Review of ChemSec SIN List of Suggested EDCs

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ChemSec, the International Chemical Secretariat, describes itself as "a non-profit organization dedicated to working towards a toxic free environment."

The SIN (Substitute it Now!) List is a database of chemicals which ChemSec believes are likely to be banned or restricted in the near future. The chemicals on the SIN List have been identified by ChemSec as Substances of Very High Concern (SVHC) based on their interpretation of the criteria established by the EU chemicals regulation REACH. The stated aim of the SIN List is "to spark innovation towards products without hazardous chemicals by speeding up legislative processes and giving guidance to companies and other stakeholders on which chemicals to start substituting."

In 2007 the EU chemicals regulation REACH entered into force. Within REACH the most hazardous chemicals are defined as Substances of Very High Concern (SVHC) and subsequently placed on the Candidate List. EU member states have decided that the use of these substances should be strictly limited. The SIN List consists of chemicals that have been identified by ChemSec as being SVHCs, based on the criteria for these defined within REACH.

The criteria for Substances of Very High Concern (SVHC) are described in REACH article 57. Three categories are included there, and the SIN List also encompasses substances from these three categories.

1. The first category is chemicals that can cause cancer, alter DNA or damage reproductive systems. These are called CMR substances (Carcinogenic, Mutagenic or Toxic to reproduction).
2. Then there are harmful substances that do not easily break down and accumulate in the food chain. These are known as PBT substances (short for Persistent, Bio-accumulative and Toxic). There is also the abbreviation vPvB, short for very Persistent and very Bio-accumulative.
3. The third category is called "substances of equivalent concern". This category covers substances that are not automatically covered by the other two categories, but which nonetheless give rise to equivalent level of concern in terms of potential damage to health and environment. This category includes endocrine disrupting chemicals.

The substances on the SIN List are grouped according to structural similarity in order to make the list more user-friendly. Almost all of the SIN List substances are divided into 31 groups, and some SIN chemicals belong to several groups. Examples of these groups are bisphenols, phthalates and perfluorinated compounds.

The SIN List is developed by ChemSec in close collaboration with scientists and technical experts they have chosen to work with, as well as an NGO advisory committee of leading environmental, health, women and consumer organizations mainly in Europe but also in the US.

All substances on the SIN List were screened to identify substances covered by the authorization provisions in REACH. Substances exempt or otherwise not regulated by REACH, such as pesticides, intermediates and unintentionally produced substances, have accordingly been removed. All information used for selection and assessment of substances for the SIN List is publicly available. For CMRs the official CLP (Classification, Labelling and Packaging) classification has been used. These substances have been agreed on a EU-wide basis to have properties corresponding to the SVHC criteria.

PBT and vPvB chemicals for the first version of the SIN List were added directly from the European PBT Working Group List developed by the former European Chemicals Bureau (ECB), the duties of which have been taken over by ECHA.

For the initial round in 2008, the list of suggested EDCs came from the set of chemicals listed as category 1 or 2 on the European Commission's priority list of potential endocrine disruptors.

For the second round in 2014, equivalent level of concern substances (REACH article 57f), including suspected EDCs, added to the SIN List have undergone a more in-depth scientific evaluation and case-by-case assessment, based on publicly available peer-reviewed scientific studies.

ChemSec screened a number of sources for suspected EDCs, including scientific papers, reports, priority lists from authorities, and from organizations, including the Endocrine Disruptor Exchange (TEDX). From this gross list, substances already on the SIN List were removed, resulting in more than 1000 substances.

To narrow down the number of substances, ChemSec considered the use of the substances. "Indicated consumer use" was defined as substances being present on a selection of product-type related substances lists. "Proven consumer use"

was defined as substances that have been detected in consumer articles in a number of studies (120) performed by the Danish EPA. Presence on any of these lists or studies was not considered as strict criteria, but only as guidance. About one hundred substances were prioritized and during discussions and first screenings with the scientists, 25 substances were selected for full evaluation.

For the scientific evaluation TEDX was contracted. In brief, the reviewers searched the published literature using PubMed and, in selected instances Web of Science. Two independent reviewers screened all articles for relevance by reviewing the abstract and title. Studies obtained for full review were read and data were extracted and entered into an Access database, then cross checked for accuracy. All in vivo studies (e.g. experimental animal and epidemiological studies) were assessed for risk of bias using a series of questions developed by the National Toxicology Program (NTP) Office of Health Assessment and Translation (OHAT). Two independent reviewers answered applicable questions and noted justifications for each answer. Standardized protocols evaluating in vitro study quality were not available, therefore those studies could not be evaluated for risk of bias.

