed more than one chemical and when tallied for a certain combination, each chemical for each paper will be added as one count. Therefore, the final tally for these combinations does not necessarily represent the number of unique papers. However, the final tally for each chemical or a certain functional use/product application/exposure route/exposure pathways/toxicity endpoint represents the number of unique papers.

## 3. Results

### 3.1. Chemicals in the collected literature

The total number of publications returned from the initial search was 1911 from Web of Science and PubMed. After applying the screening method explained earlier 342 papers were left for further analysis. The total number of chemicals covered by the 342 papers was 202, of which 180 were individual chemicals with identifiable CAS numbers, 15 were groups of chemicals (such as phthalates), and 7 were engineered nanomaterials.

Among the 202 chemicals, 79 chemicals in the discussed scenarios were determined to have low risks in the original 65 papers supported with quantitative risk assessment results. Of which 45 chemicals were

**Table 1**
Full names and abbreviations for functional uses, product applications, exposure routes, exposure pathways, and toxicity endpoints.

| Functional use[a] | | Product application[b] | | Exposure route | | Exposure pathways | | Toxicity endpoint | |
|---|---|---|---|---|---|---|---|---|---|
| Full name | Abbreviation | Full name | Abbreviation | Full name | Abbreviation | Full name | Abbreviation | Full name | Abbreviation |
| Antimicrobial actives | AC | Air fresheners | AF | Dermal absorption | DA | Aerosol | AS | Carcinogenicity | CG |
| Colorants | CL | Apparel | AP | Dietary ingestion | DI | Direct contact | DC | Cardiovascular toxicity | CT |
| Fragrances | FG | Baby and children use | BC | Inhalation | IH | Dust | DS | Developmental toxicity | DT |
| Flame retardants | FR | Biocides | BD | Unintentional ingestion | UI | Food & beverage | FB | Endocrine disruption | ED |
| Preservatives and antioxidants | PA | Cleaning agents | CA | | | Fugitive emission to air | FE | Irritation | IR |
| Plasticizer | PL | Cosmetics | CM | | | | | Neurotoxicity | NT |
| Polymers/monomers | PO | Electronics | ET | | | | | Pulmonary toxicity | PT |
| Surfactants | SF | Food contact | FC | | | | | Reproductive toxicity | RT |
| Solvents | SL | Flooring | FL | | | | | | |
| UV absorbents | UA | Furniture | FT | | | | | | |
| Others | OT | Hair dyes | HD | | | | | | |
| | | Personal care products | PC | | | | | | |
| | | Paint | PN | | | | | | |
| | | Sunscreen | SS | | | | | | |
| | | Others | OR | | | | | | |

[a] Based on U.S. EPA's Safer Chemical Ingredients List (US EPA, 2013b) with the addition of plasticizers, flame retardants, and ultraviolet (UV) absorbents.
[b] Aggregated from 46 consumer products types classified in CPCat (Dionisio et al., 2015), see Supplemental material part 1 Table S2 for details.

also discussed by at least another paper that considered them posing health risks to consumers in the discussed scenarios. These chemicals include a number of chemicals used as fragrance, several metals, engineered nanomaterials, and also phthalates, BPA, and PBDE. The rest of the collected papers either concluded that the chemicals in consumer products discussed exceeded certain risk thresholds by conducting quantitative risk assessments or made general remarks on the potential risks. The 202 chemicals were cited 674 times (average 3.3 citations per chemical) across 342 papers. Among them, phthalates, bisphenol-A (BPA), and polybrominated diphenyl ethers (PBDE) were the most frequently cited ones with 73, 40, and 39 citations, respectively. On the other end, 115 chemicals showed no more than one citation.

Key characteristics of these papers are summarized in Table S3 in the Supplemental material part 1. The full reference list for the 342 papers can be found in Supplemental material part 3.

### *3.2. Timing of publications*

Panel (a) in Fig. 1 shows the number of publications screened in this study. Panels (b), (c), (d), and (e) in Fig. 1 show the number of publications on phthalates, BPA, PBDE, and lead, respectively, in consumer products. Significant events including regulatory actions, product recalls, and manufacturers and retailers' responses related to the chemicals are indicated along the timelines. In general, the number of publications surged following such events.

