

# Food Contact Materials: A Road Map to Improved Safety Testing.

**Jane Muncke, PhD**



Food  
Packaging  
Forum





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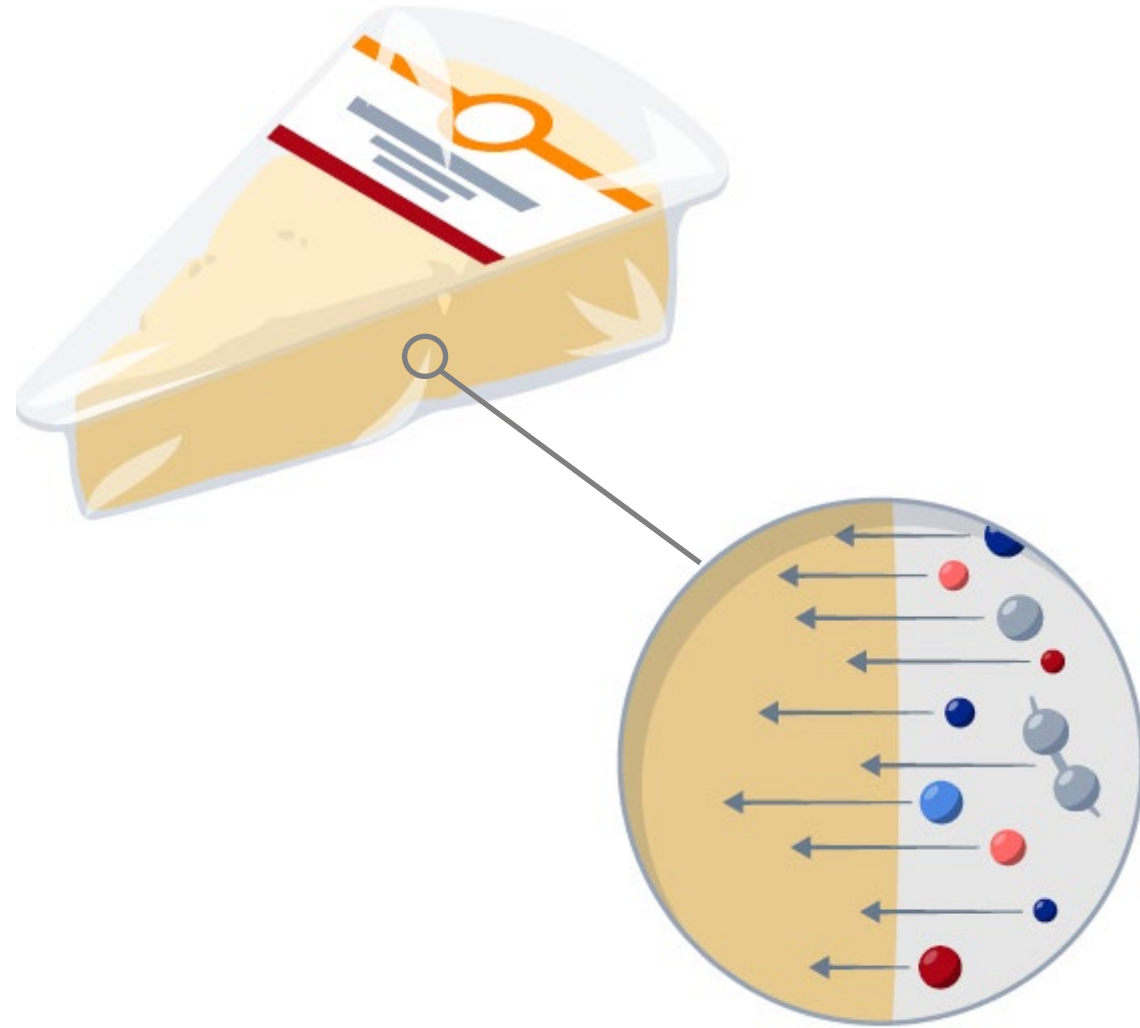




**Chemicals migrate from food  
contact materials into foodstuffs**



# chemical migration





# 1958: FDA Food Additives Amendment

1784 PUBLIC LAW 85-929—SEPT. 6, 1958 [72 STAT.]

Public Law 85-929

September 6, 1958  
[H. R. 13254]

AN ACT

To protect the public health by amending the Federal Food, Drug, and Cosmetic Act to prohibit the use in food of additives which have not been adequately tested to establish their safety.

*Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled, That this Act may be cited as the "Food Additives Amendment of 1958".*

SEC. 2. Section 201, as amended, of the Federal Food, Drug, and Cosmetic Act is further amended by adding at the end of such section the following new paragraphs:

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Food Additives Amendment of 1958.  
52 Stat. 1041.  
21 USC 321.

Definitions.

<https://www.govinfo.gov/content/pkg/STATUTE-72/pdf/STATUTE-72-Pg1784.pdf>



2014



\* Study by the Food Packaging Forum  
[TheGreenDivas.com](http://TheGreenDivas.com)





# Key Terms

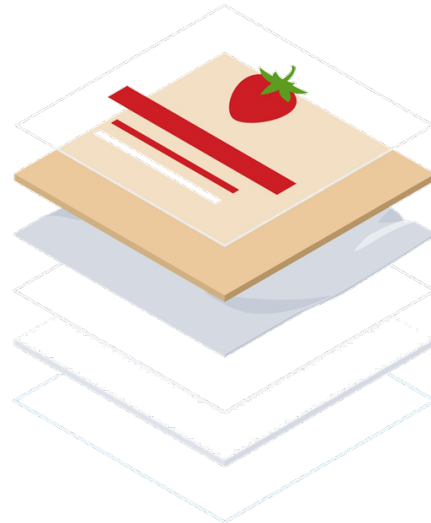
## food contact article (FCA):

- yoghurt cup



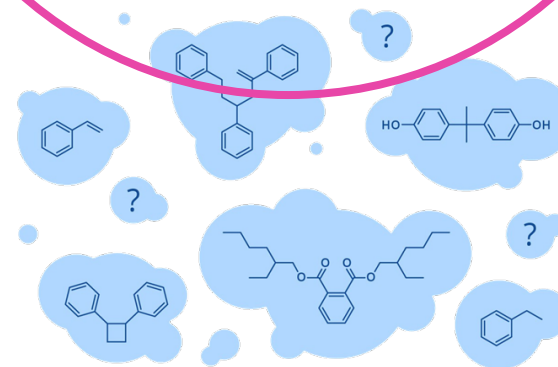
## food contact materials (FCMs):

- plastic(s)
- aluminium
- coating
- adhesives
- printing inks
- ...



