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Epistemology of contaminants of emerging concern and literature meta-analysis

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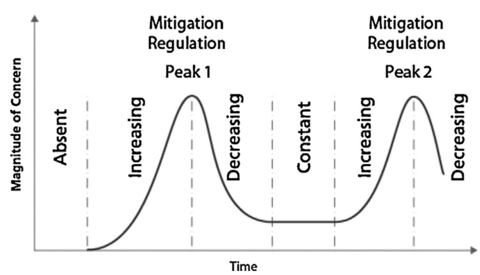
HIGHLIGHTS

- Meta-analysis of 143,000 papers reveals common pattern of emergence of contaminants.
- CECs emerge from obscurity to height of concern over a period of 14.1 ± 3.6 years.
- It typically takes 14.5 ± 4.5 years for a CEC to descend from the peak of concern to a new, lower baseline level.
- Regulatory actions are shown to play an important role in managing concern over contaminants.

GRAPHICAL ABSTRACT



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ABSTRACT

A meta-analysis was conducted to inform the epistemology, or theory of knowledge, of contaminants of emerging concern (CECs). The CEC terminology acknowledges the existence of harmful environmental agents whose identities, occurrences, hazards, and effects are not sufficiently understood. Here, data on publishing activity were analyzed for 12 CECs, revealing a common pattern of emergence, suitable for identifying past years of peak concern and forecasting future ones: dichlorodiphenyltrichloroethane (DDT; 1972, 2008), trichloroacetic acid (TCAA; 1972, 2009), nitrosodimethylamine (1984), methyl *tert*-butyl ether (2001), trichloroethylene (2005), perchlorate (2006), 1,4-dioxane (2009), prions (2009), triclocarban (2010), triclosan (2012), nanomaterials (by 2016), and microplastics (2022 ± 4). CECs were found to emerge from obscurity to the height of concern in 14.1 ± 3.6 years, and subside to a new baseline level of concern in 14.5 ± 4.5 years. CECs can emerge more than once (*e.g.*, TCAA, DDT) and the multifactorial process of emergence may be driven by inception of novel scientific methods (*e.g.*, ion chromatography, mass spectrometry and nanometrology), scientific paradigm shifts (discovery of infectious proteins), and the development, marketing and mass consumption of novel products (antimicrobial personal care products, microplastics and nanomaterials). Publishing activity and U.S. regulatory actions were correlated for several CECs investigated.

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1. Introduction

Harmful biological, chemical and physical agents represent a threat to humans, animals, plants, and microorganisms as well as to the totality of all ecosystems and eco-services humanity relies on. Environmental stress is a constant companion of all life. However, with the industrialization of the world, the number and sources of environmental stress have rapidly increased for both humans and wildlife. Over half of all diseases afflicting humanity are thought to be influenced directly or indirectly by environmental factors. And among the large spectrum of known pollutants, contaminants of emerging concern are considered one important group contributing to environmental diseases of uncertain etiology [1].

The term *contaminants of emerging concern* or CECs, has been in wider use since the early 2000s [2], and has gained popularity over the terminology "*emerging contaminants*." The latter word suggests the need for the discovery of a new agent of concern, when indeed all that is required is a change in the view of the risks posed by a given substance, irrespective of whether it is newly discovered or has already been known to exist for some time. The term CEC has been defined appropriately as: "*A chemical for which there are increasing concerns regarding its potential risks to humans and ecological systems, including endocrine disruption and neurotoxicity*," while adding the qualifying statement that "*Within the broad category of CECs monitored, however, agencies have widely different definitions as to what a CEC actually is*" [3].

As knowledge of environmental hazards increases, so does the count of specific, harmful CECs, which currently are estimated at a total of more than 40,000 substances, with an estimated six new compounds of CEC potential being added to the chemical inventory of the world every day [3].

Intuitively, one may postulate a course of knowledge generation for CECs progressing through multiple, distinct stages (Fig. 1), *i.e.*, (a) absence of concern due to ignorance of a potential hazard or risk; (b) increase in concern upon realization of a potential threat or knowledge gap; (c) initial height or peak of concern; (d) decrease in concern as a result of accumulating knowledge and risk management strategies, including behavioral changes, exposure control, voluntary phase-out of substances and regulatory actions taken; (e) establishment of a new baseline of residual concern; (f) potential renewed increase in concern possibly due to novel adverse effects observed; (g) second peak of concern; (h) decrease to a new baseline level of concern and so on.