### *3.3. Information on the methods used in the reviewed literature*

About 81% of the literature reviewed provided some information on the method used for quantitative exposure or risk assessment. 126 papers used concentration measurements in the consumer products and/or the indoor environment where the products are used, and 111 papers used exposure models and compared the results with established safety threshold levels (reference dose, lowest observed adverse effect level, tolerable daily intake, etc.). 88 papers provided biomonitoring data corresponding to the described exposure pathways. Many papers used various combinations of these approaches.

### *3.4. Patterns of chemical-product-exposure combinations*

For each individual paper, the combinations of the chemical's functional use, product application, and corresponding exposure route and exposure pathway were examined and mapped. The ten most discussed combinations based on numbers of reports are summarized in Table 2 below.

Five of the ten most discussed combinations were flame retardant chemicals used in either furniture or electronics with the most frequently reported associated exposure route and pathway being unintentional ingestion and dust. These two combinations both had 47 reports in the collected papers. Two other flame retardant chemicals related combinations are applications in furniture or electronics, with human exposure through inhalation of dust, accounting for 41 and 36 reports. Flame retardant chemicals used in electronics, exposed to human through dermal absorption through direct contact accounted for 31 reports.

One of the most frequently reported chemical-product-exposure patterns involves plasticizers. They were applied to food contact products, such as baby bottles, tuna cans, bread bags, juice boxes, etc., and with human exposure through dietary ingestion of food & beverage, accounting for 46 reports. The same pattern was also frequently reported for polymers/monomers such as BPA and polyethylene terephthalate (PET), which was among the ten most frequently reported combinations with 35 reports. Another two frequently discussed combinations for plasticizers were applications to personal care products and cosmetics with human exposure through dermal absorption via direct contact, accounting for 42 and 30 reports.

UV absorbents used in sunscreen exposed through dermal absorption due to direct contact was the fourth frequently reported chemical-product-exposure combination. 23 chemicals were covered by 39 reports for this combination.

Table 3 shows the top three chemical-product-exposure patterns for each of the five most frequently reported chemicals and chemical groups. When organized per chemicals or chemical groups, phthalates, BPA, and PBDE and corresponding exposure patterns dominated the list followed by lead used for colorants and with human exposure through direct contacts or dust, and nano-silver used for antimicrobial actives in a variety of products, exposure routes, and pathways.

The complete 168 combinations can be found in Table S4 in the Supplemental material part 1.