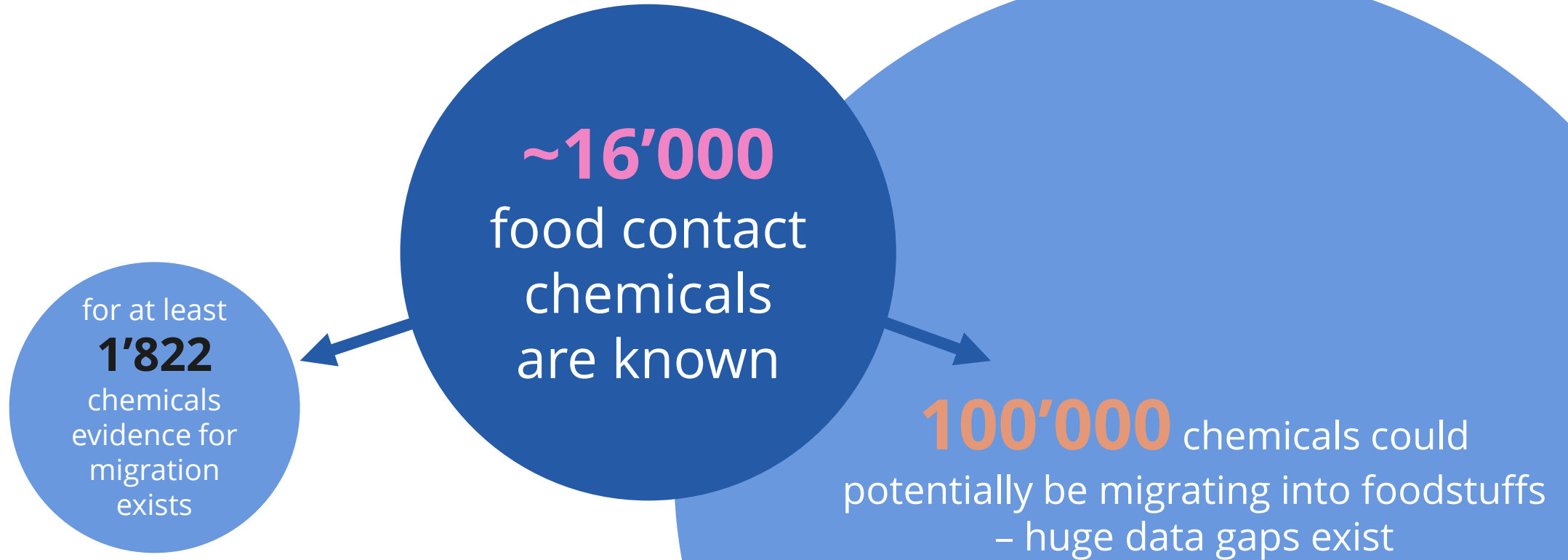
## food contact chemicals (FCCs):

- monomers
- polymers
- oligomers
- additives
- pigments
- metals
- impurities
- reaction by-products
- degradation products
- ...





# How many food contact chemicals are there?





# *In perspective:* Food Contact Materials are an underestimated source of chemical food contamination



	PESTICIDES	FOOD CONTACT MATERIALS (FCM)
Number of Substances	~1,500	Possibly 100,000
Level of food contamination	µg/kg (ppb)	mg/kg (ppm)
Toxicological evaluation	yes	mostly no

Source: presentation by Dr. Gregor McCombie, Official Food Control Authority Zurich, January 26, 2016, [EU Parliament Workshop](#).



# FCCmigex

Database on Migrating and  
Extractable Food Contact Chemicals



The **FCCmigex database** informs about **Food Contact Chemicals** that have been measured in **migrates** and **extracts** of food contact materials.

### Explore



All  
Food Contact Materials

### Have a closer look



Plastic  
Food Contact Materials

### Find out more



References



## Food Contact Materials (FCMs)



How many chemicals in FCMs are of concern?



What are their hazards?

## 388 Food Contact Chemicals of Concern

(harmful according to the EU's Chemicals Strategy for Sustainability but currently legally used)

**352 CMRs**  
(carcinogenic, mutagenic, or toxic to reproduction)

**32 Persistent, bioaccumulative**

**3 STOT**  
(specific target organ toxicity)

**22 EDCs**  
(endocrine-disrupting chemicals)

**Evidence for migration:  
97 chemicals**



## Legal definition of *indirect food additive* safety in the US

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**“Safe or safety** means that there is a reasonable certainty in the minds of competent scientists that the substance is not harmful under the conditions of its intended use.”

