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# Identifying further chemicals of emerging arctic concern based on '*in silico*' screening of chemical inventories

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ABSTRACT

In the past 12 years several studies have screened lists of thousands of chemicals available in the industrial chemical inventories of the European Union, the USA and Canada with the goal of identifying and prioritizing chemicals which are persistent (P), bioaccumulative (B) and toxic (T). Most studies have selected chemicals based on whether their predicted P and B properties and their long-range transport potential exceed guideline thresholds for evaluation of persistent organic pollutants (POPs). A major goal of this study was to review this recent literature on computer-based or '*in silico*' screening for POPs. A second goal was to review other approaches for finding previously unidentified chemicals of concern including targeted and non-target analytical approaches that might use lists of suspect chemicals developed from 'in silico' screening studies. Eight studies were reviewed along with several others which examined the screening process and its uncertainties. From these studies we assembled a list of 3421 chemicals, after removing duplicates and substances already on the Stockholm Convention on POPs. About 52% of these were halogenated, while 48% consisted of a broad range of non-halogenated organics. This list was then further analysed by calculating an overall "POPs score" for transport and accumulation in the Arctic for each substance using predicted partition coefficients, overall persistence, transfer efficiency, and bioaccumulation factor. A shorter list of twenty-five substances was developed based on their POPs score ranking. These substances had not been previously analysed in environmental media but were nevertheless on current or recent chemical inventories indicating significant commercial use.



## 1. Introduction

The recent Arctic Monitoring and Assessment Program (AMAP) assessment of chemicals of emerging arctic concern included 150 individual chemicals and groups of substances reported in the arctic environment [1]. However, these data represent just a tiny fraction of the roughly 150,000 substances that have been registered for use in Europe, USA and Canada over the past 30 years, or the more than 140 million that have been assigned Chemical Abstracts Service (CAS) Registry Numbers as of September 2018 (www.cas.org/content/chemical-substances). So are there additional chemicals with Arctic accumulation potential? Here we examine several approaches to answering this question. We first review the recent literature on computer-based or '*in silico*' screening for persistent organic pollutants (POPs) as well as the literature on ocean transport, and on recent non-target analytical screening of Arctic samples. We then evaluate the POPs characteristics of a list of 3421 chemicals identified in eight previous screening studies studies and assemble a list of possible target chemicals.

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## 2. Review of '*in silico*' screening of chemical inventories

Over the past 12 years, a number of studies have addressed the question of how many of the thousands of chemicals in commerce constitute additional POPs, i.e. organic contaminants that might meet the Stockholm Convention criteria [2]. These studies can be described as '*in silico*' screening since they have been carried out by estimating environmentally relevant physical-chemical properties using Quantitative Structure Property Relationship (QSPR) models for thousands of individual compounds with known molecular structures and then identifying those compounds with predicted persistence (P), bioaccumulation (B), toxicity (T) and/or long-range transport potential (LRTP) that exceed threshold values in various regulatory guidelines [3–14]. The starting point for all of these studies are lists of chemicals in various publicly available databases developed by chemical regulators. For example, the European Inventory of Existing Chemical Substances (EINECS); the European List of Notified Chemical Substances (ELINCS); the US Toxic Substances Control Act Inventory Update Rule (TSCA-IUR); the Canadian Domestic Substances List (DSL); and the European Chemicals Agency (ECHA) list of pre-registered substances under REACH (Registration, Evaluation, Authorization and Restriction of Chemicals); as well as the database (SMILECAS) that is included with the US EPA EPI Suite program [15] (Table 1). To be listed on the TSCA, EINECS, ELINCS or REACH inventories, these substances must be produced or imported in quantities of over 1 t/y (Europe) or 4.5 to 11.6 t/y (USA). The substances included in the studies are limited mainly to neutral organic chemicals for which existing QSPR models for predicting P and B are most applicable [8,12]. Thus most organometallics, all inorganic salts, and most polymers and surfactants, were not included. Furthermore, these screening studies were focused on industrial chemicals and did not specifically target current use pesticides or pharmaceuticals, although some of these latter substances were included due to being listed on other databases, e.g. EINECS and SIMILESCAS.

Many screening studies have included consideration of long-range transport potential and whether substances might undergo deposition and accumulate in remote regions [3,5,8,10–12,14,17]. Results of these screening studies are summarized in Table 1. The criteria used for screening varied with each study but generally followed Stockholm Convention [2], USEPA [18] and/or REACH guidance [19].

Muir and Howard [3] used a database of 11,317 organic chemicals for which physical-chemical properties had been estimated as part of the categorization of the Canadian DSL [20]. They identified 28 substances with POP-like characteristics, i.e. with modeled LRTP characteristics and bioconcentration factors (BCF) exceeding the Stockholm Convention criteria (BCF >5000, atmospheric oxidation half-life (AO $t_{½}$) ≥ 2 days). Of this group, 18 were listed in the EINECS or TSCA databases (i.e. with production volumes >1 t/yr or 4.5 t/y, respectively). Howard and Muir [8] assembled a database of 22,263 chemicals based on the DSL and TSCA-IUR. This list represented chemicals in commerce in North America, with production generally >4.5 t/y during one or more inventory updates between 1992 and 2006. Using more conservative criteria than Muir and Howard [3], they identified 105 chemicals with modeled P, B and LRTP characteristics based on a log octanol-water partition coefficient (log $K_{OW}$) > 3, AO $t_{½}$ ≥ 2 days, and log air-water partition coefficient (log $K_{AW}$) > −5 and < −1.

