Revised Protocol: UCSF **IRB/CHR Number:** 15-17703

Approved by IRB/CHR

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Study Title: Clinical blood profile assays as biomarkers to directly assess potential health effects resulting from the controlled elimination of suspected dietary and environmental chemical toxins.

This study is the first of its kind to go beyond simply measuring serum and urine concentrations of the subject chemicals. Instead, this study will measure clinically useful outcomes using widely accepted diagnostic tests available at most medical facilities.

The investigators of this study recommend a revised protocol to increase reproducibility and decrease costs.

This revision is based on 2-1/2 years of intensive research that has determined that the original protocol would be impractical, too expensive for allocated resources, and could not be replicated by other investigators.

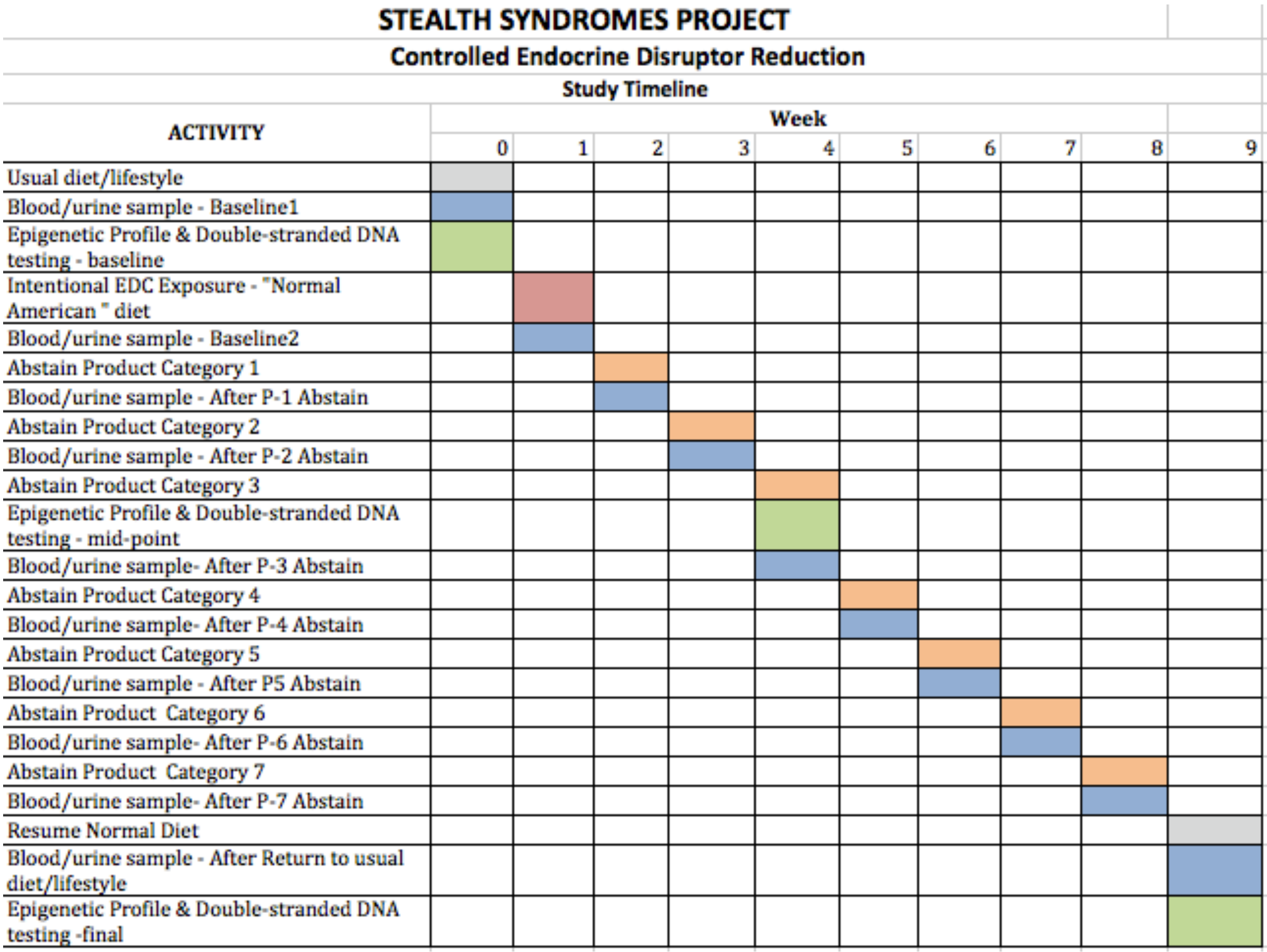
These revisions did not result from a single incident of sudden enlightenment. Instead, they are the result of a steady accumulation of insight built upon the closer scrutiny of previously published diet intervention studies. Underpinning that was the accumulated discovery of confounding basic science factors never before considered in these previous studies. which rendered them irreproducible.

Chief among the non-replicability of is the fact that the food supply chain is ubiquitously contaminated with widely varying and uncontrolled levels of Bisphenol A, phthalates and other environmental chemicals.

The investigators believe they have developed a reliable method of preparing and sourcing foods that will allow consistent results across other investigations.

NOTE: This revised protocol is followed by four appendices containing supplemental material excerpted from our internal reproducibility problem-solving working paper that offers greater perspective on the rationale and feasibility of the revised protocol.

ORIGINAL PROTOCOL AS APPROVED BY UCSF IRB/CHR



Expense and Practicality Issues

As we proceeded to implement the original protocol, we were continually confronted with a self-reinforcing cascade of confounding factors.

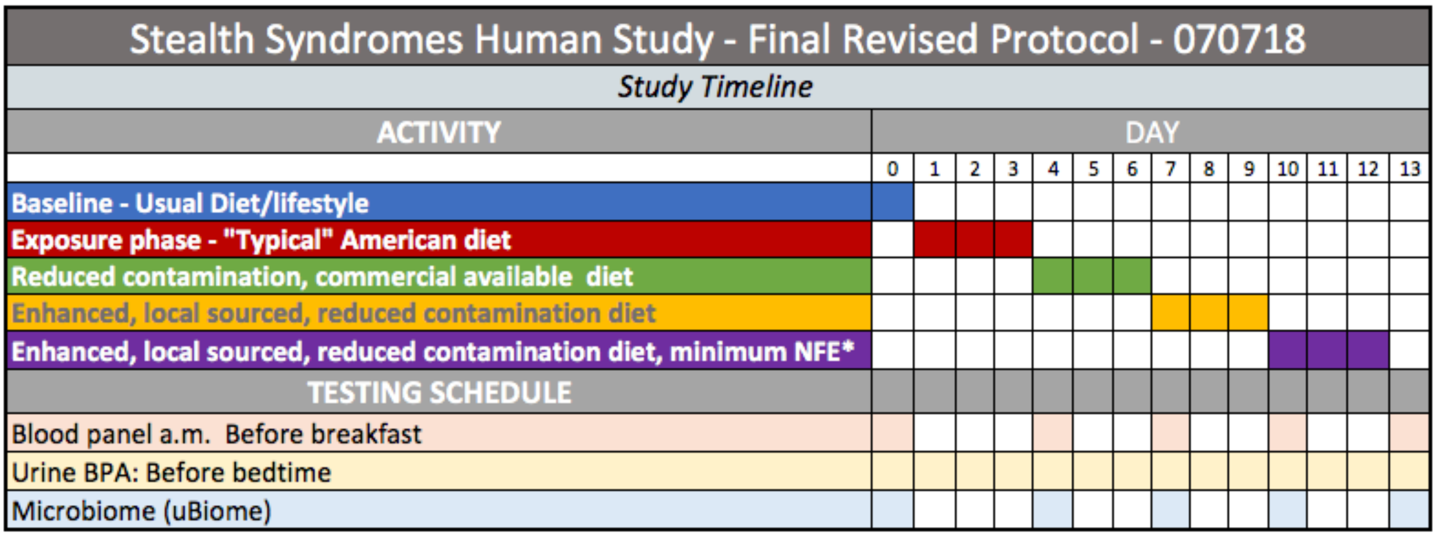
Among these confounding factors we discovered were:

1. Extreme variations among published studies that measured BPA and phthalate concentrations in many common food items.[1,2,3,4,5,6,7]
2. Evidence of inherent contamination in production and processing and not solely from food contact materials.[8,9,10,11,12,13,14]
3. Ubiquitous contamination of all commonly available foods. See Appendix 3.
4. The necessity to test every food ingredient for nutrition and contamination levels.
5. Substantial controls that needed to be imposed on non-food contamination sources.
6. Lengthy testing regime a barrier to subject compliance.