<https://www.ecfr.gov/current/title-21/chapter-I/subchapter-B/part-170> (3. Definitions (i))



2017

## Commentary

<https://doi.org/10.1289/EHP644>

### **Scientific Challenges in the Risk Assessment of Food Contact Materials**

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<sup>11</sup>Institute for Chemical and Bioengineering, Swiss Federal Institute of Technology (ETH), Zurich, Switzerland



## U.S. Government Accountability Office (2022)

«Food processing and packaging can introduce non-food substances [...] into food. Some of these substances **may pose health risks.**»

GAO 2022. <https://www.gao.gov/products/gao-23-104434>

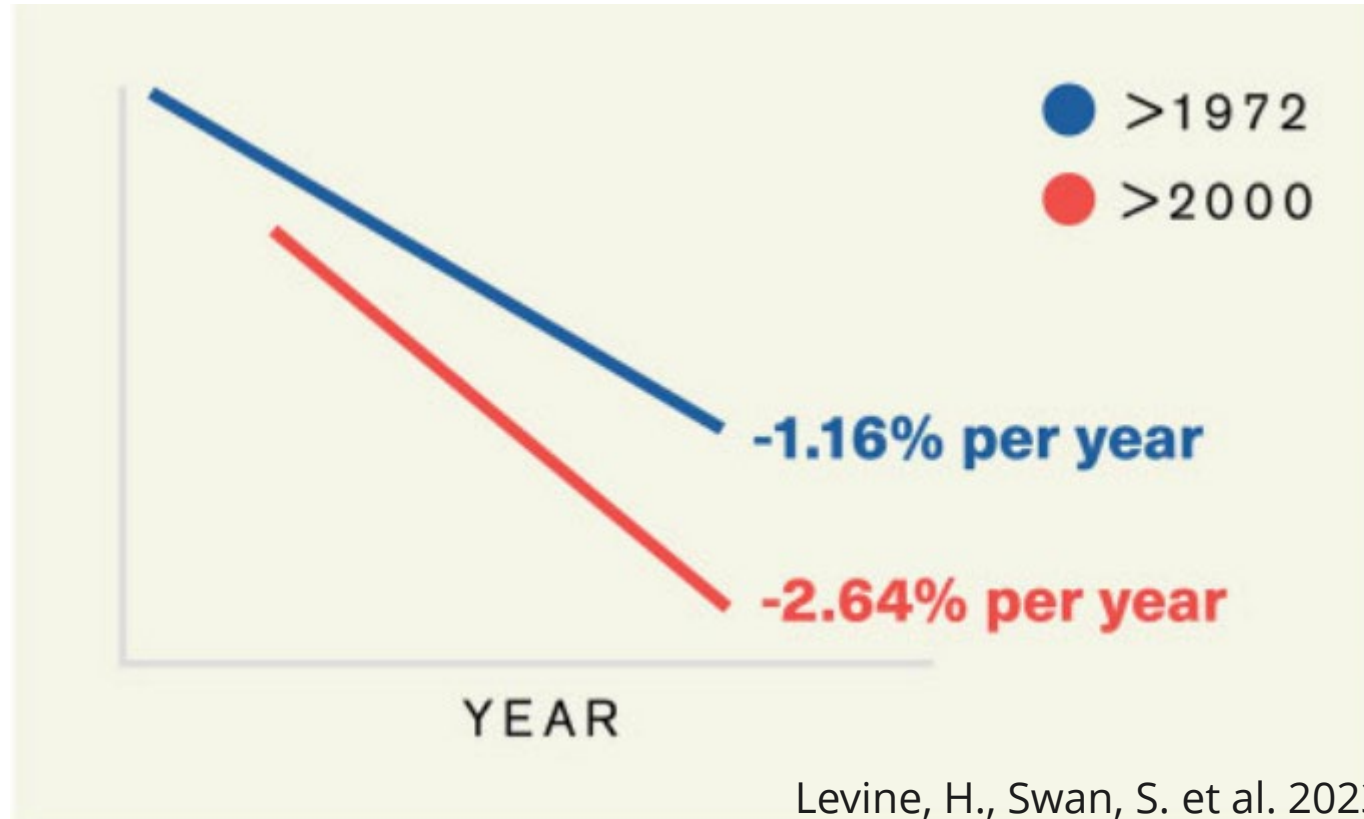




**Chemicals contribute to chronic diseases.**

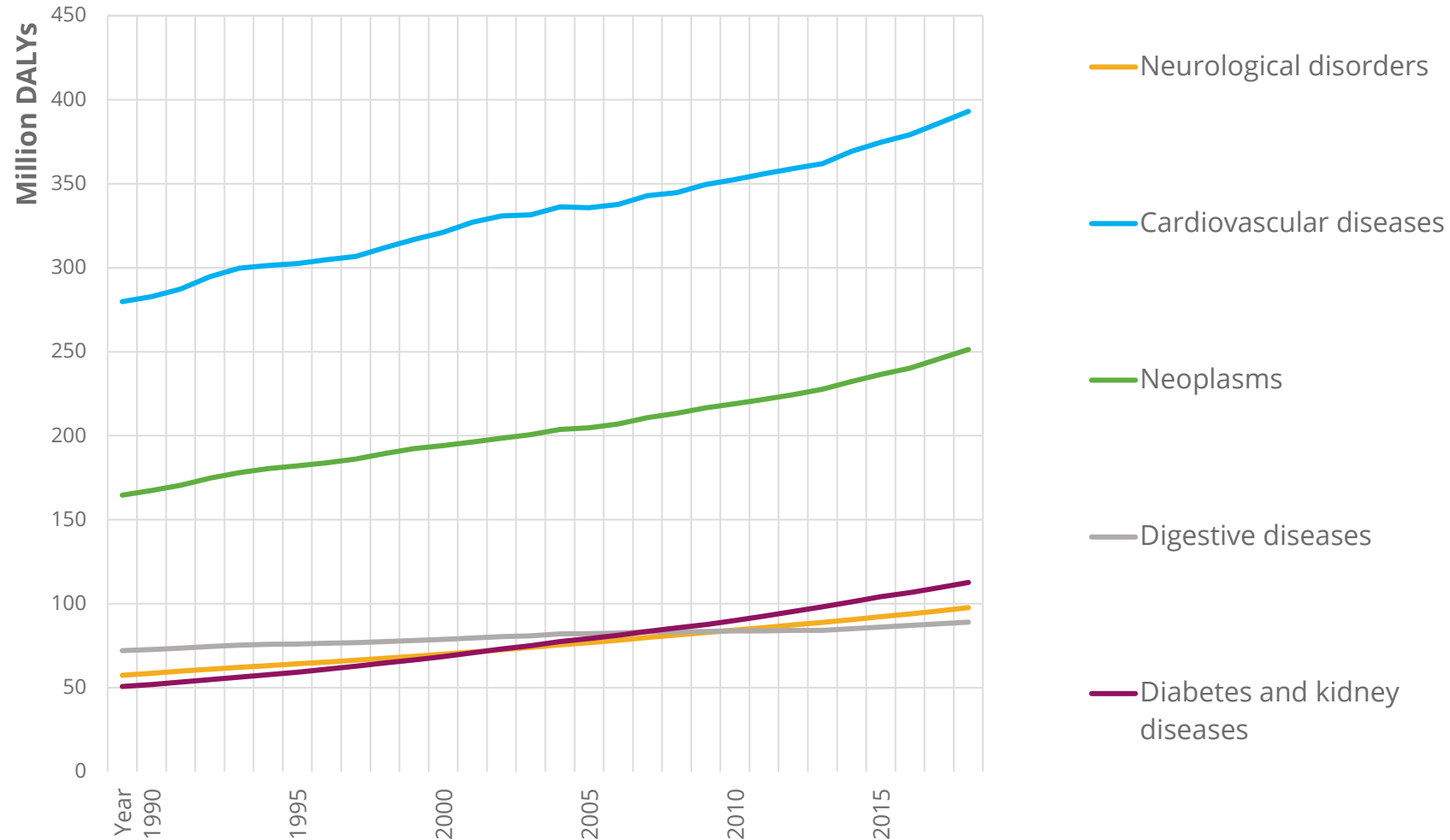


# Sperm count is declining at an accelerated pace globally





# Chronic disease burden is increasing globally



Disability-Adjusted Life Years (DALYs).  
Data: Global Burden of Disease 2021.




COMMENTARY

Open Access

# Impacts of food contact chemicals on human health: a consensus statement



Jane Muncke<sup>1\*</sup> , Anna-Maria Andersson<sup>2</sup>, Thomas Backhaus<sup>3</sup>, Justin M. Boucher<sup>4</sup>, Bethanie Carney Almroth<sup>3</sup>, Arturo Castillo Castillo<sup>5</sup>, Jonathan