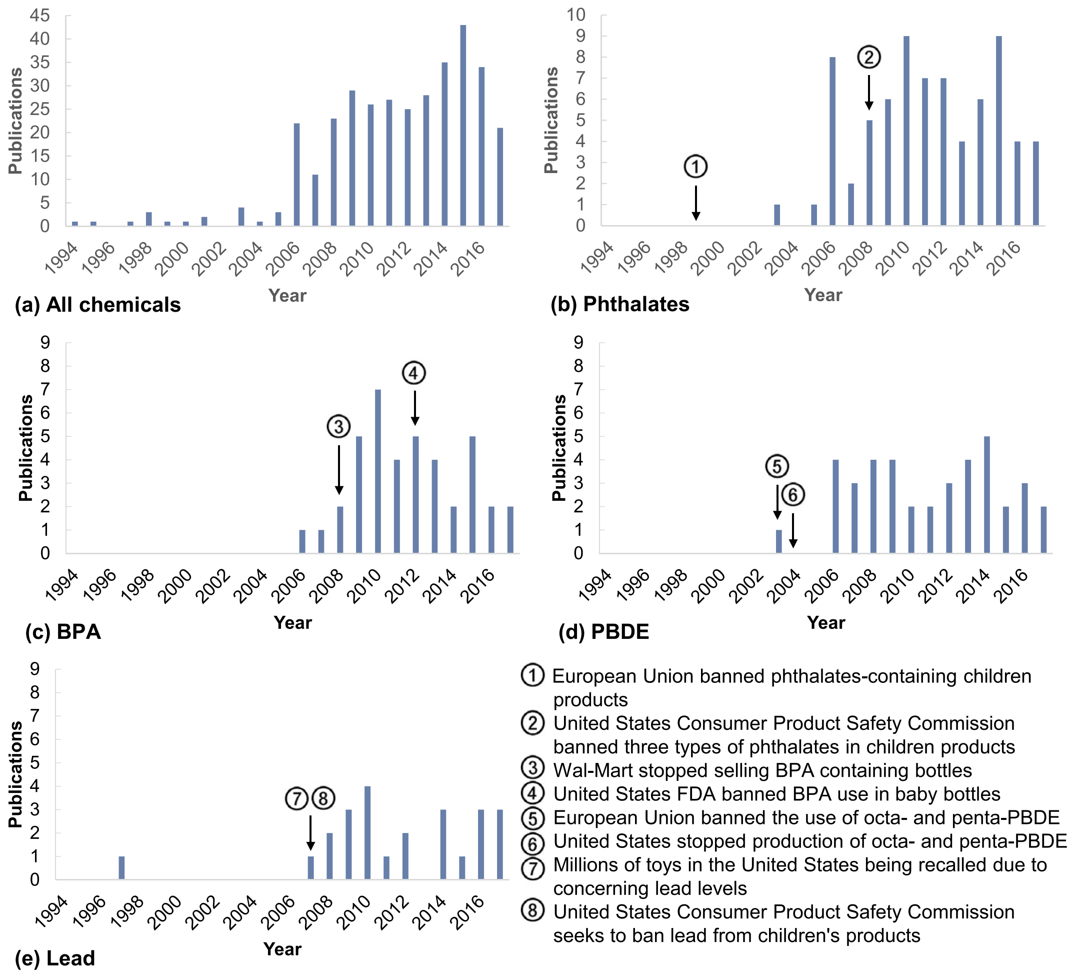


**Fig. 1.** Numbers of publications from year 1996 to 2016 using the key words "consumer products", "use", "human", "health", "exposure", and "toxicity" for (a) all chemicals, (b) phthalates, (c) bisphenol-A, (d) polybrominated diphenyl ethers, and (e) lead.

### 3.5. Distribution of reports for exposure routes and pathways

Fig. 2 shows the number of reports on different exposure routes and pathways across all chemicals from papers collected in this study. As an exposure pathway reported may be matched with multiple exposure routes (and vice versa), the sum of reports for all exposure routes is not equal to that for all exposure pathways. Dermal absorption represented the largest share of reports on different exposure routes with 42% of the total. This was mainly due to fact that direct contact being the most widely reported exposure pathway (47% of the total). Inhalation was the second largest exposure routes reported in the literature, representing 25% of the total. The sources for inhalation were more diverse, as dust, aerosol, and fugitive emission to air (which were the least three reported exposure pathways) all contributing to this exposure route. Unintentional ingestion represented 20% of reports with regard to exposure routes. The corresponding exposure pathways were

**Table 2**
Top ten combinations of functional use/product application/exposure route/exposure pathway discussed in literature.

| Functional use[a] | Product application[b] | Exposure route[c] | Exposure pathways[d] | Number of reports[e] | Chemicals[f] |
|---|---|---|---|---|---|
| FR | ET | UI | DS | 47 | 10 chemicals, see Table S4 in Supplementary data part 1 for complete list |
| FR | FT | UI | DS | 47 | 11 chemicals, see Table S4 in Supplementary data part 1 for complete list |
| PL | FC | DI | FB | 46 | Phthalates, DEHA, DEHP |
| PL | PC | DA | DC | 42 | Phthalates, DEHA, DEHP |
| FR | FT | IH | DS | 41 | 10 chemicals, see Table S4 in Supplementary data part 1 for complete list |
| UA | SS | DA | DC | 39 | 23 chemicals, see Table S4 in Supplementary data part 1 for complete list |
| FR | ET | IH | DS | 36 | 7 chemicals, see Table S4 in Supplementary data part 1 for complete list |
| PO | FC | DI | FB | 35 | Acrylamide, BPA, PET, Styrene |
| FR | ET | DA | DS | 31 | 7 chemicals, see Table S4 in Supplementary data part 1 for complete list |
| PL | CM | DA | DC | 30 | Phthalates |

[a] Abbreviations: FR (flame retardants); PL (plasticizer); PO (polymers/monomers); UA (UV absorbant).
[b] Abbreviations: CM (cosmetics); ET (electronics); FC (food contact); FT (furniture); PC (personal care products); SS (sunscreen).
[c] Abbreviations: DI (dietary ingestion); DA (dermal absorption); IH (inhalation); UI (unintentional ingestion).
[d] Abbreviations: FB (food & beverage); DC (direct contact); DS (dust).
[e] Publications may discuss several combinations for one chemical, thus overlapping in the number of reports over different combinations.
[f] Abbreviations: BPA (bisphenol-A); DEHA (di-(2-ethylhexyl) adipate); DEHP (di(2-ethylhexyl) phthalate); PET (polyethylene terephthalate).