Brown and Wania [5] screened a list of chemicals derived from the SMILECAS database for chemicals with high Arctic Contamination and Bioaccumulation Potential (AC-BAP) and POP-like properties (octanol-air partition coefficient, log $K_{OA}$ ≥ 6, log $K_{AW}$ ≥ −7 and <0.5, log $K_{OW}$ ≥ 3.5) in combination with a novel approach, based on a structural profile of known Arctic contaminants defined by halogenation, internal connectivity, and molecular size. They identified 2025 chemicals with elevated Arctic bioaccumulation potential and persistence in air. Of these, 822 matched the structural profile of known Arctic contaminants with 120 of these also found on chemical inventory lists (i.e. having high production). Harju et al. [21] applied a similar methodology to examine the Arctic accumulation potential of 21 'new' brominated flame retardants (BFRs), i.e. BFRs already commercially available as replacements for polybrominated diphenyl ethers (PBDEs). They

**Table 1**
Screening studies for chemicals on European or US/Canadian chemical inventory lists with persistence (P), bioaccumulation (B), and long-range transport potential (LRTP).

| Reference | Databases/lists used | Total chemicals initially screened | Final list for which parameters estimated | P and B | P, B and LRTP |
|---|---|---|---|---|---|
| Muir and Howard, 2006 | Environment Canada DSL[a] organics | 11,317 | 11,317 | 30 | 28 |
| Brown and Wania, 2008 | SMILECAS[b] + HPV lists[c] | 105,584 | 105,584 | 2025[d] | 120 |
| Howard and Muir, 2010 | DSL, TSCA-IUR[e] | 22,263 | 22,263 | 610 | 105 |
| Strempel et al., 2012 | EINECS, ELINCS[f] & SMILECAS | 127,281 | 94,483 | 1202 | Not determined |
| Scheringer et al., 2012 | EINECS & SMILECAS | 122,000 | 93,144 | Not determined | 510 |
| Rorije et al., 2011 | EINECS, pesticides (US/EU), pharmaceuticals (EU/WHO) | 107,337 | 64,721 | 1986 | 1171 |
| Öberg and Iqbal, 2012 | REACH[g] pre-registration | 118,285 | 48,782 | 829 | 125 |
| Gramatica et al., 2015 | Reassess results of above studies | 4412 | 3567 | 1313 | Not determined |
| | Total (duplicates removed; POPs removed)[h] | | | 3421 | 2258[i] |

[a] Domestic Substances List, Environment Canada.
[b] SMILECAS Database http://esc.syrres.com/interkow/database.htm; SMILES is an acronym for Simplified Molecular Input Line Entry System.
[c] HPV= High production volume chemicals (>454 or >1000 t annual production, depending on the list).
[d] Elevated Arctic Contamination and Bioaccumulation Potential (AC-BAP) and persistent in air;
[e] Toxic Substances Control Act (TSCA) Inventory Update.
[f] European List of Existing/Notified Chemical Substances.
[g] Registration, Evaluation, Authorization and Restriction of Chemicals pre-registration list [16].
[h] Chemicals listed on the Stockholm Convention including PCBs, PCDD/Fs, PBDEs, hexabromobiphenyls, chlorinated pesticides, along with petroleum oils, were not included.
[i] Number of substances (POPs removed) with predicted Log $K_{AW}$ > -9.0 and < 1.5, as discussed in relation to Table 2.

**Table 2**
Top 25 substances with high POP scores and intermediate log $K_{AW}$ values that are also on US and European inventory lists and have limited or no analyses in Arctic environmental media as of November 2018.

| CASRN | Name | Class | Log $K_{ow}$ | Log $K_{AW}$ | P–B-LRTP Score[a] | Arctic POP Score[b] | Overall Score[c] | TSCA[d] 2018 | TSCA[e] 1990-2006 | REACH[f] 2018 | REACH[g] Pre-reg | Source |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 369371437 | Ethane, 1,2-dichloro-1-[difluoro[1,1,2,2-tetrafluoro-2-(trifluoromethoxy)ethoxy]methoxy]-1,2,2-trifluoro- | Cl/F | 6.1 | −1.9 | 7.9 | 4.0 | 5.8 | | | | x | [11] |
| 369371426 | Ethane, 1,2-dichloro-1-[difluoro(pentafluoroethoxy)-methoxy]-1,2,2-trifluoro- | Cl/F | 5.3 | −0.6 | 7.1 | 3.2 | 5.3 | | | | x | [11] |
| 144728596 | Ethaneflulfonyl fluoride, 2(1,2-diChloro-1,2,2-trifluoroethoxy)-1,1,2,2-tetrafluoro- | Cl | 5.7 | −3.2 | 7.2 | 2.9 | 5.3 | | | x | x | [11] |
| 375451 | Flutane, 1,2,3,4-tetrachloro-1,1,2,3,4,4-hexafluoro- | Cl | 5.3 | 1.5 | 7.1 | 1.7 | 5.1 | | | x | x | [11] |
| 3064708 | Bis(trichloromethyl)sulfone | Cl | 3.1 | −6.5 | 5.6 | 2.6 | 4.5 | x | | | x | [8] |
| 354585 | 1,1,1-Trichloro-2,2,2-trifluoroethane | Cl/F | 3.1 | 0.8 | 5.5 | 2.1 | 4.4 | x | x | | x | [8] |
| 29091096 | 2,4-Dichloro-1,3-dinitro-5-(trifluoromethyl)benzene | Cl/F | 3.9 | −5.0 | 6.2 | −1.0 | 4.3 | x | x | x | x | [8] |
| 116165 | Hexachloroacetone | Cl | 2.5 | −5.6 | 5.1 | 0.8 | 4.0 | x | x | x | x | [8] |
| 1134049 | 2,3,4,5-Tetrachloro-6-(trichloromethyl)pyridine | Cl | 5.3 | −3.8 | 4.9 | 0.9 | 3.9 | x | x | | x | [13] |
| 7497087 | Bis(pentachlorophenyl) carbonate | Cl | 9.7 | −4.0 | 5.7 | −1.5 | 3.9 | x | | | | [16] |
| 2227170 | Dienochlor | Cl | 8.4 | −1.8 | 4.0 | 0.8 | 3.5 | | | | x | [10] |
| 71216041 | Carbonic acid, pentabromophenyl 2,4,6-tribromophenyl ester | Br | 10.3 | −5.9 | 4.8 | −2.3 | 3.4 | x | | | | [16] |
| 393759 | 2-Chloro-1,3-dinitro-5-(trifluoromethyl)benzene | Cl/F | 3.2 | −4.9 | 4.5 | −1.6 | 3.3 | x | x | | | [8] |
| 56480069 | 1,2,3,5,7,8-hexabromonaphthalene | Br | 8.5 | −4.3 | 4.2 | −1.7 | 3.2 | | | | x | [16] |
| 83682706 | 1,1,1,2,2,3,3-heptachlorobutane | Cl | 5.9 | −2.6 | 3.5 | 0.4 | 3.2 | | | | x | [16] |
| 52135269 | 1H-Isoindole, 1,1,3,4,5,6,7-heptachloro- | Cl | 7.5 | −4.3 | 3.4 | 0.5 | 3.2 | x | | | | [16] |
| 108770 | 2,4,6-Trichloro-*s*-triazine | Cl | 1.7 | −4.9 | 2.5 | 2.5 | 3.1 | x | x | x | x | [8] |
| 632791 | 4,5,6,7-tetrabromo-1,3-isobenzofurandione; tetrabromophthalic anhydride | Br | 5.6 | −5.4 | 3.1 | −1.0 | 2.8 | x | x | | x | [12] |
| 67990323 | bis(2,4,6-tribromophenyl) carbonate | Br | 8.6 | −5.1 | 3.8 | −3.3 | 2.7 | x | | | x | [16] |
| 37710579 | 1H-Isoindole-1,3(2H)-dione, 4,5,6,7-tetrabromo-2-(2,4,6-tribromophenyl)- | Br | 7.9 | −8.7 | 3.5 | −3.5 | 2.6 | x | | | | [16] |
| 2943706 | 1,3-bis(dichloromethyl)-1,1,3,3-tetramethyldisiloxane | Cl/Si | 6.1 | −0.9 | 1.5 | 2.0 | 2.5 | x | | | x | [11] |
| 155613937 | 1H-Indene, 2,3-dihydro-1,1,3-trimethyl-3-phenyl-, octabromo deriv. | Br | 11.8 | −7.1 | 3.7 | −4.9 | 2.4 | x | x | | x | [8] |
| 37853615 | Benzene, 1,1'-(1-methylethylidene)bis-3,5-dibromo-4-methoxy- | Br | 8.3 | −5.7 | 3.3 | −7.2 | 1.9 | x | | | x | [12] |
| 2554065 | 1,3,5,7-Tetramethyl-1,3,5,7-tetravinylcyclotetrasiloxane | Si | 8.2 | 0.3 | 1.4 | −5.0 | 1.3 | x | x | x | x | [8] |
| 70942040 | 1-Bromo-3-(4′-bromo(1,1′-biphenyl)-4-yl)-1,2,3,4-tetrahydronaphthalene | Br | 8.5 | −4.5 | 2.8 | −11.9 | 0.9 | x | | | x | [12] |