Chevrier<sup>6</sup>, Barbara A. Demeneix<sup>7</sup>, Jorge A. Emmanuel<sup>8</sup>, Jean-Baptiste Fini<sup>7</sup>, David Gee<sup>9</sup>, Birgit Geueke<sup>1</sup>, Ksenia Groh<sup>1</sup>, Jerrold J. Heindel<sup>10</sup>, Jane Houlihan<sup>11</sup>, Christopher D. Kassotis<sup>12</sup>, Carol F. Kwiatkowski<sup>13</sup>, Lisa Y. Lefferts<sup>14</sup>, Maricel V. Maffini<sup>15</sup>, Olwenn V. Martin<sup>16</sup>, John Peterson Myers<sup>17,18</sup>, Angel Nadal<sup>19</sup>, Cristina Nerin<sup>20</sup>, Katherine E. Pelch<sup>13</sup>, Seth Rojello Fernández<sup>21</sup>, Robert M. Sargis<sup>22</sup>, Ana M. Soto<sup>23</sup>, Leonardo Trasande<sup>24</sup>, Laura N. Vandenberg<sup>25</sup>, Martin Wagner<sup>26</sup>, Changqing Wu<sup>27</sup>, R. Thomas Zoeller<sup>28</sup> and Martin Scheringer<sup>4,29</sup>

**Source:** <https://ehjournal.biomedcentral.com/articles/10.1186/s12940-020-0572-5>





**Use modern science.**



**To prevent illness,**  
**test all food contact chemicals**  
**for their impact on increasingly**  
**prevalent chronic diseases.**



2023



Contents lists available at [ScienceDirect](#)

## Environment International

journal homepage: [www.elsevier.com/locate/envint](http://www.elsevier.com/locate/envint)