**Table 3**
Combinations of functional use/product application/exposure route/exposure pathways for the five most cited chemicals.

| Chemical | Top three combinations for each chemical | | | | | Total unique papers for each chemical |
|---|---|---|---|---|---|---|
| | Functional use[a] | Product application[b] | Exposure route[c] | Exposure pathway[d] | Number of reports[e] | |
| Phthalates | PL | FC | DI | FB | 41 | 73 |
| | PL | PC | DA | DC | 39 | |
| | PL | CM | DA | DC | 30 | |
| Bisphenol-A | PO | FC | DI | FB | 32 | 40 |
| | PO | OR[f] | DA | DC | 8 | |
| | PO | PC | UI | DC | 6 | |
| Polybrominated diphenyl ethers | FR | ET | UI | DS | 31 | 39 |
| | FR | ET | IH | DS | 28 | |
| | FR | FT | UI | DS | 26 | |
| Lead | CL | CM | DA | DC | 8 | 24 |
| | CL | BC | UI | DC | 7 | |
| | CL | PN | UI | DS | 7 | |
| Nano-silver | AC | AP | DA | DC | 7 | 19 |
| | AC | FC | DI | FB | 6 | |
| | AC | PC | IH | AS | 6 | |

[a] Abbreviations: AC (antimicrobial actives); CL (colorant); FR (flame retardants); PL (plasticizer); PO (polymers/monomers).
[b] Abbreviations: AP (apparel); BC (baby & children use); CM (cosmetics); ET (electronics); FC (food contact); FT (furniture); OR (others); PC (personal care products); PN (paint).
[c] Abbreviations: DI (dietary ingestion); DA (dermal absorption); IH (inhalation); UI (unintentional ingestion).
[d] Abbreviations: AS (aerosol); FB (food & beverage); DC (direct contact); DS (dust).
[e] Publications may discuss several combinations for one chemical, thus overlapping in the number of reports over different combinations.
[f] Receipt paper for this combination.

dust (e.g. hand-to-mouth activities) and direct contact (e.g. lipsticks). Dietary ingestion represented 14% of reports on exposure routes and corresponded exclusively with food & beverage, which represented the third largest share of reports on exposure pathways.

### 3.6. Combinations of functional uses, product applications, and toxicity endpoints

Regarding functional uses, plasticizers had the highest number of reports across all product applications due to both of its wide coverage in product applications and including phthalates, which were most frequently cited from the reviewed papers. Flame retardants followed due to having the highly cited PBDEs as well as a variety of PBDE alternatives that have been attracting the attention of researchers lately. Although BPA was one of the most cited chemicals, its product application was highly concentrated in food contact products therefore making polymers/monomers not standing out as a functional group in terms of numbers of reports. These functional uses (plasticizers, flame retardants, polymers/monomers) represented the most of the reports for all functional use/toxicity endpoint combinations found in the reviewed papers because the chemicals in these functional groups were found to have multiple toxicity endpoints and a high numbers of reports.

Regarding product applications, cosmetics, food contact, and personal care products had much higher numbers of reports across both functional uses and toxicity endpoints compared to other product applications. These products all come within close contact with consumers, which may grant them high exposure potentials. The numbers of chemicals across all toxicity endpoints for these products were also higher compared to other products. The high numbers of reports for toxicity was further compounded by the use of highly cited chemicals with various toxicity concerns such as phthalates and BPA in these products.