[a] "P-B-LRTP" score based on log$P_{OV}$, logBAF, and logTE from the OECD $P_{OV}$-LRTP Screening Tool [22,23].
[b] Arctic POP score calculated by summing the z-values from the Arctic POP score of Brown and Wania [5].
[c] Overall score calculated as the sum of z-scores for "P-B-LRTP" score and Arctic POP score.
[d] Based on listing in the US (TSCA) chemical inventory [28].
[e] Listed in the US TSCA inventory updates from 1990 to 2006 [8].
[f] Listing in the REACH inventory as of 2018 [27].
[g] Listed in the REACH pre-registration list [16].

identified 12 of the 21 as potentially relevant for further investigation and monitoring in the Norwegian environment.

Rorije et al. [10] identified 1171 substances with POP-like P and B characteristics (BCF or Bioaccumulation Factor (BAF) >5000, half-life in water > 1440 h, AO $t_{½} \geq 2$ d). Almost all substances on the Stockholm Convention list as of 2018 were among the 1171 except for hexabromobiphenyl. Top-ranked, in terms of LRTP, were a series of volatile per- or polyfluoroalkyl substances (PFASs). They calculated a "PB score" in order to combine both P and B properties. The P-score was based on overall persistence (Pov) estimated with the OECD Pov and LRTP Screening tool [22,23], centered around the criterion of 180 d, and scaled from 0 to 1, while the B score was based on a calculated BAF-value centered around the criterion of 5000. The PB score was the sum of the P and B scores. Rorije et al. [10] were able to calculate P and B scores for 64,721 substances and identified 1986 substances with separate P- and B-scores > 0.5 and listed 250 substances with combined PB scores ≥ 1.79 in their report.

Lambert et al. [24] identified 15 chemicals as potential POPs with Arctic accumulation potential by reviewing the literature on monitoring studies for the Arctic and Antarctic published between 2005 and September 2011. The review yielded a list of 84 chemicals detected in remote regions, not including POPs already on the Stockholm Convention. Then data for the persistence, bioaccumulation, long-range transport potential, and adverse effects (eco- and mammalian toxicity) of the compounds were identified. The chemicals were selected through a scoring system and by use of the data for 250 most persistent and bioaccumulative chemicals reported by Rorije et al. [10]. All 15 have been included in lists of other screening studies (Table 1).