The strength of the body of evidence was assessed using aspects outlined by OHAT and was determined to be strong, moderate, or weak for a given endpoint. Endpoints with fewer than three studies were not assessed for strength of evidence. The findings for each chemical were summarized and categorized by the model studied (i.e. human, animal, in vitro) and then by positive effect categories (e.g. estrogenicity, androgenicity). In vivo endpoints were summarized using the study quality for human and animal studies, then where applicable, in vitro findings with evidence Assessments were used to support in vivo models.

For the final decision on inclusion on the SIN List, ChemSec based its evaluation on the summaries from TEDX as well as discussions with experts from authorities, NGOs and research institutes. Recent reports on identification and assessment of EDCs were also taken into account in the decision process.

As suggested by the expert advisory group, and in the document, "Key scientific issues relevant to the identification and characterization of endocrine disrupting substances" from the European Commission Joint Research Centre, the following aspects were considered in the discussions on the available evidence:

- an endocrine mode of action
- probability for serious effects
- possible link between the two above

What is the pool of chemicals considered for potential listing as EDCs?

ChemSec included only chemicals that have known uses relevant to the EU REACH regulation and that are not used only as intermediates. All substances on the SIN List have been screened to identify substances covered by the authorization provisions in REACH. Substances exempt or otherwise not regulated by REACH, such as pesticides, intermediates and unintentionally produced substances, have accordingly been removed.

How many chemicals are listed as EDCs?

According to a 2015 draft report by the International Panel on Chemical Pollution (IPCP), there are 84 chemicals listed as suggested EDCs; however, we could not independently confirm this.

Do the authors use the WHO/IPCS definition of an EDC?

Yes, although the evidence supporting a causal link between an endocrine mode of action and adverse health effects needs to meet a low burden of being merely "plausible".

Is the list homogeneous or does it classify different categories of EDCs?

It is homogeneous and the label used is "suggested EDC."

What scientific expertise do the authors have?

For the update conducted in 2014, ChemSec contracted with TEDX. The TEDX website lists an executive director (Ph.D. in psychology), two other staff members with doctoral degrees (a Ph.D. in reproductive and developmental endocrinology with post-docs at NTP and NIEHS and a Ph.D. in Molecular, Cellular, and Integrative Physiology, with a Designated Emphasis in Reproductive Biology), a research associate (BA and MS in Integrative Physiology) and a research assistant (BS in International Agronomy).

None of the staff members hold degrees or certifications in toxicology or epidemiology.

Do the authors of the list engage other stakeholders?

For the final decision on inclusion on the SIN List, ChemSec based its evaluation on the summaries from TEDX as well as discussions with experts from authorities, NGOs and research institutes. To our knowledge, there is neither an opportunity for other stakeholders to offer unsolicited input, nor a commitment by ChemSec to consider such input if it were offered.

Is the list based on primary research or do they rely on other lists?

Initially, in 2008 ChemSec list of suggested EDCs came from the set of chemicals listed as category 1 or 2 on the European Commission's priority list of potential endocrine disruptors. However, since then, they have used primary research to add to the list of suggested EDCs.

Is the list updated on a regular basis with new information?

Although the authors say the SIN list is continuously updated, it would appear more accurate to say that the list of suggested EDCs is episodically updated with major updates having occurred in 2011 and 2014.

Is there a process to appeal the listing of a chemical?

No such process is described anywhere on the ChemSec website.

What are the strengths of the list?

- The methods used are reasonably scientifically sound and are fairly well described on the website.
- The database is easily accessed and searched.
- ChemSec is using the WHO/IPCS definition of an EDC, although the burden for establishing a causal link between endocrine activity and an adverse health effect is low (merely plausible).
- The label of "suggested EDC" is preferable to that of known or probable EDC and seems to appropriately reflect the level of confidence ChemSec has in the underlying evidence.

What are the weaknesses of the list?

- The reviewers may lack sufficient qualifications to undertake a robust evaluation of the evidence.
- The standard for assessing evidence of a causal link between endocrine activity and adverse health effects (i.e., merely plausible) is too low thus resulting in too many chemicals that truly are not EDCs being listed as suggested EDCs.
- Once a chemical is listed, no amount of new contradictory data appears sufficient to get it unlisted.
- A limited multi-stakeholder process with no apparent process for handling unsolicited input from other experts.
- A process that relies solely on published studies, and that ignores high quality unpublished evidence generated for regulatory purposes and that is in the hands of regulators, will not always generate the best evaluation.

What are the implications of the list for the Value Chain?

If downstream users rely on the SIN list they will deny themselves access to valuable chemicals that actually do not possess endocrine disrupting properties.