Among the toxicity endpoints considered, irritation was the most prevalent by far as accounting for 50% of all chemicals reviewed. Following irritation were neurotoxicity and endocrine disruption, found in 16% and 15% of the chemicals, respectively. On the contrary, cardiovascular toxicity was the least common endpoint in the literature accounting for 5% of the chemicals reviewed. As much as 33% of the chemicals reviewed reported more than one toxicity endpoint. BPA, phthalates, and polychlorinated biphenyls were associated with six toxicity endpoints. Formaldehyde and lead were associated with five

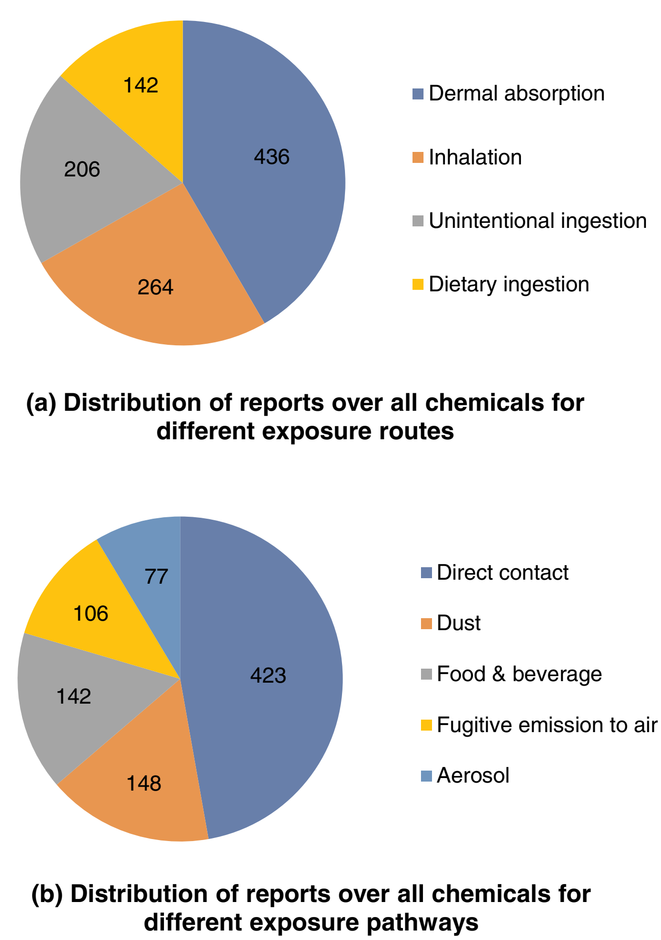


**Fig. 2.** Numbers of reports on (a) four exposure routes and (b) five exposure pathways across all chemicals published from year 2006 to 2016.

toxicity endpoints. More details can be found in Table S3 in Supplemental material part 1. No clear patterns could be found in either combination with functional uses or product applications.

## 4. Discussion

### 4.1. Knowledge gap

As shown in this study, published literature on health risks of chemicals in consumer products largely focused on a handful of high-profile chemicals, namely phthalates, BPA, PBDE, lead, and several engineered nanomaterials (Fig. 1 and Table S3). We also observed a tendency in the literature to focus on several functional use/product application combinations such as plasticizers in food contact applications, leaving variety of the other combinations unexplored (Table 4). When these frequently discussed chemicals are excluded, the number of chemicals found in the literature under our criteria is reduced to 195, which is a tiny fraction of the chemicals used in consumer products. For example, recent applications of high-resolution mass spectrometry for non-target analysis have revealed hundreds to thousands of unique chemicals in house dust samples, many of which are originated from consumer products (Moschet et al., 2018; Rager et al., 2016). In another study, suspect screening analysis of 100 consumer products tentatively identified 1602 chemicals, 1404 of which were not found in public database of known consumer product chemicals (Phillips et al., 2018). Although the importance of the frequently discussed chemicals in the literature is indisputable, the possibility that an under-researched chemical in consumer products turns out to be a substantial threat to human health cannot be completely ruled out until they are properly studied. At the same time, providing the information needed by modern risk assessment and regulators in a timely fashion via traditional toxicity testing has become increasingly challenging due to its high cost of laboratory animal testing and the time needed to generate and review data (Andersen and Krewski, 2009; Krewski et al., 2010). This creates a fundamental, structural challenge in understanding adverse human health impacts of the many chemicals in consumer products that has little information available, which is illustrated by the aforementioned works of non-target and suspect screening analysis.