Need to Increase Reproducibility

1. Expanded data capture and transparency
2. More demanding and selective food sourcing standards
3. Minimization of non-food contamination sources
4. More rigorous controls over experimental apparatus

NEW PROPOSED PROTOCOL:



*NFE = Non-Food Exposure

Protocol Phases

Baseline

Testing establishes the study subject's pre-trial parameters. This also allows a comparison with NHANES data to see how test subject levels compare with the national median.

PHASE 1: Exposure, Typical American Diet

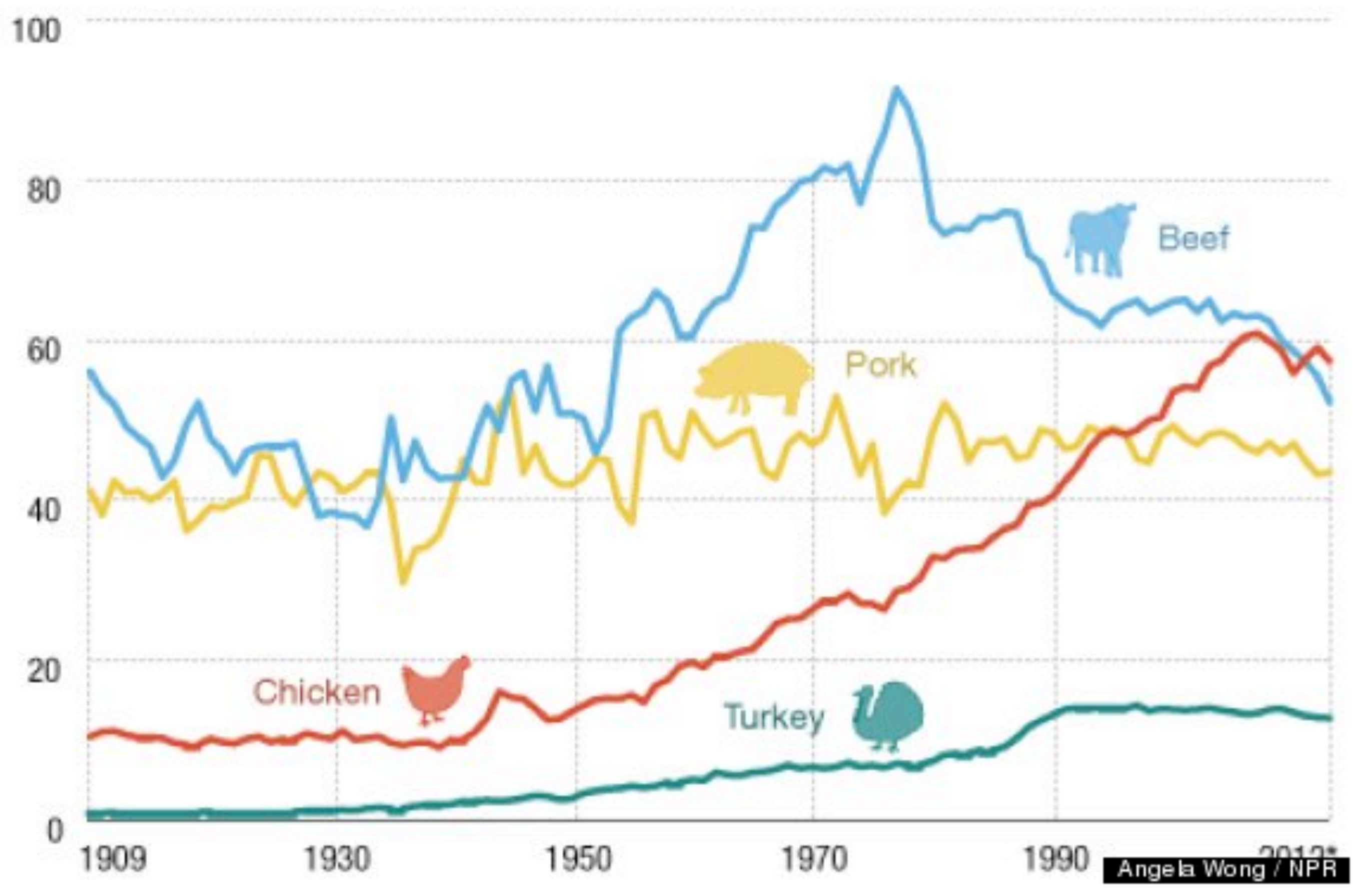
During this three-day period, study subjects will consume a diet designed to emulate a "typical" American diet.

To create that diet, investigators will rely, in part, upon the U.S. Department of Agriculture's 2016 study: *Americans' Eating Patterns and Time Spent on Food: The 2014 Eating & Health Module Data*[15]. A more recent edition will be relied upon if available.

The search will begin in the frozen foods section of a supermarket. Ultimately, the retailer may be Walmart because they are located in all American states making specific brands easily accessible to other investigators.

Our assumption for this strategy is that a branded frozen food is likely to be consistent in content, nutrition and contaminant exposure regardless of the location of purchase. This is not a certainty because processing may have taken place at different facilities depending upon distribution and location of sale. We will make an effort to determine the processing facility for all goods.

Because data from numerous sources indicate that chicken, beef and pork are the most popular meats, we will reflect this by using each for one of the evening dinner menus during the 3-day exposure phase.



Because people in all demographics increasingly choose convenient foods that save time, we will choose complete meals with an emphasis on being as nutritionally balanced as possible -- meat + vegetable (preference on leafy green or cruciform) + carbohydrate (pasta, potato etc.).

In cases where a suitable complete meal is not available, we will select multiple items and combine as a meal. Items will be prepared as indicated on their labels. This will, inevitably mean microwaving frozen foods in plastic containers or in paper containers with plastic liners.

To best reflect "typical American" meal and to assure widespread availability and reproducibility, we will select best-selling brands.

PHASE 2 - Reduced contamination, commercial

Once a menu has been established for the typical exposure phase, the components of this diet phase will be structured to emulate the typical exposure phase meals as closely as possible using less-contaminated food choices.

This phase, which has been missing from all other diet intervention studies of BPA and phthalates, offers study participants a "standard dose" of BPA and phthalates. This phase is intended not only to assess the effects of a typical American diet, but also to "standardize" food-exposure levels for each participant.

Standardized food exposure levels, combined with the final phase (minimum non-food exposure - NFE) may be useful in establishing estimates of overall individual NFE.

Foods and beverages will be obtained from Organic Certified sources, selected for minimum processing and plastic food contact materials. Currently, Whole Foods is the only national chain that prohibits biosolid use in its foods and may be a primary source because its availability facilitates reproducibility by other investigators.

Other widely available sources will be sought, especially from among direct-shipping vendors who adhere to the enhanced organic rules developed by this study's investigators.

1. No plastic contact. Exceptions are not preferred, but may include BPA and phthalate-free nitrile gloves and tubing such as Tygon S3 B-44-3 Beverage Tubing or other manufacturer's equivalent.
2. Any plastic product used must be tested to assure manufacturer claims because studies have shown that some manufacturer claims are false.[16,17,18]

Preparation & cooking

The following are forbidden:

- Sous vide
- non-stick pans
- most cooking oils
- plastic utensils
- plastic prep bowls
- synthetic gloves
- plastic bags
- plastic wrap
- drip coffee makers
- Sodastream
- Keurig and other "pod" beverage makers
- Beverages in cans, plastic bottles or glass.