The term *concern* in the CEC moniker is subject to interpretation and may mean different things such as *interest*, *importance* or *cause of anxiety*; all of these interpretations have in common that they are difficult to measure objectively. However, regardless of the nature of *concern*, the latter almost certainly will trigger an elevated activity in scientific research. Thus, research activity may serve as a proxy to track and quantify *concern* regarding specific contaminants. This approach was adopted in the present study, as it promises both convenient access to relevant data and a low risk of study bias, due to reliance on rigorously maintained scientific databases.

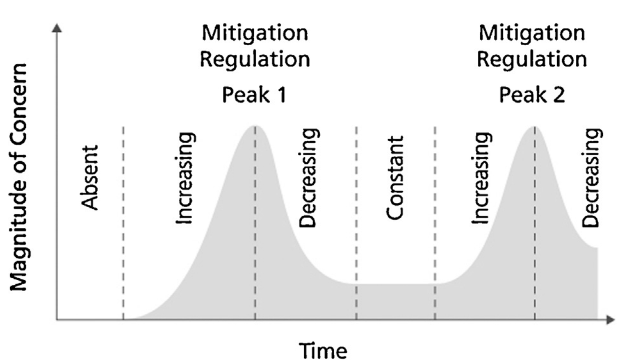

Fig. 1. Hypothesized time course and stages of the emergence of contaminants of concern.

The present meta-analysis of the scientific literature was designed to elucidate the process of CEC emergence and to determine over what timeframe CECs emerge as a threat, and what factors are responsible for triggering their emergence. This work was carried out to better understand past emergences of chemicals and to predict future ones from available data. Twelve case studies were chosen and examined for commonalities and differences in CEC emergence. The selection process was guided by: (i) the need to include substances whose combined emergence histories covered a sufficiently broad time interval of at least four decades; (ii) evidence of public health importance of the substances; (iii) representation of a spectrum of chemical compositions and properties. The agents selected and discussed in the following represent a convenience sample, reflecting these qualities. They include chemical compounds and biological materials that have received extensive attention in scientific journals and the news media alike.

2. Time course of CEC emergence

Although common trends of CEC emergence have been speculated to exist [4], yet unanswered questions regarding the epistemology of CECs include:

- How long does the process of CEC emergence take?
- Upon CEC emergence, how long does it take for concern to subside to a lower baseline?
- Can one and the same CEC emerge repeatedly, as suggested in the hypothetical scenario shown in Fig. 1?
- Does the emergence of CECs follow a distinct temporal pattern?

Identifying and characterizing an inherent pattern of CEC emergence would be quite valuable for conceptualizing the ongoing emergence of CECs. If CEC emergence and subsidence indeed are occurring along a common timeline, this may enable one to forecast future developments, *e.g.*, predict future years of peak concern for currently emerging CECs. Such insights into the periodicity of scientific progress have proven beneficial in other scientific disciplines, where for example, Moore's realization in 1965 [5] of the constant rate of miniaturization of microprocessors (known as *Moore's Law*), has enabled fairly accurate forecasting of technical developments for 50 years and counting.

To begin to answer the above questions and probe for an underlying "law of emergence", a metal-analysis of the peer-reviewed literature was performed in January/February 2014 for the twelve prominent CECs listed in Table 1. Annual publishing activity was chosen as a study metric and proxy for the amorphous term *concern*. Published papers compiled in the Chemical Abstract Service (CAS) database were extracted using SciFinder Web software (v2014). The SciFinder registry was queried using the substance identifier to establish a CAS registry number for each contaminant. References for each registry entry were retrieved for the substances selected. Additional queries were limited to the following categories, or combinations of categories: (1) *adverse effect, including toxicity*; (2) *biological study*; and (3) *occurrence*. Contaminant classes for which no CAS registry numbers were available (*i.e.*, nanomaterials, prions, and microplastics) were queried by research topic and categorized by Chemical Abstract Section Title.

Data on publishing activity per calendar year were extracted from the literature and analyzed systematically. The time point of peak publishing activity was defined as the year for which the most publications for the compound were on record, not the 3-year

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