Full length article

### A vision for safer food contact materials: Public health concerns as drivers for improved testing

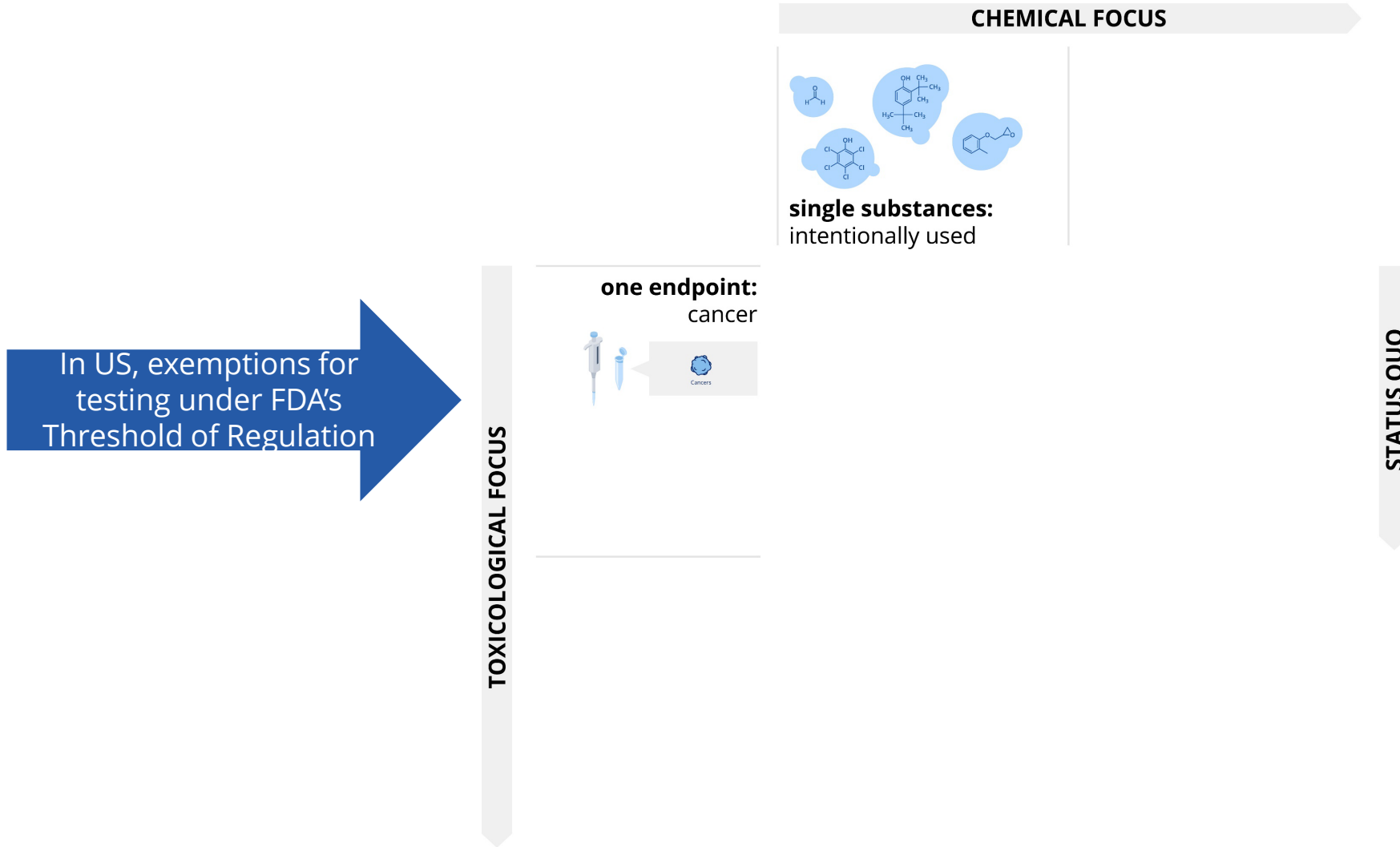
Jane Muncke<sup>a,\*</sup>, Anna-Maria Andersson<sup>b</sup>, Thomas Backhaus<sup>c</sup>, Scott M. Belcher<sup>d</sup>, Justin M. Boucher<sup>a</sup>, Bethanie Carney Almroth<sup>c</sup>, Terrence J. Collins<sup>e</sup>, Birgit Geueke<sup>a</sup>, Ksenia J. Groh<sup>f</sup>, Jerrold J. Heindel<sup>g</sup>, Frank A. von Hippel<sup>h</sup>, Juliette Legler<sup>i</sup>, Maricel V. Maffini<sup>j</sup>, Olwenn V. Martin<sup>k</sup>, John Peterson Myers<sup>e,l</sup>, Angel Nadal<sup>m</sup>, Cristina Nerin<sup>n</sup>, Ana M. Soto<sup>o,p</sup>, Leonardo Trasande<sup>q</sup>, Laura N. Vandenberg<sup>r</sup>, Martin Wagner<sup>s</sup>, Lisa Zimmermann<sup>a</sup>, R. Thomas Zoeller<sup>r</sup>, Martin Scheringer<sup>t,u,\*</sup>