PHASE 3: Enhanced organic

This diet will work to provide identical menu items served in previous phases but will follow a set of guidelines developed by this study's investigators for sourcing local food and beverage products. Those guidelines eliminate many sources of endocrine disruptors -- such as recycled wastewater irrigation -- that are allowable under USDA organic regulations. Adherence to these rules should facilitate reproducibility.

The guiding principals are summarized below. More details are available in Appendix 2 of this document.

1. Commercially processed foods are unacceptable.
2. All food will be obtained directly from local Certified USDA Organic sources whose premises have been voluntarily inspected for compliance with those and the following enhanced requirements.
3. Do not consume any ingredient whose composition cannot be traced to, and inspected at its origin.

4. No recycled wastewater is allowed in irrigation or other on-premises uses.
5. No biosolids are allowed in irrigation or other on-premises uses.
6. No food contact with plastics or recycled paper or cardboard. Minimum or incidental contact may be approved depending upon the plastic composition.
7. Irrigation water must not be transported via plastic pipes. Drip irrigation is discouraged, but if used must not contact edible surfaces.
8. Harvest and food transport must be in metal containers.

PHASE 4 - Enhanced, local sourced, reduced contamination diet, minimum Non-Food Exposure

The unknown -- and possibly unknowable -- variabilities in this class of exposures offers the greatest set of hazards to reproducibility.

Numerous non-food sources of BPA are present in the environment and likely pose significant "background" contamination which will vary depending upon the test subjects' lifestyles and environments.

This is particularly critical because the major health effects being measured in this study; estrogen/testosterone disruptions, inflammation, and metabolic events such as insulin resistance and lipid imbalance, can also be affected by a wide variety of chemicals other than BPA and phthalates.

This is why this final phase of the protocol has been added to reduce non-food exposures of all harmful chemicals as much as possible.

In addition, the personal environments of participants (personal care products, medications, etc.) must be noted for the record and reduced in a manner that can be illuminated by comparison with measured BPA, phthalate, and microbiome levels and indicators.

The path to a revised protocol: Confounding factors lead to greater complexity and expense

This study's investigators, from the beginning, recognized that basic nutritional levels -- protein, fat, and sugar/carbohydrates would need to be the same at each level of the study. While unnecessary in previous dietary intervention studies that measured only BPA levels, the present study also measures health effects which can be affected by nutritional composition.

The widespread variance in BPA concentrations in source foods led to the realization that reproducibility of this study would require testing of all source food for BPA concentrations. Otherwise, any record of increase or decrease in subject BPA concentrations would be invalid.

That recognition led to the conclusion that a reproducible investigation required the establishment of specific baseline food concentrations -- leading to accurate dose levels of BPA consumed.

Further investigation led to published papers that indicated interactions between folic acid and BPA levels[19]. That realization made it necessary to eliminate foods which would be concerned considered methyl contributors including genistin, and soy products among others.

This was further confounded by the revelation that BPA interacts with a key blood panel indicator, Prostate-Specific Antigen (PSA)[20]. A clinical study included as part of this paper indicates that BPA may suppress serum levels of PSA in men under 65 years of age.

The potential confounding factors regarding PSA and folic acid led us to the realization that, in addition to assuring that the intervention diet nutritional content was equal in macronutrients to the baseline, we would also need nutritional analysis of micronutrients as well as every food item consumed. This compounded the complexity of the investigation as well as the costs.

Investigators' further research indicated that the American food chain was so contaminated at every level by BPA and phthalates. The resulting food sourcing and testing demands increased the costs of the study far beyond the previous budget and would require extraordinary -- and expensive -- food production and processing methods to be implemented at the farm level and continuing in a highly controlled regime through processing, and preparation for table consumption.

This would require financial and personnel resources far beyond those originally anticipated.

The original study had, as its expressed outcomes to:

1. Determine direct health effects: Determine if reducing BPA and phthalate levels correlated significantly with health effects that could be measured using well-accepted diagnostic blood panel elements, and
2. Clinical usefulness: Offer consumers and their health professionals practical, evidence-based dietary intervention steps to improve personal health.

The ubiquitous, and inconsistent contamination of food, along with the limited availability of minimally, contaminated foods made those two goals impossible without testing every sample of food destined for the consumer's mouth. This was obviously impractical.

This situation led us to a deeper re-examination of the handful of previous dietary interventions aimed at reducing bisphenol A concentrations in a test population. Not surprisingly, none of those previous could be replicated. Only one of those studies devoted significant attention to the reasons for non-reproducibility.

A more detailed discussion of those previous studies and this new protocol's replication improvements is presented at the end of this document.

The evolution of this new protocol

Taking into account the results of previous published studies that indicated the ubiquitous presence of BPA and/or phthalates in every type of readily available food, the investigators sought to identify contamination sources, categorize them by food type and develop a simple, cost-effective method for selecting minimally contaminated foods.

The limited number of foods available for the intervention and variability of contamination meant that the granularity of measuring health effects by the stepwise reduction of seven different categories of food and beverages would yield little in useful data.

The original protocol offered a finer "granularity" of data because it called for nine test phases, each one week long which involved the step-wise elimination of seven contaminated product categories.

The theory was that, if BPA levels in test subjects dropped after eliminating a category, then that category was probably the cause of a certain level of contamination as indicated by blood and serum levels.

Cost constraints -- primarily associated with testing costs -- make the original protocol's granularity goal impractical. For that reason, we propose four phases of three days each.

In addition, using week-long intervention periods for each category required extensive, and expensive meal preparation expense, increased risk of inadvertent contamination from non-food sources and -- most likely -- decreased compliance by test subjects.

The numerous additional phases and longer duration in the original protocol would not only increase the cost of testing, but would also increase food expense, impose unacceptable demands on test subjects, and place additional efforts on the reduction of non-food exposure sources.

Adjusting protocol phases to accommodate CRP pharmacokinetics

While BPA levels rise and drop quickly within a day, our key health indicator -- C-Reactive Protein (CRP) requires a different protocol.

Given CRP's rapid response to initial stimulus, 3-day phases should allow adequate time for accurate measurements even though more data need to be located regarding the concentration of BPA needed to stimulate an adequate CRP synthesis response.

According to Pepys and Hirschfield (2003)[21], CRP is very responsive to inflammatory compounds: *"De novo hepatic synthesis starts very rapidly after a single stimulus, serum concentrations rising above 5 mg/l by about 6 hours and peaking around 48 hours. The plasma half-life of CRP is about 19 hours ...."*