### 4.2. Potential solutions under development

Recently, in vitro high-throughput techniques are often applied to screen a wide variety of chemicals in a short period of time. U.S. EPA initiated the ToxCast program in 2006 with the purpose of generating data and predictive models to screen thousands of chemicals (Dix et al., 2007). To date, ToxCast has data on over 9000 chemicals from high-throughput assays (U.S. EPA, 2016b). The ExpoCast program was established following ToxCast with the goal of creating tools that can rapidly estimate human exposure potential to support risk-based prioritization for chemicals (Wambaugh et al., 2013). Developments of high-throughput based methodologies in both exposure and toxicity have created the possibility to conduct high-throughput risk assessment (Wetmore et al., 2015). The emerging microphysiological systems approach, or "organs-on-chips", also presents a potential pathway for providing human relevant toxicity information of chemicals at key organs before actual population exposure (Fabre et al., 2014), which

**Table 4**

Combinations of functional uses, product applications, and toxicity endpoints for all chemicals found in the reviewed papers. Numbers indicate number of reports and chemicals (in parenthesis) in the matching combinations. The three sections represent combinations of functional use/product application, functional use/toxicity endpoint, and product application/toxicity endpoint. Color coding from green to red for lower to higher numbers of reports in 20 percentiles was done for each section.

| | | Functional uses[a] | | | | | | | | | | | Toxicity endpoints[c] | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | AC | CL | FG | FR | PA | PL | PO | SF | SL | UA | OT | CG | CT | DT | ED | IR | NT | PT | RT |
| Product applications[b] | AF | 1 (1) | | 21 (12) | | 2 (1) | 5 (1) | | | 4 (4) | | 1 (1) | 5 (4) | 1 (1) | 5 (1) | 5 (1) | 30 (17) | 15 (8) | 10 (5) | 9 (4) |
| | AP | 12 (2) | 4 (3) | | | | 4 (2) | | 11 (3) | 1 (1) | | 1 (1) | 8 (4) | | 12 (3) | 13 (4) | 10 (5) | 16 (6) | 15 (4) | 17 (6) |
| | BC | 8 (3) | 9 (2) | 1 (1) | 14 (8) | 2 (2) | 34 (4) | 3 (2) | 2 (2) | | 1 (1) | 2 (2) | 10 (3) | 16 (4) | 49 (10) | 37 (7) | 54 (16) | 48 (7) | 33 (4) | 44 (8) |
| | BD | 20 (6) | | | | | | | | | | | | 14 (2) | | 1 (1) | 3 (3) | 3 (1) | 18 (4) | |
| | CA | 19 (9) | | 19 (15) | | 5 (2) | 6 (1) | 2 (1) | 13 (10) | 7 (4) | 1 (1) | 4 (4) | 8 (5) | 3 (2) | 17 (5) | 14 (7) | 55 (8) | 30 (11) | 23 (9) | 23 (6) |
| | CM | | 23 (4) | 19 (17) | | 19 (7) | 36 (1) | 5 (3) | 17 (14) | 5 (4) | 11 (10) | 26 (8) | 27 (8) | 20 (4) | 52 (6) | 55 (10) | 101 (32) | 70 (13) | 55 (9) | 59 (9) |
| | ET | | | | 52 (11) | | 4 (2) | 2 (1) | | | | | 5 (2) | 36 (2) | 42 (6) | 46 (6) | 11 (7) | 43 (5) | 2 (1) | 11 (6) |
| | FC | 7 (1) | 6 (3) | | 1 (1) | 1 (1) | 52 (4) | 37 (4) | 32 (16) | 1 (1) | 4 (3) | 3 (3) | 18 (7) | 35 (3) | 92 (7) | 109 (14) | 90 (11) | 94 (9) | 61 (8) | 109 (12) |
| | FL | | | | 12 (4) | 6 (2) | 30 (3) | 1 (1) | 17 (3) | | | | 18 (6) | 9 (1) | 49 (5) | 55 (5) | 39 (8) | 44 (5) | 34 (3) | 54 (8) |
| | FT | | | | 57 (12) | 10 (6) | 1 (1) | 1 (1) | | | | | 7 (3) | 29 (1) | 45 (6) | 35 (4) | 25 (11) | 39 (4) | 7 (3) | 17 (5) |
| | HD | | 13 (6) | | | | | | | 3 (3) | | | 4 (3) | 3 (2) | 2 (1) | | 10 (4) | 3 (2) | 7 (2) | 4 (3) |
| | PC | 31 (6) | 13 (4) | 35 (32) | | 16 (4) | 47 (3) | 11 (3) | 14 (8) | 3 (3) | 25 (22) | 26 (12) | 18 (9) | 19 (4) | 74 (7) | 82 (16) | 145 (51) | 82 (15) | 69 (12) | 80 (11) |
| | PN | 2 (1) | 13 (4) | | 2 (2) | | 8 (2) | | 1 (1) | 11 (7) | 3 (3) | | 11 (4) | 10 (3) | 18 (4) | 10 (4) | 20 (10) | 32 (7) | 17 (7) | 22 (7) |
| | SS | | 17 (3) | | | | | | 14 (12) | | 45 (23) | | 1 (1) | | 1 (1) | 26 (10) | 15 (5) | 15 (2) | 11 (4) | 5 (3) |
| | OR | | | 7 (5) | | 3 (2) | | 11 (3) | | 12 (5) | | 4 (3) | 10 (6) | 11 (3) | 13 (4) | 9 (2) | 29 (12) | 29 (11) | 5 (3) | 18 (5) |
| Toxicity endpoints[c] | CG | | 23 (2) | 2 (2) | 4 (1) | 13 (1) | 9 (2) | 6 (2) | 12 (1) | 12 (4) | | 26 (5) | | | | | | | | |
| | CT | 15 (3) | 22 (1) | | 41 (1) | | | 40 (1) | | 8 (4) | | 11 (1) | | | | | | | | |
| | DT | 16 (2) | 22 (1) | | 58 (4) | | 80 (4) | 40 (1) | 23 (3) | 9 (2) | | 3 (1) | | | | | | | | |
| | ED | 5 (3) | | 3 (1) | 49 (3) | 18 (3) | 82 (3) | 41 (2) | 30 (7) | | 29 (8) | | | | | | | | | |
| | IR | 28 (14) | 8 (2) | 49 (30) | 19 (6) | 36 (8) | 89 (6) | 47 (7) | 19 (16) | 35 (12) | 10 (4) | 33 (12) | | | | | | | | |
| | NT | 20 (2) | 50 (3) | 10 (5) | 45 (2) | 12 (2) | 77 (2) | 46 (3) | 1 (1) | 29 (11) | | 10 (4) | | | | | | | | |
| | PT | 38 (8) | 25 (3) | 1 (1) | | 13 (1) | 81 (2) | 1 (1) | 7 (4) | 14 (5) | | 7 (2) | | | | | | | | |
| | RT | 16 (2) | 23 (4) | | 13 (3) | 14 (2) | 89 (6) | 44 (2) | 23 (3) | 18 (4) | 5 (2) | 4 (1) | | | | | | | | |