<https://doi.org/10.1016/j.envint.2023.108161>





# Assessing the safety of food contact articles: STATUS QUO





low levels  $\neq$  safe levels



“cancer” ≠ proxy for all  
relevant chronic diseases



# Six Clusters of Disease (SCOD)



## Cancers

- Breast cancer
- Prostate cancer
- Kidney cancer



## Cardiovascular diseases

- Hypertension
- Atherosclerosis
- Myocardial infarction



## Reproductive disorders

- Male infertility
- Female infertility



## Brain-related disorders

- Hypothyroidism
- Abnormal neurodevelopment



## Immunological disorders

- Immunosuppression
- Asthma
- Allergies



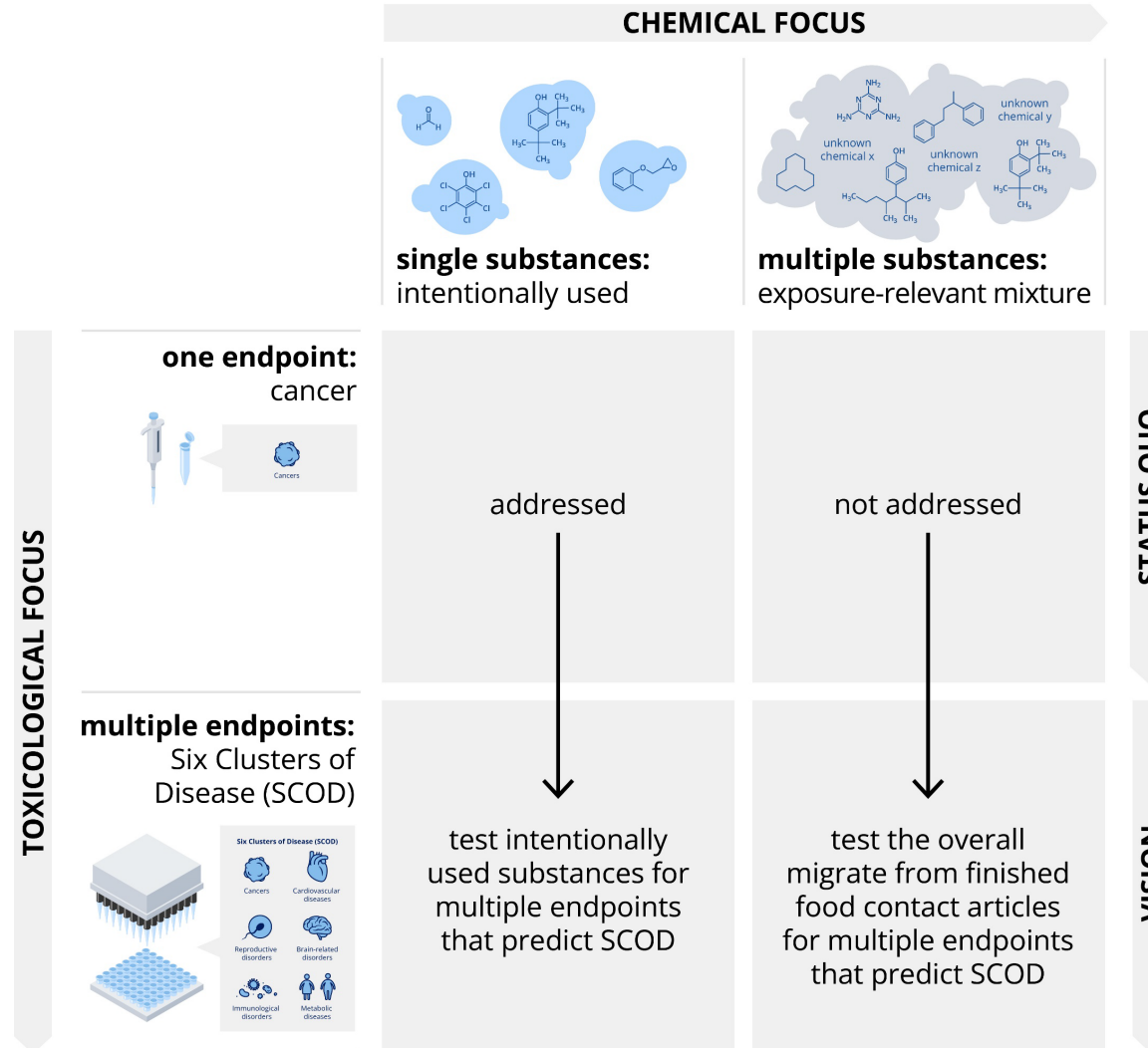
## Metabolic diseases

- Diabetes type 1/2
- Obesity
- Non-alcoholic fatty liver disease

Muncke et al. 2023. Env. Int. <https://doi.org/10.1016/j.envint.2023.108161>



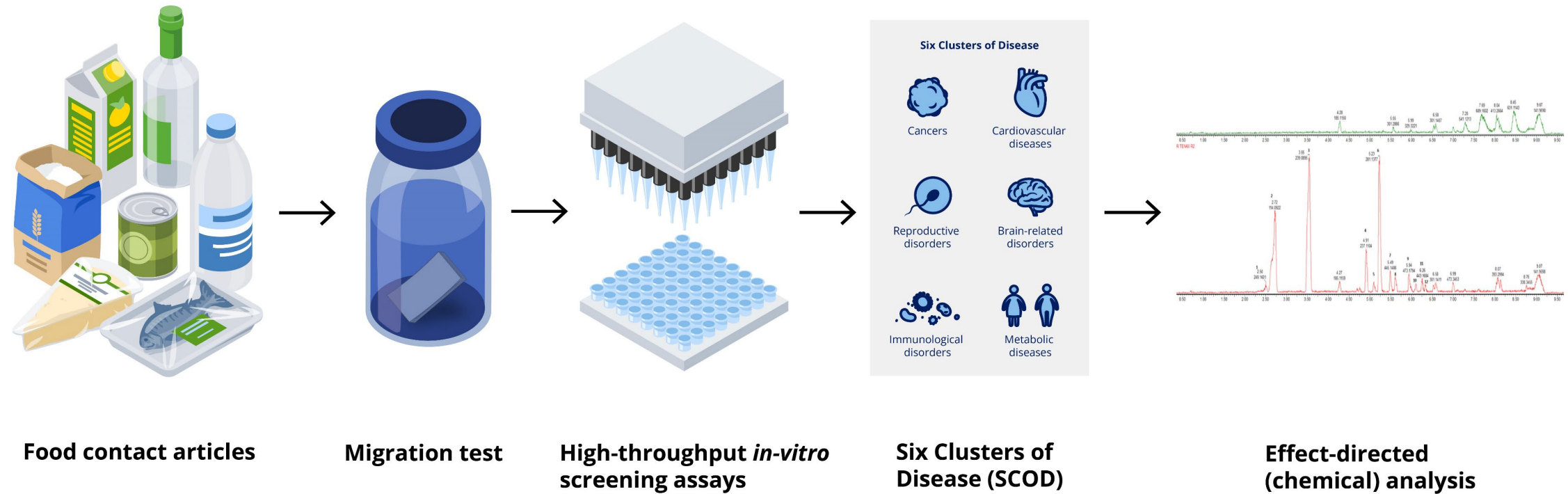
# Fully safe food contact articles: the FPF vision



testing of ALL migrating food contact chemicals



# Fully safe food contact materials and articles are *properly* tested





# How to confirm food contact materials are **fully safe**?



# Different approaches to identifying chemical hazard

## Toxicology

- Does a chemical cause **cancer**?
- *In-vivo* testing (animals)
- observational
- not at molecular level
- high cost, long time
- ethical considerations
- relatively good scientific certainty (?)

## Adverse Outcome Pathway

- How does a chemical cause **breast cancer**?
- What is the molecular initiating event for breast cancer?
- (linear) cause-effect relationship needs to be established
- highly challenging to develop
- when available: highly useful for development of *in-vitro* testing
- cost efficient, fast
- relatively good scientific certainty (?)

## Key Characteristics

- Does a chemical have the **key characteristics of carcinogens**?
- *In-vitro* assays to test chemical for these molecular-level properties of interacting with biological molecular targets
- (soon) available for all of the SCOD
- highly useful for development of *in vitro* testing
- cost efficient, fast
- relatively good scientific certainty (?)