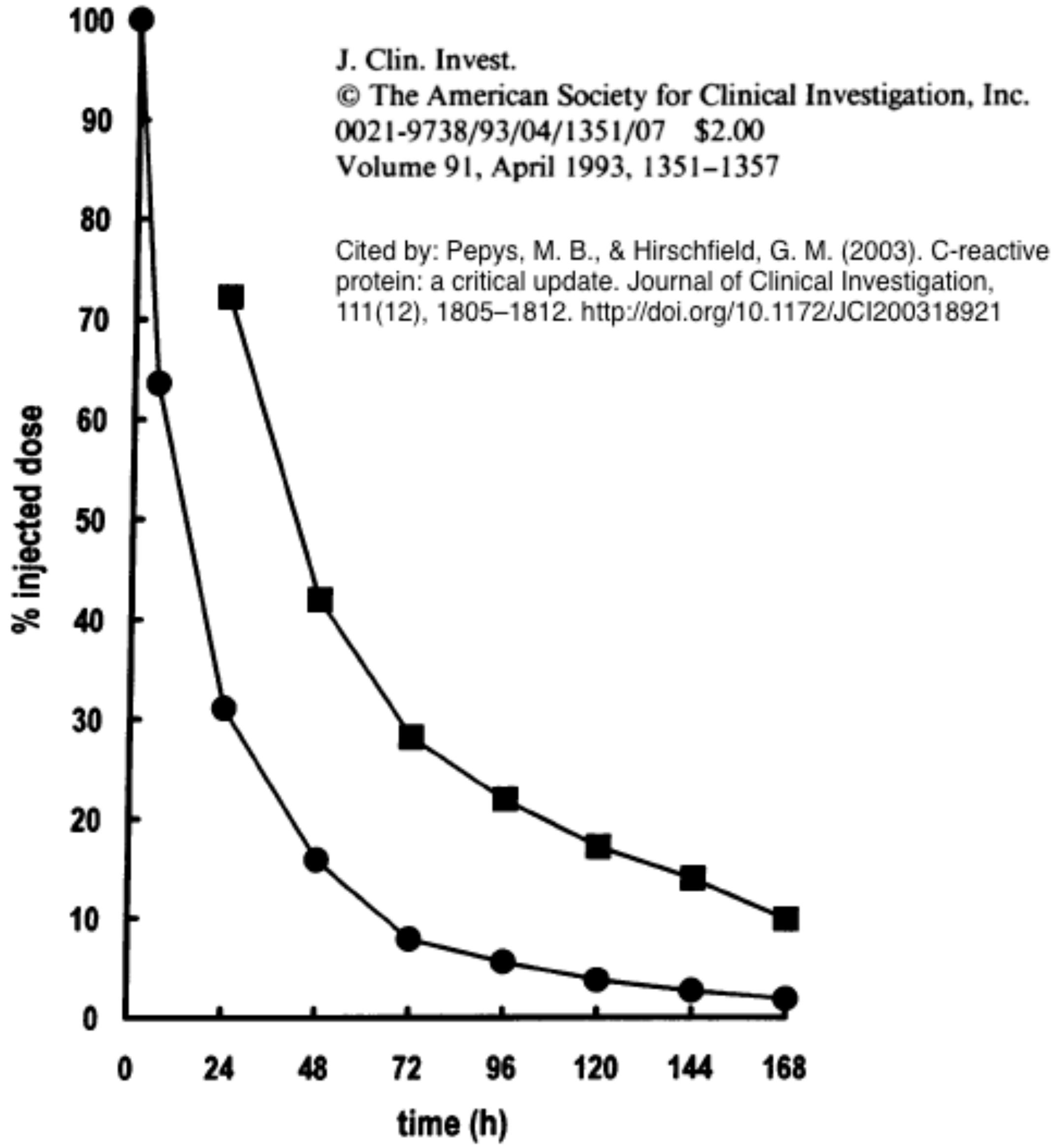


Figure 1. Clearance of ^{125}I-human CRP in vivo in normal controls. Each point represents the arithmetic mean of the values in eight healthy normal subjects. The standard deviations fell within the range 0.6–6.4% for plasma clearance (●), and 4.7–7.1% for whole body retention (■).

Proposed blood panel markers

It would be desirable, if the pharmacokinetics and costs fit the protocol schedule and budget, to add additional data including a panel of inflammation markers including IL-1β, IL-6, IL-10, and TNF-α and an oxidative stress panel.

While those biomarkers include indications of conditions related to Type 2 diabetes and carcinomas, it would also be desirable to include measurements of leptin, and appropriate members of the VEGF and FGF families.

Finally, given that Bisphenol A is an estrogenic compound and phthalates are anti-androgenic, a measurement of the androgen/estrogen ratio for all test participants would be appropriate because Bisphenol A is associated with hormone related cancers including breast and prostate.[22]

PSAs tests for men should be included as well since a study published in 2014 found exposure to bisphenol A correlates with early-onset prostate cancer[23] and that BPA exposure may lower serum PSA levels, thus complicating diagnosis. *See also: Role of diet in prostate cancer: the epigenetic link*[24].

Regardless of which tests may be appropriate and affordable (beyond CRP) this revised protocol will save significant time and cost.

New testing regime: Epigenetic profile, BPA serum dropped, gut microbiome added

The epigenetic profiling will be eliminated as a budget move unless a suitable co-investigator or testing source can be located and additional funds allocated.

One potentially useful result from the original protocol was investigating the health effects of reduced BPA and phthalate concentrations on a diagnostic blood panel and comparing the results with BPA serum and urine concentrations. However, The BPA serum testing is included in the revised protocol but may also need to be eliminated for budgetary reasons.

As previously noted in the protocol, some controversy has lingered over the presence of free BPA in serum. Many investigators -- primarily traditional toxicologists -- have insisted that free serum BPA does not exist and that all BPA is absorbed by digestive tract mechanisms, metabolized by the liver and excreted.

The controversy exists because alternate pathways for dietary BPA to enter the bloodstream have been proposed including transdermal absorption by buccal tissues including the dental gums.

Samples for BPA serum testing. if retained in the testing schedule, would be obtained at the same time as the blood panel.

Gut Microbiome added

One additional testing method proposed for this revised protocol includes gut microbiome measurements.

The science of gut microbiome measurements and the ability to sample and analyze the results conveniently and inexpensively has advanced greatly in the past three years.

In addition, development of clinical diagnostic techniques have also made great strides.

Therefore, the relationships among these methods: diagnostic blood panel, urine, and gut microbiome, offer the possibility of yielding novel and significant health effects of BPA and phthalates on gut biome composition.

Data gathered from the use of these methods could be the subject of a separate paper.

Economics: Testing for BPA Only

In addition, testing will be restricted to BPA. Phthalates and other endocrine disruptors are frequently detected together in the same samples. In this case, BPA becomes a "marker" for chemicals having similar health effects.

Both Bisphenol A and phthalates are rapidly metabolized[25] and decline rapidly within 8 hours, which makes a three-day cycle appropriate for testing.

While one important study indicated that BPA had a longer half life, the methodology of that study indicated that a slower decline could be due to release from adipose stores or continual contamination from non-food sources[26]. Significantly, the three-day period for each diet segment, and daily urine BPA testing, should accommodate data for both studies.

Phthalate testing would be valuable, but is prohibitively expensive given that its ubiquitous environmental presence requires specialized and extensive laboratory precautions which vastly reduces the number of qualified testing facilities.

Data also indicate[27] that Bisphenol A will serve as an appropriate marker for phthalates because urinary concentrations of both decrease together with very similar data curves[28] for most (but not all) phthalates. In addition, phthalates, parabens, bisphenol A and triclosan have shown similar concentration correlations[29].