Strempel et al. [12] identified 1202 substances that were potentially very persistent and very bioaccumulative (vPvB). Although they did not estimate LRTP, their list is also useful in the context of Arctic contamination because most of the chemicals were at one time in commerce in Europe (i.e. on EINECS which included chemicals in production as of 1981). Of the 1202 substances, 130 were also identified by Brown and Wania [5]. In a related study, Scheringer et al. [17] screened a group of 94,483 substances and identified 510 chemicals with potential POP-like properties that had not been evaluated as potential POPs under the Stockholm Convention at the time of publication. This latter study is also described in a technical report prepared for the German Environment Agency [25]. Many of the compounds are well-known halogenated aromatics (polychlorinated naphthalenes (PCNs); PBDEs; chlorobenzenes), however, other groups with possible POP-like characteristics included triazines with fluorinated or chlorinated substituents, perfluorinated alkanes and perfluorinated alkyl ethers (linear, branched, and cyclic) and 1,3-

dichloro-6-(trifluoromethyl)-phenanthrene-9-carbonyl chloride (CAS 94133-67-2). Of the 510 compounds, 193 were defined as "very POP" by the authors (biodegradation half-life in water > 180 d, BAF > 20,000, and a half-life in air >10 days). Ten of the 510 substances were high production volume chemicals (HPVs), with production or use in Europe of >1000 t/y and so more likely to be detectable in remote locations. In addition to developing a list of chemicals with POP-like properties, Scheringer et al. [17] also reviewed the lists of Öberg and Iqbal, Rorije and co-workers, and Howard and Muir. Their comparison was used as the starting point for a list published in the AMAP assessment on chemicals of emerging arctic concern [1].

Öberg and Iqbal [11] screened chemicals on the ECHA pre-registration list for REACH. They selected 48,782 neutral organic chemicals for detailed screening based on the applicability domain of QSPR estimation models. Similar to Rorije et al. [10] they used $P_{OV}$ and LRTP calculated with the OECD $P_{OV}$ and LRTP Tool [22,23]. They used threshold values of 195 days for $P_{OV}$ and a Characteristic Travel Distance (CTD) > 5097 km, which is the CTD of 2,4,4′-trichlorobiphenyl (CB28). They identified 68 neutral organic chemicals on the REACH preregistration list as potential POPs, many of which were known or candidate POPs at the time of the study, for example PCNs, polychlorinated biphenyls (PCBs), or identified in studies by Scheringer et al. [17], Strempel et al. [12] and Rorije et al. [10] because the substances were also in EINECS.

Gramatica et al. [13] used a PBT Index, that was originally derived from a Principal Component Analysis of available experimental data of half-lives, bioconcentration, and aquatic toxicity data for 180 representative non-PBT and PBT chemicals, and modeled by simple molecular descriptors (e.g. number of halogen atoms, number of multiple bonds etc.), to assess the results from most of the studies listed in Table 1. The combined list was 4412 substances. After screening with the PBT Index model they identified 1313 substances meeting PBT criteria.

Reppas-Chrysovitsinos et al. [26] evaluated 464 individual chemicals mentioned in the AMAP report on chemicals of emerging arctic concern [1]. Using a similar scoring approach as Rorije et al. [10], they identified substances using a POPs Score ($S_{POP}$) which was the product of BAF from EPI Suite's BCFBAF Quantitative Structure Activity Relationship (QSAR) [15] and Overall Persistence (Pov), and transfer efficiency (TE) from the OECD Pov-LRTP Screening Tool [22,23]. They found that 44%, mainly polychlorinated diphenyl ethers and PCNs, were identified as having high $S_{POP}$ values, similar to known POPs. Other chemicals identified as having high $S_{POP}$ were undecachloropentacyclooctadecadiene (a mirex derivative), the dechloranes 602, 603, 604, and perfluoroalkyl substances including perfluorooctanesulfonamide and perfluorobutane sulfonamide.

The combined list of chemicals identified by all studies in Table 1 contains 3421 substances after removing the POPs listed on the Stockholm Convention (consisting of about 360 CAS RNs for PCDD/F and PCB, PCN, hexabromobiphenyl, PBDE congeners, and organochlorine pesticides) as well as petroleum distillates. Depending on the study, 1.3–3.1% of chemicals that were screened were P and B under REACH criteria and 0.1–1.8% were P, B and LRTP by Stockholm Convention criteria. The 3421 substances meeting P and B criteria can be roughly categorized into eight classes; brominated, chlorinated, fluorinated compounds, organophosphate esters, siloxanes, musks, polycyclic aromatics, and a broad class of other non-halogenated organics (Fig. 1). The full list is provided in Supporting Information (Table S1). Of the 3421 substances, 253 were also on the REACH inventory available as of November 2018 (16755 substances with CAS RNs) so had been subject to recent evaluation and registration [27]. Also 1138 were in the TSCA inventory of 67951 publicly available CAS RNs [28].

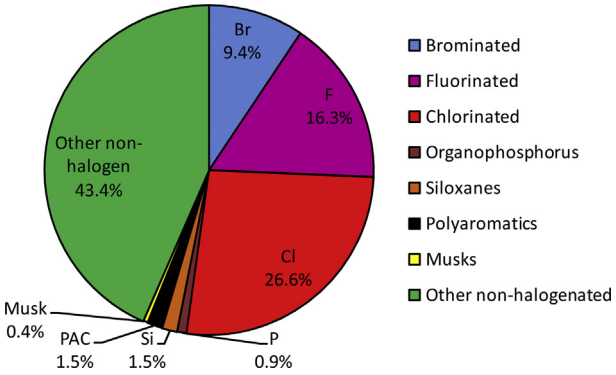


**Fig. 1.** Broad classes of the 3421 chemicals with POP-like properties identified by the eight screening studies listed in Table 1 after removing duplicates and known POPs. A similar figure based on 3743 chemicals (including some POPs) appears in Chapter 4 of the recent AMAP assessment of chemicals of emerging arctic concern [1].

## 3. Review of long-range transport potential in oceans

Identifying P and B chemicals that may undergo long-range transport via oceans is challenging because screening criteria are influenced by the selection of water flow velocities in rivers and ocean currents. Some POPs are known to be preferentially transported in ocean waters and this has been confirmed for perfluorooctane sulfonate (PFOS) [29,30] and β-hexachlorocyclohexane (β-HCH) [31]. Gouin and Wania [32] used a zonally averaged global distribution model to estimate the time it would take for organic contaminant concentrations to decline in Arctic Ocean waters after global emissions have been reduced due to regulatory measures. They concluded that "swimmers", i.e. persistent water soluble chemicals that reach the Arctic by slow long-range oceanic transport, would need to have a half-life in water of more than 10 years for a significant lag in their response to declining emissions to occur. Chemicals in this category would be PFOS and perfluorocarboxylates. They also noted that "multimedia hoppers" that exchanged with ocean water and with air, and were slow to degrade e.g. perfluorinated alcohols (e.g. perfluoropropanol), would also have high Arctic Contamination Potential due to continued exchange with water and terrestrial surfaces.