**Table 1. Key characteristics of carcinogens.**

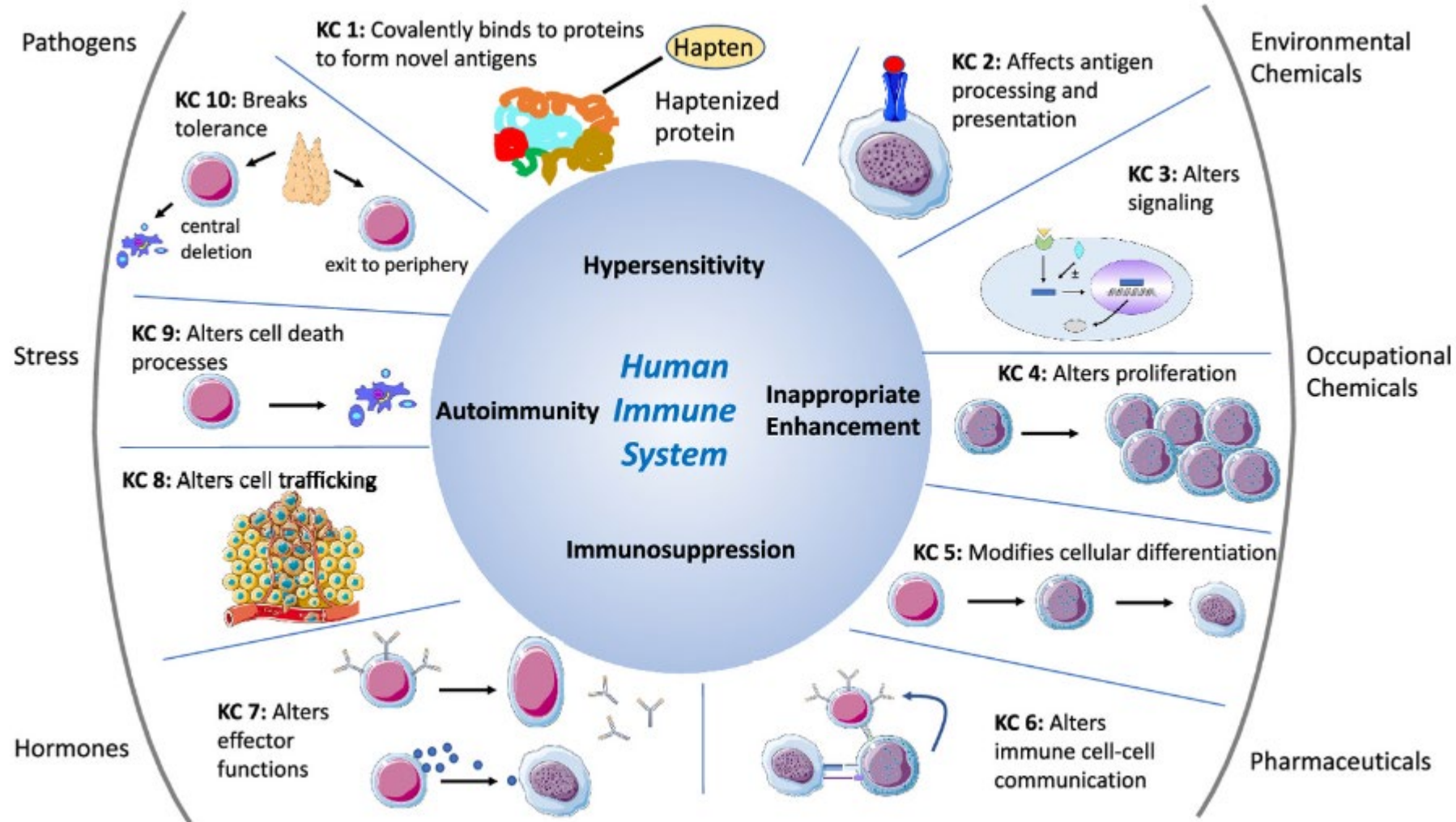
Characteristic	Examples of relevant evidence
1. Is electrophilic or can be metabolically activated	Parent compound or metabolite with an electrophilic structure (e.g., epoxide, quinone), formation of DNA and protein adducts
2. Is genotoxic	DNA damage (DNA strand breaks, DNA–protein cross-links, unscheduled DNA synthesis), intercalation, gene mutations, cytogenetic changes (e.g., chromosome aberrations, micronuclei)
3. Alters DNA repair or causes genomic instability	Alterations of DNA replication or repair (e.g., topoisomerase II, base-excision or double-strand break repair)
4. Induces epigenetic alterations	DNA methylation, histone modification, microRNA expression
5. Induces oxidative stress	Oxygen radicals, oxidative stress, oxidative damage to macromolecules (e.g., DNA, lipids)
6. Induces chronic inflammation	Elevated white blood cells, myeloperoxidase activity, altered cytokine and/or chemokine production
7. Is immunosuppressive	Decreased immunosurveillance, immune system dysfunction
8. Modulates receptor-mediated effects	Receptor in/activation (e.g., ER, PPAR, AhR) or modulation of endogenous ligands (including hormones)
9. Causes immortalization	Inhibition of senescence, cell transformation
10. Alters cell proliferation, cell death or nutrient supply	Increased proliferation, decreased apoptosis, changes in growth factors, energetics and signaling pathways related to cellular replication or cell cycle control, angiogenesis