Figure 1

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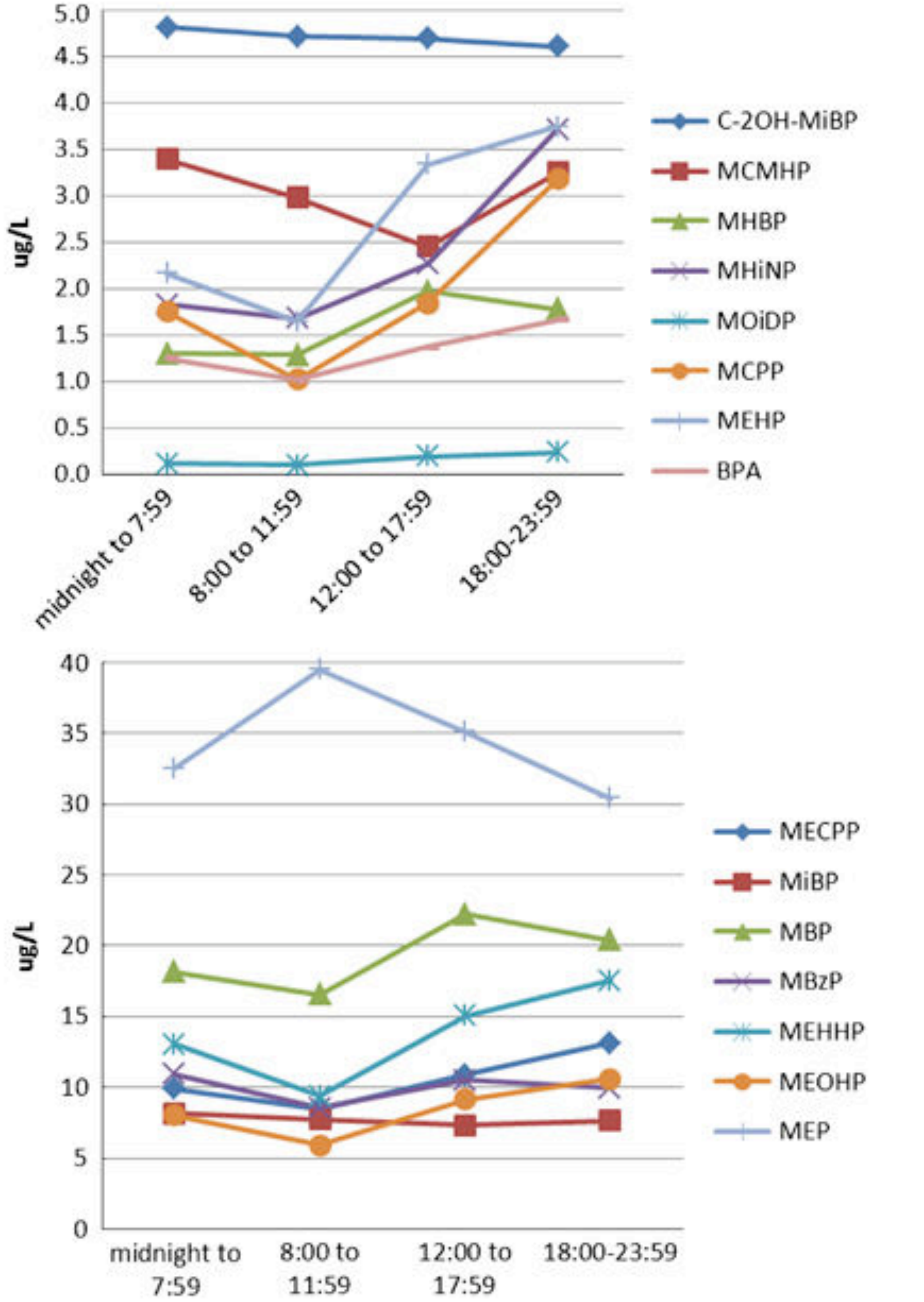
doi:10.1038/jes.2014.65



Specific gravity adjusted geometric mean chemical levels by time of day.

Focus on reproducibility as a function of usefulness, practicality, cost, and transparency.

Indeed, the inability of other investigators to reproduce previous dietary studies on this subject (see discussion below) can be laid at the feet of the numerous confounding factors the current researchers have thoroughly investigated in an effort to source appropriate food and beverage for the study.

Those previous dietary studies attempted only to correlate test subject urine concentrations of BPA metabolites. Our study, on the other hand, intends to extend the knowledge gained in those by correlating BPA and phthalate levels to direct human health effects as determined by accepted laboratory blood tests and other indicators.

Lessons from the Non-Replicability of Previous Studies

There have been five dietary intervention studies regarding BPA, phthalates, or both.

Three are not relevant because of fundamental flaws:

1. One involved members of a single family, all of whom had very low baseline BPA levels (some below LOD) because of an existing habit of avoiding plastics: *Life without plastic: A family experiment and biomonitoring study.*[30]
2. A second recruited a cohort of guests at a spiritual retreat: *Influence of a five-day vegetarian diet on urinary levels of antibiotics and phthalate metabolites: a pilot study with "Temple Stay" participants.*[31]
3. The third was self-administered by high-school students given a list of foods to avoid: *An engaged research study to assess the effect of a 'real-world' dietary intervention on urinary bisphenol A (BPA) levels in teenagers.*[32]

Of these, only two are relevant:

1. The first broke new ground as the first of its kind with solid scientific underpinnings: *Food Packaging and Bisphenol A and Bis(2-Ethyhexyl) Phthalate Exposure: Findings from a Dietary Intervention.*[33]
2. The second attempted to replicate the first study. And found that some of the participants had higher levels of BPA and phthalates after intervention: *Unexpected results in a randomized dietary trial to reduce phthalate and bisphenol A exposures*[34].

According to Sathyanarayana *et al.* (2013)[35], "tested food ingredients from the same suppliers but were unable to test the exact same food ingredients used in the intervention because testing was performed 3 weeks after the study was completed."

In the absence of data, the investigators reasoned that the unexpected increases came from far more than food contact material and reasoned that "the food supply is systematically contaminated...."

Finally, they concluded "Federal or industry wide regulation aimed at reducing phthalate and BPA concentrations in foods may be the only effective mechanism to ensure the food supply is safe from contamination."

See Appendix 3 for a discussion of food contamination sources which occur prior to contact with plastic packaging materials.

Learning from the replication efforts of the past

This revised protocol has been expanded to address the confounding factors discovered above along with numerous other serious problems discovered by investigators over the past 2 1/2 years.

Our research has revealed numerous contamination source and factors that afflict every level of the food chain from production to preparation for consumption.

Therefore, the lessons of Sathyanarayana *et al.* (2013) comprise the first of several novel recommendations/innovations to improve replicability for food intervention studies

Current investigators took careful note of the following conclusions of Sathyanarayana *et al.* (2013) who had worked "to develop a controlled dietary replacement focused on fresh, organic, and local foods without the use of plastics.

- "We conclude that currently accepted methods to reduce phthalate and BPA exposures (both dietary replacement and written recommendations) may not lead to anticipated changes in urinary phthalate and BPA concentrations."
- "Our study team undertook several measures to ensure that our dietary replacement would consist of fresh, local, organic food prepared, stored, and transported without plastics. For example, the caterer called local farms and asked that fresh foods be delivered in wood crates instead of plastic cartons.
- "All dairy was delivered in glass (milk/cream) or paper except for one delivery of butter in plastic. In the kitchen, the cooks prepared dishes without the use of plastic utensils, appliances, or storage containers.
- "Families were instructed to eat using ceramic dishes and metal utensils. We provided glass containers for food storage and transport. Despite these measures, DEHP metabolite concentrations increased significantly ...."

And, yet, those efforts were not enough.

We therefore conducted a thorough investigation to discover and circumvent every possible contamination in the food chain.

Reproducibility depends on the availability of the exact same foods, prepared the exact same way

Creating a practical, useful study which could be economically replicated must focus on foods which are widely available nationwide. As much as the investigators would like to conduct the study with the minimum-possible contamination, the "enhanced organic" sourcing would make it both expensive and impossible to replicate.

This is because replication requires total data transparency and that requires (among other things) the ability to source materials used in the original study.

Previous dietary studies of BPA and related endocrine disruptors have not made that information available.

Those studies have given instructions to food preparers to use only "fresh" ingredients and to avoid any plastic contact. However, specific food sources and the details of their production are not available. Neither are specific cooking protocols or the identities of the utensils, pots, pans, cleaning regimen (surfactants an issue), recipes, ingredients (processing & methyl contributors an issue).

In addition, no details are available on non-food-contamination variables, environmental conditions or precautions regarding the avoidance of those.

Data regarding those conditions cannot account for the wide variability of contamination in the growing, processing, and sourcing stages. As a result, instructions in previous dietary studies account only for contamination transfer from food packaging materials and preparation.

No studies have been found that parse the growing, production, and processing contamination from that of food contact materials and preparation.

This study cannot afford to measure all of those disparate contributions directly, but will attempt to control for that lack of information and facilitate replication using the guiding principles for enhanced organic, previously described above.

Obtaining food only from sources with nationwide availability and will make that full data available.

Treat the kitchen as a laboratory and pots, pans & utensils as lab equipment.

Along with enabling replication by controlling for the systematic contamination of the food supply, we will present detailed methods and procedures, preparation, apparatus standardization, cleaning and maintenance.