[a]Abbreviations: AC (antimicrobial actives); CL (colorants); FG (fragrances); FR (flame retardants); PA (perservatives and antioxidants); PL (plasticizer); PO (polymers/monomers); SF (surfactants); SL (solvents); UA (UV absorbents); OT (others).

[b]Abbreviations: AF (air fresheners); AP (apparel); BC (baby and children use); BD (biocides); CA (cleaning agents); CM (cosmetics); ET (electronics); FC (food contact); FL (flooring); FT (furniture); HD (hair dyes); PC (personal care products); PN (paint); SS (sunscreen); OR (others).

[c]Abbreviations: CG (carcinogenicity); CT (cardiovascular toxicity); DT (developmental toxicity); ED (endocrine disruption); IR (irritation); NT (neurotoxicity); PT (pulmonary toxicity); RT (reproductive toxicity).

offers an opportunity to prevent possible future tragedies similar to the pulmonary fibrosis outbreak in South Korea caused by certain disinfectants in humidifiers. Progress is also being made specifically on the topic of chemicals in consumer products. Components and their weight fractions in thousands of consumer products are compiled across multiple sources and recorded in the Chemical/Product Categories Database (CPCat) (Dionisio et al., 2015). Predictive models have been developed to estimate the functional uses and weight fractions of chemicals in personal care products (Isaacs et al., 2016), and to explore alternative chemicals that would avoid becoming the unfortunate "regrettable substitutions" (Phillips et al., 2017). Systematic exposure models and frameworks dedicated to near-field consumer exposure have emerged as well (Delmaar et al., 2015; Isaacs et al., 2014; Jolliet et al., 2015). These new developments could inform Green Chemistry, which aims to design and manufacture safer chemicals to reduce the use or generation of hazardous substances (US EPA, 2013a). Successfully implementing this "safe by design" paradigm at the stage of development of chemicals in consumer products, the inherent risks to consumers could be lowered and the occurrence of regrettable substitutions could decrease.