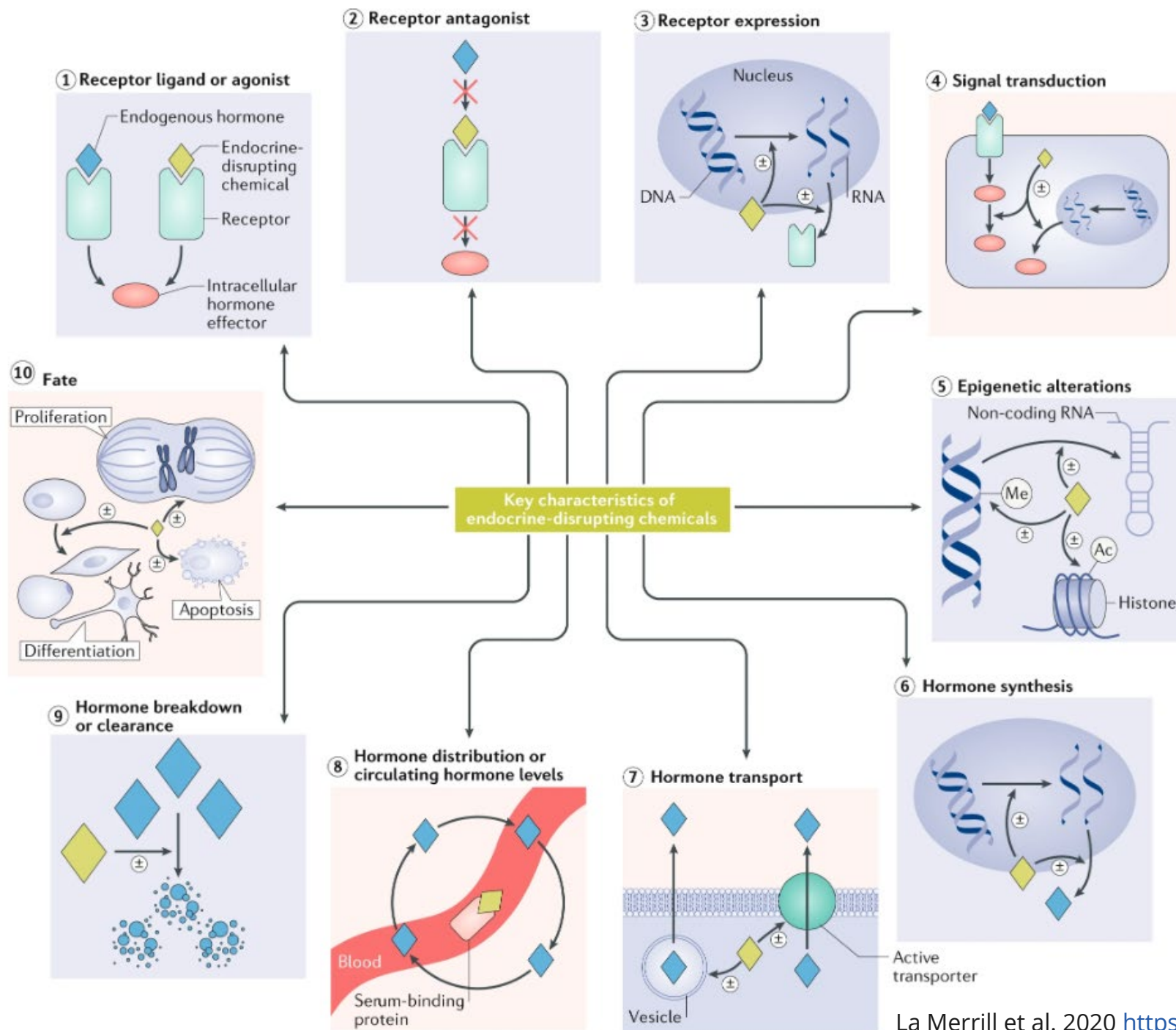
**Abbreviations:** AhR, aryl hydrocarbon receptor; ER, estrogen receptor; PPAR, peroxisome proliferator–activated receptor. Any of the 10 characteristics in this table could interact with any other (e.g., oxidative stress, DNA damage, and chronic inflammation), which when combined provides stronger evidence for a cancer mechanism than would oxidative stress alone.

Smith MT. et al. 2016. Key Characteristics of Carcinogens as a Basis for Organizing Data on Mechanisms of Carcinogenesis. *Env. Health Persp.* <http://dx.doi.org/10.1289/ehp.1509912>



# Key Characteristics of Immunotoxic Agents







## Key Characteristics available to date

- Carcinogens
- Cardiovascular Toxicants
- Endocrine Disrupting Chemicals
- Female Reproductive Toxicants
- Hepatotoxicants
- Immunotoxicants
- Male Reproductive Toxicants

<https://keycharacteristics.org/publications/published-papers-describing-various-sets-of-key-characteristics-kcs/>

## Public Law 85-929

## AN ACT

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Amendment of  
1958.

52 Stat. 1041.  
21 USC 321.

Definitions.



## Fully safe (2024):

Use **modern science**

to test **ALL migrating food contact chemicals** for their impacts  
on **ALL relevant chronic diseases**.



## Next steps towards fully safe food contact materials (FCMs)

- Identify suitable *in-vitro* assays
- Refine protocols for FCM sample preparation
- Establish protocols for (high-throughput) *in-vitro* testing
- Develop novel relevant *in-vitro* assays
- Expand chemical analysis methods for FCMs
- Collaborate with relevant stakeholders:
  - food and FCM industry,
  - regulators,
  - academia,
  - civil society
  - scientific services industry
- Build capacity with commercial testing labs
- Adjust regulatory requirements
- ...



## Conclusions

- **Underestimated:** Food contact materials, including food packaging, are a relevant source of man-made, synthetic chemicals
- **Preventing exposure prevents disease:** Some food contact chemicals contribute to human chronic disease
- **Inadequate regulations:** Food contact chemicals are currently not appropriately tested for their impacts on human health
- **Use modern science:** Fully safe food contact materials have to be tested for all migrating chemicals and for all disease-relevant properties
- **Collaboration Imperative:** Only by including all stakeholders' expertise can food contact materials be made «fully safe»





**«If you don't test,  
you don't know.»**

**J. Pete Myers**







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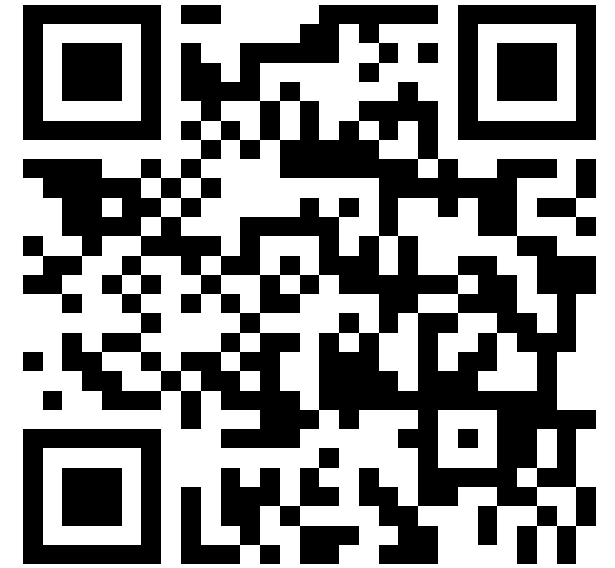
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