All of those previous details have been omitted from all previous studies.

The precise manufacturer, model, and size of pots, pans, dishes should be disclosed as well as food preparation utensils, and appliances. The source vendor should be noted.

To minimize incidental contamination, pots, pans, and their handles should be glass and/or stainless steel and un-coated (no Teflon or other non-stick treatments).

Cooking, serving and eating utensils should be stainless steel. Wooden utensils may be used for scraping if needed.

Glass must be used for all serving items including plates, bowls, cups, and drinking glasses. This practice avoids the possibility of incidental contamination from unknown substances leaching from glazes.

Effort must be made to assure that the lowest-priced suitable items are used and that exact duplicates are widely and easily available to encourage replication.

Automatic dishwashers may be used. Appropriate residue-free cleaning agents such as one of the Extran products from Millipore/Sigma, or those from Alconox may be used.

Several cycles using the detergent should be run to remove any residues present from commercial household products. The number of those cycles should be noted along with whether the input water to the dishwasher is filtered and whether it is fed by plastic pipes. The type of plastic should be noted.

Carbon filtered water is desirable, but the volume required is impractical and too expensive for most research efforts.

Cleaned items must be followed by a rinse in properly carbon-filtered water to remove any remaining residues including those left by the unfiltered water utilized by the home dishwasher. No plastic sponges or polymer-based towels or cloths may be used.

After rinse, items should be air-dried on a stainless steel rack.

They should not be dried with a towel. Synthetic fabrics and even those from natural fibers are frequently contaminated during manufacturing.[36]

Additional contamination can come from chemicals used in laundry detergents, softeners and dryer sheets that contain phthalates used as carriers for fragrances.

In addition, home dryer drums may be coated with stubborn layers of contaminants from drying fabric contaminated by detergents and from transfer from designs imprinted on tee-shirts and other clothing. Most inks used to print the designs on fabric are phthalate-based.

Recipes are laboratory procedures

Cooking is a chemistry procedure which must be described -- and adhered to -- by cook/chemists.

Ingredients are reagents and must be obtained from specified, trusted sources, measured precisely, and added at the proper time at the proper concentrations.

Recipes are experimental procedures that must be measured and timed precisely.

All of those details are analogous to laboratory data provided by in non-dietary studies which provide the specific names of reagents and apparatus along with formulae and other information necessary for experiment replication.

All of those details will available with other study data and supplemental material.

And while expense prevents this study from testing the precise contamination concentrations or measure nutritional profiles, the use of the same materials from the same sources offers an opportunity to increase the likelihood of successful replication.

Reproducibility: Reducing non-food exposures (NFEs)

Sathyanarayana *et al.* (2013) posited that substantial non-food exposures such as those with personal care products could mask BPA and phthalate reductions from dietary intervention.[37]

However, a quick picture of the complexity of NFEs can be illustrated by this diagram from *Endocrine Disruptors and Asthma-Associated Chemicals in Consumer Products*[38]*:*

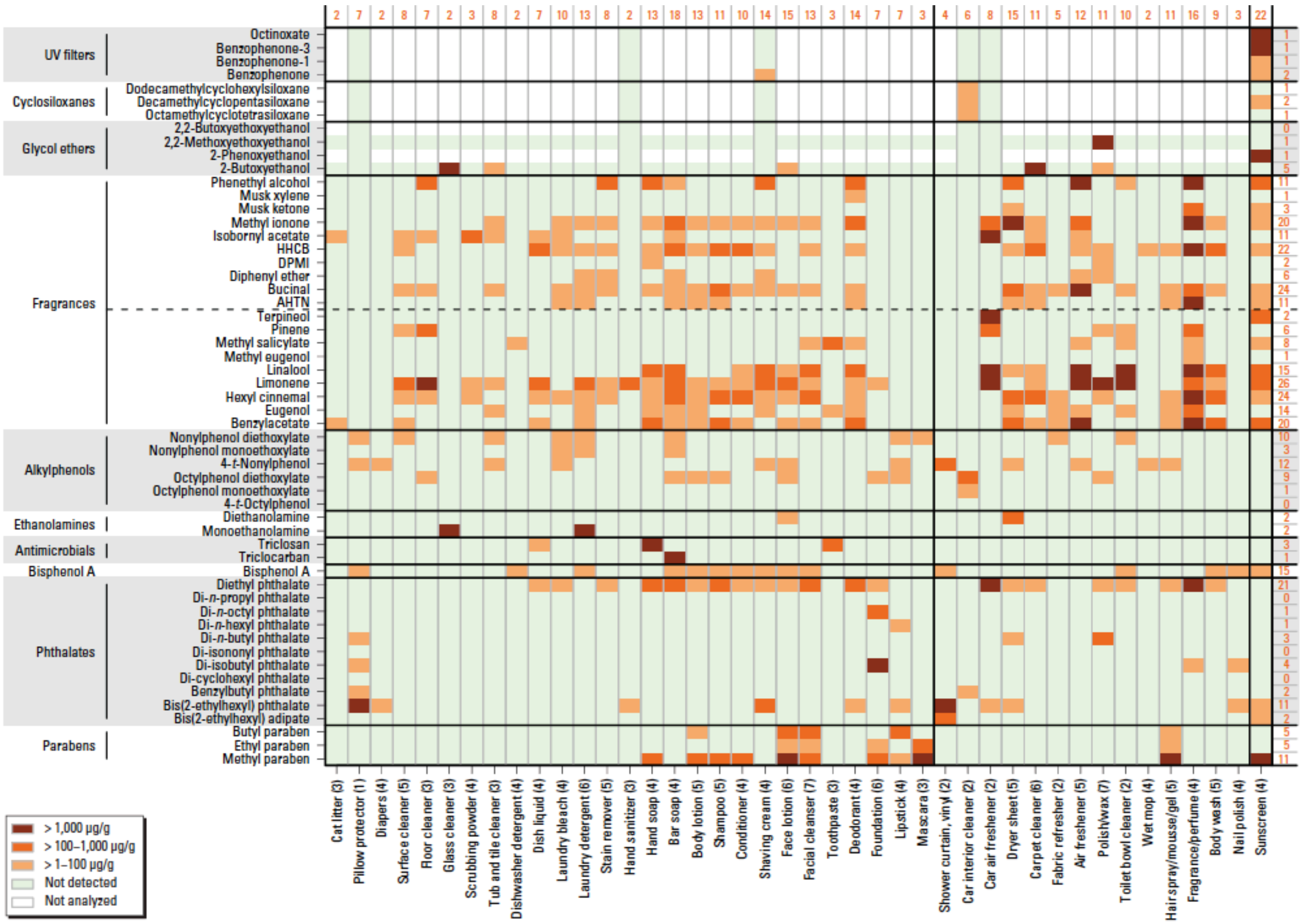


Figure 1. Concentrations of target compounds (left) in conventional consumer products (bottom) by product type. Compounds are grouped by chemical class, with natural and synthetic fragrances distinguished by a dashed horizontal line within the figure. Numbers in parentheses after product type indicate number of products in the composite. Numbers at the top of the figure indicate the number of chemicals detected in each product type; numbers on the right indicate the number of products containing each compound. The first 27 product types (left of the solid vertical line) and the last product type (sunscreen) are also shown in Figure 2, but the remaining product types differ.

Diagram from: Environ Health Perspect; DOI:10.1289/ehp.1104052 - Endocrine Disruptors and Asthma-Associated Chemicals in Consumer Products

An extensive discussion of NFE contamination sources may be accessed in Appendix 4.

Triaging NFE elimination

Given the impossibility of avoiding BPA, phthalates, and other harmful chemicals in the environment, reproducibility of studies must focus on the practical reduction of known exposures reducing those exposures that are:

1. most easily identified and,
2. practical to control,
3. likely to produce maximum reduction via minimum study subject effort, and
4. can be adequately documented and replicated.