Modelling ocean transport of PFOS, chlordecone and lindane by Zarfl et al. [33] showed a significantly higher mass fraction in water at steady-state than in air. However, the authors noted that partitioning into water is not sufficient by itself to make transport in the water compartment the dominant route. They noted that long travel CTD in water was predicted only for chemicals with a long half-life in water and a low $K_{AW}$. Zarfl et al. [33] applied the ELPOS model [34,35] to calculate the CTD for water transport. This model is a simplified version of the regional-scale model of EUSES-SimpleBox, which is legally accepted for chemical assessment in the European Union [36]. The results revealed that, among the Stockholm Convention list of POPs, only the highly soluble PFOS has a higher CTD in water ($CTD_W$) than in air. Zarfl et al. [33] also suggested the use of the ratio of the CTD in air ($CTD_A$) to $CTD_W$ to compare chemicals according to their LRTP properties, since the results obtained for the CTD are independent of emission rates. They applied their model to the Canadian DSL list of neutral organic chemicals (11,317 substances) and found that 38% of compounds had a higher $CTD_W$ than $CTD_A$. Reppas-Chrysovitsinos et al. [26] calculated exposure-based hazard profiles for waterborne persistent contaminants (WPCs) for 464 chemicals in the AMAP report on chemicals of emerging arctic concern [1] and assumed global scale

distribution by oceanic transport. Their score $S_{WPC}$ was the product of Pov and $CTD_W$ from the OECD Tool. They obtained high scores for relatively polar compounds including bendroflumethiazide (CAS 73-48-3), pentabromobenzyl acrylate (CAS 59447-55-1), 2,2-bis(chloromethyl)-1,3-propanediyl tetrakis(2-chloroethyl) bis(phosphate) (CAS 38051-10-4), and 1,2,4,5-tetrabromo-3,6-dimethylbenzene (CAS 23488-38-2). These substances had relatively low scores for atmospheric transport using a similar scoring system (Pov and $CTD_A$).

Arp et al. [37] screened a list of neutral, ionizable and ionic industrial organic compounds in the REACH inventory for their potential to be persistent and mobile organic compounds (PMOCs). They applied screening criteria to 5155 unique parents and their hydrolysis products (5043 additional structures). A PMOC score was calculated based on mobility and persistency categories. Fifty-two percent of the parent structures and 56% of the hydrolysis products were considered PMOCs. In a follow-up study, a qualitative emission score model was applied to the high scoring chemicals (PMOC = 4-5) reported by Arp et al. [37], based on the tonnage placed on the European market and on seven emission-related use characteristics [38]. This demonstrated that about 50% of the substances would likely be released to the environment. Although not directly related to ocean transport, this screening study illustrates that there may be a large number of chemicals in commerce with potential to enter surface waters and be transported in rivers and ultimately in ocean currents, and to be sufficiently persistent for long-range transport.

In addition to transport of chemicals dissolved in water, the possibility of transport on microplastic particles has been discussed by Zarfl and Matthies [39]. They noted that, besides sorption of hydrophobic chemicals from seawater, plastic polymers contain additives that might otherwise not undergo ocean or atmospheric transport, such as colorants, UV-stabilizers and matting agents, flame retardants, phthalates, bisphenol-A and anti-microbial agents [40]. Zarfl and Matthies [39] concluded that on a mass basis, transport on plastics would be four to six orders of magnitude smaller than atmospheric or seawater currents. Ocean transport of chemicals to the Arctic on microplastics has also been discussed in the AMAP assessment on chemicals of emerging arctic concern [1].

## 4. Review of analytical screening studies for arctic contaminants

While the screening of lists of chemicals in commerce is a good starting point to identify potential Arctic contaminants, it does not provide empirical evidence of P, B and LRTP. The decision on which chemicals to include in monitoring programs and/or analytical screening studies is still very challenging given limited information on uses and physical-chemical properties, as well as lack of analytical standards with which to validate methods. Targeted and non-targeted approaches specific to measurements in the Arctic environment are now briefly discussed.

### 4.1. Targeted approaches

Targeted screening refers to studies that identify contaminants of emerging concern (CECs) using reference standards as well as 'suspect' screening for substances of known molecular weight, but without a standard, that may have been identified by *in silico* screening approaches. The Northern Contaminants Program in Canada (http://www.science.gc.ca/eic/site/063.nsf/eng/h_7A463DBA.html) and the contaminant monitoring programme in Greenland (AMAP Core Programme) include sub-programs on "new or emerging contaminants", which address less-studied compounds (e.g. Refs. [41,42]). A series of reports by the Nordic Council of Ministers have reported on a wide range of chemicals in consumer products in Scandinavian countries including the Faroe Islands, Iceland and Greenland (http://nordicscreening.org/). Priority is generally given to substances used in high volumes or that are likely to be environmentally persistent and hazardous to humans and other organisms. Results from these studies, which included measurements of PFASs, BFRs, phosphorus flame retardants (PFRs), phthalates and siloxanes are cited in the AMAP assessment on chemicals of emerging arctic concern [1]. The Norwegian Environment Agency has also supported a series of targeted screening studies to determine CECs in the Arctic environment [43–48]. Several of these have used a list of priority chemicals established by Harju et al. [21] as well as expert judgement to establish targets. Gebbink et al. [49] took a similar targeted approach to determine previously unidentified PFASs in marine mammals from Greenland. Shen et al. [50] used a 'suspect' screening approach to identify two novel dechlorination products of Dechlorane 602 in beluga (*Delphinapterus leucas*) blubber using gas chromatography (GC) and very high resolution mass spectrometry (MS). Schlabach et al. [51] targeted a series of compounds listed as possible priorities in the AMAP report on chemicals of emerging arctic concern [1] using GC-HRMS and detected a series of fluorinated and chloro/fluoro compounds including perfluoroperhydrophenanthrene (PFPHP), tris(perfluorobutyl)-amine (PFTBA), 1,2,3,4-tetrachlorohexafluorobutane (TCHFB), and 3,5-dichloro-2,4,6-trifluoropyridine (DCTFP), in arctic air for the first time. Therefore, there appears to be growing use of 'suspect' screening using information from lists of priority substances in Arctic environmental samples.