In addition, the recently reformed Toxic Substances Control Act (TSCA) allows the U.S. EPA to more flexibly identify chemicals for in-depth reviews and relaxes the stringent requirement for U.S. EPA to hold the burden of proof that the risk of the substance in question poses is greater than its commercial benefits. The first step of risk evaluation process under the current TSCA is prioritization to identify chemicals of high-priority that should undergo the second step of more detailed reviews (U.S. EPA, 2016a). This is similar with the tiered approach taken by the Endocrine Disruptor Screening Program (US EPA, 2015). The recent developments in high-throughput toxicity and exposure techniques and predictive methodologies are poised to perform rapid screening level assessments on thousands of chemicals. These new developments will help researchers and regulators alike prioritize the chemicals for in-depth reviews and take regulatory measures before empirical evidences on human health risks are materialized.

### *4.3. Limitations of this study*

The papers collected and analyzed in this study may not cover all relevant studies conducted, especially if they were published outside the peer-reviewed journal space. This creates a potential bias in the sample of published literature, as negative studies that show no observable effects rarely get published. In addition, publicly funded researches tend to focus on the public health concerns that have already been raised by earlier researches. As a result, the peer-reviewed journal space could have a self-reinforcing trend of over-representing the chemicals with known concerns.

It should also be noted that some chemicals have multiple functional uses, while we chose the most dominant functional use for each chemical. An example is the grouping of phthalates. Despite categorized as plasticizer together in this review, several phthalates such as diethyl phthalate and dimethyl phthalate are used as solvents in personal care products and cosmetics as carriers of fragrance (Schettler, 2006).

## 5. Conclusions

Modern lifestyle relies on increasingly diverse synthetic chemicals, and consumer products often act as an interface between them and humans. These chemicals are designed and, in most cases, successfully applied to improve the quality of life, while they too may pose human health risks. We reviewed the published literature and examined how human health risks of synthetic chemicals in consumer products were reported and communicated. First, our review indicates that there is a structural issue: given that negative studies (i.e., studies that result in no observable effects) rarely get published, and that peer-reviewed publications are widely used as the primary measure of research productivity in academic and research institutions, the list of chemicals targeted by funded research tend to be biased toward the ones with known health risks. Furthermore, second, we found that the volume of the peer-reviewed literature that addresses human health risks of the chemicals in consumer products did grow over the last two decades, while its growth could by no means match the speed of increasing volume and diversity of the chemicals produced and used in consumer products by the society. This growing gap between increasing reliance on chemicals in consumer products and our knowledge on their human health risks raises a potential public health concern, given the pervasive nature of today's mass production and consumption practice.

As a result, peer-reviewed journal publications largely failed to serve as an early warning or a preventive mechanism. The humidifier disinfectant incident in South Korea is a stark example that shows the potential vulnerability in chemical exposure through consumer products and its consequences, as well as the limited role for peer-reviewed journal publications to prevent them. It also highlights the needs for understanding the risks of chemicals before putting them into consumer products, while the rapidly growing diversity of synthetic chemicals often makes the generation of necessary data cost-prohibitive. As a result, we observed that scientific literature tends to appear only after the outbreak of major exposure incidents, or they tend to be concentrated in the chemicals or chemical groups of which human health risks have been previously reported. This is a structural problem that is poised to grow under the current practice.

We believe that there is an urgent need for creating the framework conditions that encourage more exploratory and speculative risk assessments and their publications in peer-reviewed journal space in the absence of known human health risks. Reducing the costs and time needed for toxicity and exposure assessments is a key, to which the developments in predictive toxicity and risk assessment techniques for screening-level assessment, as well as the use of systematic prioritization for high-risk exposure pathways and chemicals in consumer products would be crucial.

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## Appendix A. Supplementary data

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