An ideal scenario would be to conduct trials in a well-defined residential/dormitory setting where all study subjects experience near-identical environmental conditions for the entire term of he study.

However, expense and practicality dictate that many studies must engage subjects who will modify their diets while living in their own homes as well as engaged in multiple additional sites for work, school, shopping, and recreation.

Because of those practical limitations investigators should -- to the best of their ability -- thoroughly document the environmental circumstances under which a dietary intervention is conducted. This should include questionnaires about known exposure sources for their:

1. External environment (home, work, school, recreation including floor surfaces) and,
2. Personal environment (pharmaceuticals, personal care products, appliances, fabrics for clothing and bedding, presence of plastic dental and other implants and prosthetics, etc.).

Participants with excessive and/or uncontrollable external environmental exposures will be excluded.

Study subjects should then be counseled on contamination sources and given a checklist of specific controllable sources to avoid during the trial.

Investigators should schedule frequent reminders and follow-ups with each participant to assess and assure the best possible compliance.

As a potential starting point for assessing personal environmental exposures, investigators will consider the EDC Footprint Calculator developed by the Pennsylvania State University Extension Service. While this Excel version was designed to offer an indication of contamination products found in municipal wastewater and is not all-inclusive, it could be modified and updated to better serve the purposes of this study, or future efforts.

Personal environment controls

As the above chart from "Endocrine Disruptors and Asthma-Associated Chemicals in Consumer Products" illustrates, most personal care products contain relevant chemical contaminants that can potentially confound this study's chosen health effects markers.

Select three-day reduction actions for personal environment:

NOTE: To make these reductions possible and assure the greatest possibilities for reproducibility, study subjects must be healthy, non-smoking adults without recent dental work or invasive medical procedures. Male subjects should not have body fat more than 32% for women and 25% for men. Subjects should not be taking any medicines or dietary supplements other than low-dose or 325 mg aspirin.

- Use recommended toothpaste without Triclosan and reduced or zero-levels of contaminants.
- No mouthwash.
- Uncoated nylon fiber dental floss (no plastic strips).
- No hand creams or lotions.
- No perfumes or any other products containing fragrances.
- Use recommended shampoo with reduced or zero-levels of contaminants.
- Use recommended hand soap with reduced or zero-levels of contaminants.
- No cosmetics.
- No hair color treatment.
- No teeth whitener.
- No hand sanitizers.

- Use recommended deodorant.
- No contact lenses. Use of eyeglasses only.
- No contact with cash register receipts.
- No hair spray, gel or other treatment.
- No body wash.
- No sunscreen.
- No nail polish.
- No tee-shirts, sweatshirts, or other clothing with printed designs.

In addition, subjects must note synthetic composition of clothing and bedding items. That data may be valuable for investigating possible confounding factors.

External environment controls

In addition to food contamination issues, home, workplace, and public spaces also provide significant -- but widely variable -- exposure to humans to endocrine disruptors, CECs and, other environmental chemicals[39].

- Do not use ink jet printers, gel rollerball pens, ballpoint pens.
- No use of volatile adhesives such as rubber cement or from spray cans.
- Use no household cleaners.
- No reusable, non-paper grocery/shopping bags with printed designs.
- No plastic wallets/purses/backpacks.
- Inform investigators if beds or pillows have plastic covers.
- No air fresheners.
- Avoid areas irrigated with recycled wastewater.
- Do not get into a vehicle until the interior has been thoroughly ventilated with outside air.
- Ride in vehicles with all windows open. Do not use an air freshener. Avoid new vehicles and those whose interiors have been recently cleaned commercially.
- Wear only those clothes that have been washed with phthalate-free laundry detergents.
- Unless a phthalate-free laundry detergent has been used previously, run two loads of towels, then dry.
- If fabric softeners have been used in the dryer, run two additional loads of towels after decontaminating washer and dry them in the dryer to reduce accumulated phthalate levels.
- Avoid bathing in homes whose water supply is delivered with plastic plumbing: PVC, Pex etc.

Dust particles

Household dust presents a significant confounding factor because it is the residual detritus from many environmental sources shown to contain BPA, phthalates, and other chemicals relevant to this study: *Phthalates in Indoor Dust and Their Association with Building Characteristics*[40]. That study contains a home materials inventory that will be adapted for the study subject questionnaire. See also *PM 2.5*[41].

Reduction actions for dust particles:

Frequent and thorough cleaning (before the start of phase 4) of all surfaces (floor, walls, ceilings) with a mop dampened with water only. No cleaning compounds which may introduce their own unique, unknown, and uncontrollable contaminants.

If the cleaning/dusting is performed by the test subject, then tasks should be performed wearing an N-95/p100 mask/filter. Significantly, masks of that particular quality do not filter all of the most hazardous particulates -- those in the 2.5 micron (PM 2.5) and smaller size.

The PM 2.5 size class is most likely to reach and be retained by alveoli and thus have direct access to the bloodstream.

As a consequence, PM 2.5 is implicated in a wide range of serious health effects[42,43,44].

The type and age of the HVAC system should be noted as well as the type of filter used and the ducting materials (metal versus plastic).

Immediately after dusting, the HVAC filter should be changed and the system fan run continuously for four hours to collect as much dust as possible which has been stirred up from cleaning. A fresh filter should then be installed.

The slightly-used filter may be preserved for future use if handled gently and immediately inserted into a suitably-sized plastic bag. Investigators note the ironic necessity to use plastic to help protect against plastic.

Study subjects who already have a HEPA-class air purifier should report the make, model, capacity and whether it is portable or installed with the HVAC system. If portable, the location should be noted along with the distance from the HVAC air return.

More supplemental references may be found in Appendix 5.

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APPENDIX 1 - Reproducibility

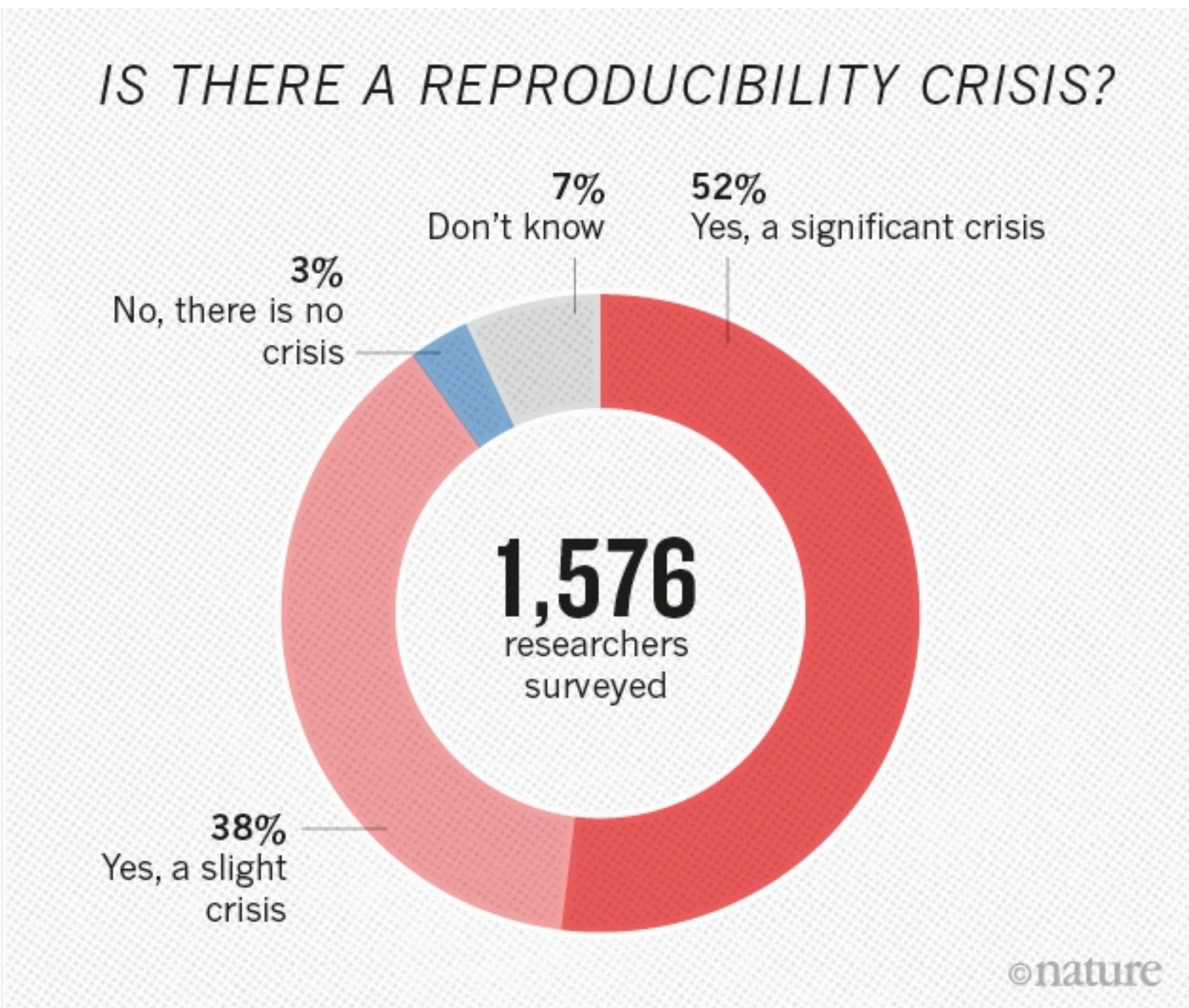
REPRODUCIBILITY - *THE SCIENTIFIC PROBLEM THAT DEMANDED ENHANCED SOURCING OF THE STUDY DIET*