### 4.2. Non-targeted approaches

A relatively new approach is non-target screening which uses HR-MS coupled to 1- or 2-dimensional gas chromatography (GC or GC×GC) or liquid chromatography (LC) to search for chemicals in environmental extracts [51–53]. It involves processing of instrumental data to search for complete unknowns starting from the exact mass, isotope, adduct, and fragmentation information. Schlabach [52] analysed air samples from a remote site in Norway (Birkenes) and identified 'suspect' unknowns using GC×GC-MS, GC-HRMS and LC-HRMS. The non-target analysis detected many polymer additives including phthalates and one adipate, three organophosphates, polymer antioxidants, fungicides, pharmaceuticals, and unknown fluorinated compounds. Routti et al. [54] used non-target approaches with LC-HRMS to screen for unknowns in polar bear adipose and identified phthalates, tonalide and nonylphenol. Schlabach et al. [51] analysed extracts from the Nordic screening program, including air and biota from Svalbard, by GC-HRMS and detected an average of 123 components in air and 84 in polar bear fat. Most components could not be identified although hexachlorobutadiene (HCBD), a relatively well known contaminant, was present in most samples (See Balmer et al. [55] for further information on HCBD in the Arctic). Schlabach et al. [51] also screened the same sample extracts by LC-HRMS and found each sample to contain approximately 8000 mass spectral "features" but were unable to identify them although they did note that chlorinated compounds could be observed when using Van Krevelen diagrams and mass defect plots [56].

Liu et al. [57] detected three new classes of per/polyfluorosulfonic acids (PFSAs) in pooled polar bear plasma from the Canadian Arctic using a non-targeted LC-HRMS method. One group were cyclic or unsaturated PFSAs indicating a ring or double-bond in the core structures. A second group had unique $[C_2F_5O]^-$ ions and were characterized by the simultaneous detection of PFSA-specific ions (e.g. $[SO_3]^-$ and $[SO_3F]^-$ while a third group included

unsaturated ether-, cyclic ether-, or carbonyl-PFSAs. Liu et al. [57] also detected x:2 chlorine-substituted perfluoroalkyl ether sulfonates including F–53B previously reported by Gebbink et al. [49] in polar bear liver. In addition to the polyfluoroalkyl compounds, Liu et al. [56] also identified a series of novel PCB metabolites in polar bear plasma including more than 50 PCB-sulfates and >40 OH-PCB-sulfate congeners, hydroxylated $SO_2CH_3$-PCBs >40 congeners) and >20 dihydroxylated $SO_2CH_3$-PCBs. Given the rapid developments in the non-target analysis field [58] the lists of chemicals with Arctic accumulation potential in this and other studies will provide analysts with plenty of 'suspects' to try to identify.

## 5. Further prioritization of the substances in terms of arctic accumulation potential

### 5.1. Methodological approach

SMILES were assigned for all 3421 chemicals identified in Table 1. Physical-chemical properties, partition coefficients ($K_{OW}$, $K_{AW}$ and $K_{OA}$) and BAFs were calculated with EPI Suite [15]. Overall persistence (Pov) and transfer efficiency (TE) were calculated with the OECD Pov-LRTP Screening Tool [22,23]. The P-B-LRTP score we derived is slightly different from Reppas-Chrysovitsinos et al. [26] who derived a POP score as the product of Pov, BAF and TE. Considering the values and distributions of these three POP indicators, we derived the P-B-LRTP score as the sum of z-scores for logPov, logBAF, and logTE. The log-transformation and scaling help eliminate the influence of any extreme value for one of the indicators on the score. In addition to the P-B-LRTP score, we also calculated the Arctic POP score, which was developed by Brown and Wania [5] based on chemical structural features (numbers, types and connections of atoms and bonds) of known Arctic POPs. Their POP score indicates how closely a chemical matches the profile of known Arctic contaminants. The P-B-LRTP scores and the Arctic POP scores were combined and used for ranking of the chemicals according to equation (1) (Table S1).

$$\text{Overall score} = \text{z-score(P-B-LRTP score)} + \text{z-score(Arctic POP score)} \quad (1)$$

### 5.2. Results of POPs score profiling and ranking

Results for all substances are provided in the Supplementary Material (Table S1 and Figs. S1 and S2). These chemicals cover a broader area on the $K_{OA}$~ $K_{AW}$ chemical space than the region where chemicals have elevated Arctic Contamination and Bioaccumulation Potential (AC-BAP) determined by Brown and Wania [5] via model simulations of chemicals emitted in mid-latitude and accumulated in Arctic human food web (Fig. S2). We have widened the $K_{OA}$-$K_{AW}$ space to capture a wider range of chemicals that were on chemical inventories. The chemicals to the upper left of the elevated AC-BAP region are highly volatile. Their high overall scores are driven by their persistence and long-range transport potential but they have lower tendency to reach Arctic surfaces where they could be accumulated in the local food web, and thus do not show elevated AC-BAP. Some chemicals with overall scores are located to the lower right of the elevated AC-BAP region (Fig. S2). They have log $K_{OW}$ higher than 10 which makes them less likely to undergo bioaccumulation.

Not surprisingly, given that the eight studies in Table 1 were focusing on P, B and LRTP in most cases, 2258 substances within the larger list could be categorized as having atmospheric LRTP based on predicted log $K_{AW} \geq -9$ and $\leq 1.5$. From the 2258, 25 with high POPs scores were selected (Table 2). This was done by first confirming which substances were on the US and European chemical inventories. Of the 2258, the greatest number were in the REACH pre-registration list (1071) while 681 were in the TSCA inventory. The top 25 were then selected based on presence in those two inventories although listings on earlier versions of the TSCA inventory and on the REACH list of registered substances (to December 2018) was also checked (Table 2). Most (24/25) were halogenated with chlorinated compounds predominating (14/25). Chemicals reported to be used as intermediates (i.e. within a manufacturing process) were excluded, on the assumption that releases would be small although this assumption may not be correct. However, this information was generally available only for a small number of substances on the REACH inventory of registered substances [27]. Table 2 is not a priority list, but is intended to show that chemical inventories contain many substances with POP-like characteristics. As of November 2018, these chemicals had not been included in Arctic monitoring programs to our knowledge.

Bänsch-Baltruschat et al. [14] have commented on the challenges on taking chemical lists such as Table 2 further to recommend risk assessments and/or further monitoring. They extended the studies of Blepp et al. [25] by evaluating a list of 17 chemicals prioritized by Lambert et al. [24] as well as other chemicals identified as potential POPs based on expert judgement and two studies on P and B substances conducted by the German Environment Agency [59,60]. They noted that relevant data for QSPR screening were typically not readily available for most substances that were predicted to have POP-like properties, such as pentachlorothiophenol and tetrachlorobenzenes. They concluded that monitoring in remote regions such as the Arctic was needed to confirm the LRTP and bioaccumulation of newly identified POP candidates, including monitoring in biota and in air and including non-target-screening.

## 6. Uncertainties in identifying additional chemicals of emerging concern

### 6.1. Methodological issues and information sources

The results in Table 2 and Table S1 show that chemical inventories in Europe and North America contain many substances that have POP-like characteristics even after recent updates. Strempel et al. [12] found that 5.2% of chemicals registered between 1982 and 2007 in the ELINCS had PBT characteristics (they did not include LRTP characteristics). Their results also suggest that when substances are banned or phased out by national or global regulation there are typically many potential replacements among lists of existing, registered chemicals. However, as noted previously 253 of the 3421 substances were also on the current REACH (2018) inventory. Also 1138 are on the US EPA TSCA list [28], and 279 were on the USEPA Chemical Data Reporting list, which includes 8700 substances in active use (manufacture or import) in the US as of 2016 [61]. In the case of PBDEs, for example, they were substituted by many brominated and phosphorus flame retardants with highly varied molecular structures which were in existing chemical inventory lists [62,63]. A good working methodology that takes into account the potential POP-like properties of replacement chemicals is not yet in place. In the Stockholm Convention assessment process, substitutes or alternative chemicals are briefly discussed in Risk Management Evaluations (e.g. see Stockholm Convention [64] for technical octabromodiphenyl ether substitutes). Alternative assessments for identifying, comparing and selecting safer alternatives to chemicals of concern is an emerging area of science and policy [65]. A framework for improved chemical substitution was recently proposed by the U.S. National Research Council [66] and

best practices have been reviewed by the OECD [67] but these approaches have not yet been adopted by chemical risk assessment agencies.

To date, peer reviewed studies related to screening of lists of chemicals in commerce for POP-like characteristics have used the chemical inventories of the USA, Canada and Europe. Chemical inventories exist for many other countries [68]. For example, the Chinese Inventory of Existing Chemical Substances (IECSC) has 45,600 substances, and the Japanese Existing and New Chemical Substances Inventory (ENCS) has about 26,000. A recent report of a chlorinated polyfluoro ether sulfonic acid, 6:2-Cl-PFAES, in Arctic biota [49], is an illustration of the need for knowledge about chemical use in Asian countries that are major producers of synthetic organic chemicals. China is apparently the only country with documented usage of this PFAES [69].

*'In silico'* screening studies for chemicals with POP-like characteristics have mainly focused on registered chemicals rather than on degradation products. Yet degradation or transformation products may be more persistent and bioaccumulative. The anisoles, for example pentachloroanisole, are one such example. These degradation products of phenols, which also have possible natural sources [70], have no commercial applications, so are absent on any of the lists. Chemicals with perfluoroalkyl chains, such as the fluorotelomer alcohols or halo-perfluoroalkanes predominate on some lists of chemicals that have LRTP in the atmosphere [10,17]. However, most are likely to degrade to perfluorocarboxylates [71]. Thus, monitoring of the degradation products in the Arctic may be more important for many fluorinated substances.

### 6.2. Uncertainties in parameter estimates

*'In-silico'* based chemical screening results are subject to uncertainty from different sources [72]. The P-B-LRTP score is derived from model-predicted Pov, BAF and TE. Similar to other model predictions, uncertainty of the model-derived P-B-LRTP scores comes from three sources: (1) Chemical properties ($\log K_{OW}$, $\log K_{AW}$, degradation half-lives in air, water and soil) used as input of the model; (2) Environmental characteristics (e.g. volume of different phases). Environmental parameters differ from location to location but in model simulations fixed environmental parameters for a representative environment are used; (3) Model structure. A model to simulate environmental fate and hazards is a simplification of the real environment (e.g. representing global air, water and soil with one compartment each). Uncertainties originating from environmental parameters and model structures apply to all chemicals but are difficult to characterize unless by comparing with environmental monitoring data. The Arctic POP score is based on chemical structures of known chemicals detected in the Arctic environment [5]. It serves as a guide to look for chemicals with a high probability to reach the Arctic. Brown and Wania [5] discussed research needs which would reduce uncertainties of the Arctic POP score such as verification of the physical-chemical property data, improved measures of biotransformation and adjustment of model thresholds for partitioning and atmospheric oxidation.

Here, we analyze the uncertainty of the P-B-LRTP scores propagated from the uncertainty of model input parameters while noting that uncertainty of the results also comes from environmental parameters and the model structure, which can hardly be characterized. As described by MacLeod et al. [72], confidence factors are used to describe uncertainty of input parameters. Similar to MacLeod et al. [72], we used confidence factors of 1.1 for $\log K_{OW}$, 1.5 for $\log K_{OA}$, 2.0 for BAF and 3.0 for reaction half-lives in air water and soil. The chemical 2,2′,3,4,4′,5,5′-heptachlorodiphenyl ether (CASRN: 83992-69-2) has a P-B-LRTP score at the 95 percentile of the scores for all the chemicals and it was selected for uncertainty evaluation. Monte Carlo simulation was conducted by sampling 10,000 times from distributions of these parameters, i.e. P-B-LRTP scores were derived for these 10,000 combinations of input parameters. Distributions of model input, output and derived P-B-LRTP score are shown in Fig. S3. Without considering uncertainty and using a single value of each input parameter, the P-B-LRTP score is 3.58. When considering uncertainty propagation as revealed from the Monte Carlo simulation, the P-B-LRTP score ranges from 2.33 to 4.20. The P-B-LRTP scores of 189 chemicals (5.5% of all the evaluated chemicals) are within this range. These chemicals deserve attention if the prioritization criterion is set to the value of 95 percentile. Although these additional 189 chemicals possibly have the same P-B-LRTP scores as the chemicals at the 95 percentile, the probability is directly related to the difference between two scores. This is the advantage of having a scoring system in which values follow a normal distribution.

Strempel et al. [12] estimated uncertainty factors of predicted chemical properties: 4-fold for half-lives and for BCF, and 3.5 for $K_{OW}$. Thus their initial estimate of 2930 actually ranged from 153 to 12,493 chemicals classified as potential PBTs. Similar uncertainties apply to the study by Scheringer et al. [17] where a range of 190–1200 chemicals with POP-like characteristics was estimated.

Another problem is the 'street-light effect' whereby only chemicals that are similar to well-characterized existing substances are identified due to the use of QSPR models that are 'trained' with (incomplete, possibly non-representative) measurements of physical-chemical properties. Most studies to date have relied on the same suite of models based on the USEPA EPI Suite software [15], although other approaches using molecular descriptors have also been employed, especially for identifying PBT chemicals [9,13]. These approaches are best suited for identifying neutral organics. Thus while substances with phenolic, sulfonic and carboxylic acid moieties have been included in most studies (as neutral forms), most inorganics and organometallic compounds have been left out. Although substances that are ionized at environmentally relevant pH are unlikely to be transported in the atmosphere, except on particles, they could undergo transport via ocean currents. It has been estimated that 50% of the chemicals on the REACH preregistration list are ionogenic i.e. acids, bases, or zwitterionics [73]. In their study of aquatic persistency and mobility, Arp et al. [37] found that of 5155 organic chemicals on the REACH inventory 41.1% were ionizable and 8.4% classified as ionic. The categorization of the Canadian DSL showed that 10%, or about 2300 of 23,000 compounds, were inorganic, organometallics and organic-metal salts [74]. Future assessments should consider ionogenic compounds more thoroughly and especially their potential for transport in ocean currents or on particles due to particular use patterns and persistence.

UVCBs (Unknown and Variable composition, Complex reaction products and Biologicals) represent another challenge for assessments of chemicals in commerce with Arctic accumulation potential. The DSL categorization identified 20% of substances as UVCBs [74]. Included in this group are well-known substances such as the chlorinated paraffins, which are characterized by chain length and chlorine content, but generally not by individual congeners. Representative components can often be used for UVCB assessment [75].

It is important to note that this study has not explicitly considered toxicity or potential for adverse effects, which are among the criteria for defining POPs characteristics. However, three of the screening studies listed in Table 1 did include toxicity [11,12,17]. All three used aquatic toxicity predicted by ECOSAR, the EPI Suite QSAR [15], and toxicity thresholds defined under REACH regulations [76]. Predicted toxicity was then used to help identify and assess which substances should be priorities. As Scheringer

et al. [17] have noted, it is challenging to include toxicity in a screening study on POPs because no quantitative criteria are defined under the Stockholm Convention. Furthermore, ECOSAR, the most widely used QSAR for baseline aquatic toxicity, mainly derives estimates from the $K_{OW}$ and may not perform well for chemicals with specific modes of action [12]. In their uncertainty analysis, Strempel et al. [12] found uncertainty factors of 100 for chronic (aquatic) toxicity and 45 for acute toxicity, far higher than the factor of 4 that they estimated for BCF.

## 7. Conclusions/recommendations

Screening for chemical inventories in Europe and North America has shown them to contain many chemicals in commerce with POP-like characteristics. Exact numbers are difficult to estimate due to uncertainties in the information on physical-chemical properties and model domains. The combined total from eight recent studies was 3421 when including all identified as P and B. Scheringer et al. [17] estimated the range for substances with a combination of POP-like characteristics for persistence, bioaccumulation and long-range transport potential to be from 190 to 1200 chemicals, while here we estimated 2258 substances had atmospheric LRTP based only on air-water partitioning (log $K_{AW} \geq -9$ and <1.5). Further screening of inventories particularly those for China and Japan would be useful to provide a global picture of the production of chemicals with POP-like characteristics.

Screening studies for chemicals with POP-like characteristics have mainly focused on registered chemicals rather than on degradation products. Further screening for degradation products of chemicals in commerce for POP-like characteristics would be worthwhile given the many examples of degradation products detected in Arctic environmental media.

Some POPs are known to be preferentially transported in ocean waters and screening of a large list of neutral organic chemicals (11,317 substances) as well as 464 substances previously detected in the Arctic showed that a significant proportion could undergo ocean transport. Further screening for chemicals with POP-like characteristics and potential for ocean transport would be worthwhile given the high proportion of chemicals identified in initial screening.

Non-target screening for chemicals in Arctic samples has revealed some previously unidentified chemicals and has potential, especially when combined with lists of substances identified by *in silico* screening to widen the number of CECs identified in the Arctic. Further non-target screening for chemicals with POP-like characteristics should be conducted using priority lists developed by recent peer-reviewed studies.

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*Conflicts of interest*

The authors declare no conflicts of interest.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.emcon.2019.05.005.

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