Reproducibility + Confounding factors drive changes, increase complexity, & costs

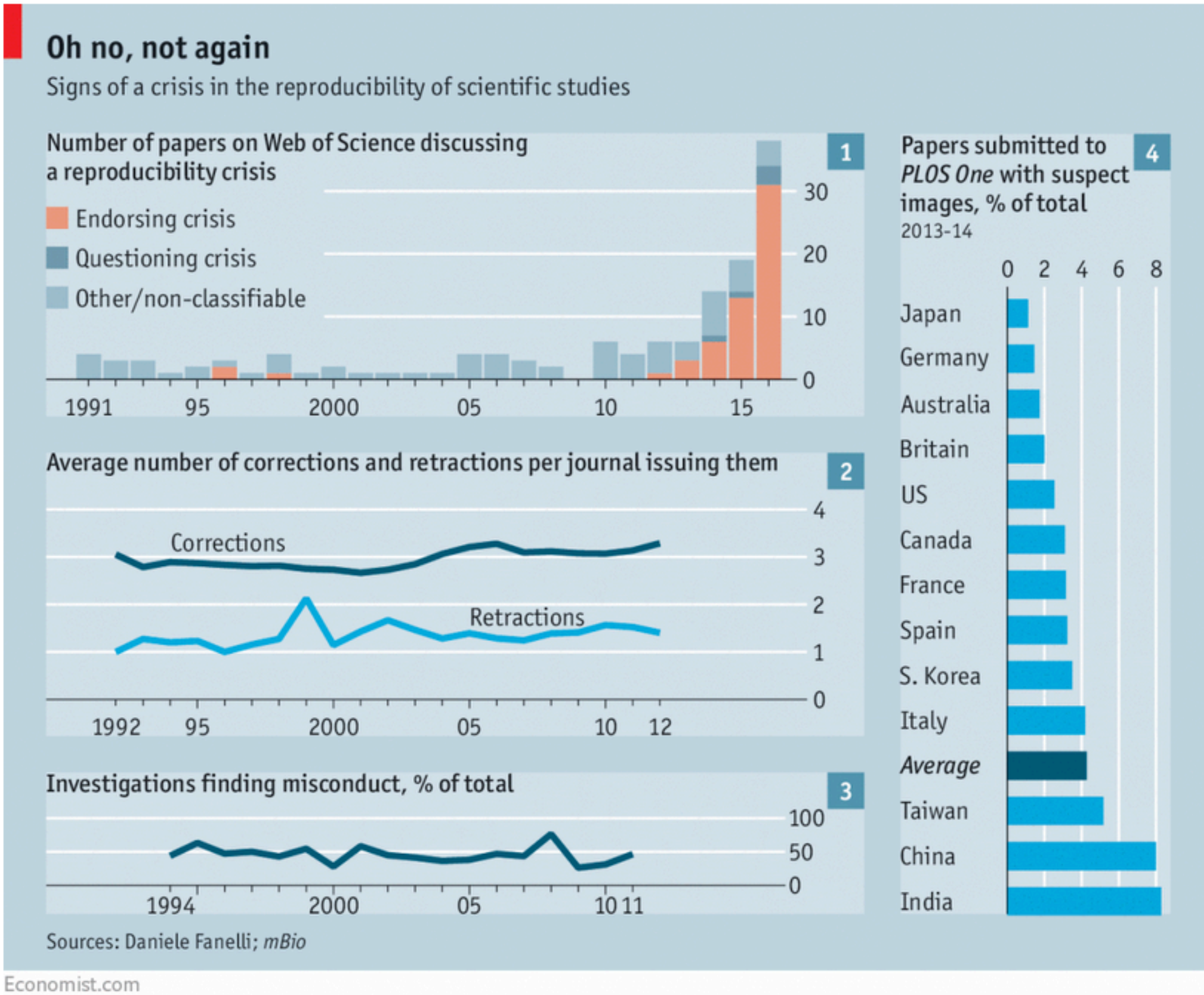
Reproducibility is the acid test of properly done studies that produce valid data. In the past couple of years, the "reproducibility crisis" has been the subject of numerous scholarly articles and comments.

The most data-based is this one from Nature (1,500 scientists lift the lid on reproducibility Survey sheds light on the 'crisis' rocking research.).

That article found that: "More than 70% of researchers have tried and failed to reproduce another scientist's experiments, and more than half have failed to reproduce their own experiments."



While data do not indicate a substantial rise in irreproducible results, the persistence of non-replicable studies is unacceptable. We should not add to that phenomenon.



See also:

- [When Quality Beats Quantity: Decision Theory, Drug Discovery, and the Reproducibility Crisis]()
- [Opinion: Is science really facing a reproducibility crisis, and do we need it to?]()

APPENDIX 2 - Detailed parameters of intervention diet selections

Water

All water consumed and/or used for cooking, washing, drinking or used to irrigate self-grown plants will be obtained from a commercial device using a solid-block carbon filter and certified by NSF for reduction of BPA and phthalates. One such device is the Aquaversa filter from Multipure which uses a carbon block filter that lists BPA among its contaminant reduction list. The list does not mention phthalates. However, the list does cover many chemical with similar phenolic structures.

If study funds are available, it would be valuable to determine BPA and phthalate levels in the water water before the filter and afterwards.

In addition, independently published research indicates that other types of carbon filters are effective in reducing many harmful compounds including organic chemicals.

- Effects of activated carbon types and service life on removal of endocrine disrupting chemicals: amitrol, nonylphenol, and bisphenol-A.
- Adsorption characteristics of selected pharmaceuticals and an endocrine disrupting compound—Naproxen, carbamazepine and nonylphenol—on activated carbon
- Bisphenol A Removal from Water by Activated Carbon. Effects of Carbon Characteristics and Solution Chemistry, Environmental Science and Technology, 39 (16) (2005), pp. 6246-6250

Beverages

Coffee

Only locally roasted and ground beans will be used.

Provider will be selected on the smallest amount of plastic involved. Beans and grounds will be handled with metal or glass only and packed in glass jars.

Beans will be ground in a mill with no plastic components.

The beans will be prepared using either an all glass and stainless steel French press or a stainless steel percolator with all metal parts.

Also acceptable is the Moka pot-style espresso maker or a pour-over, glass and metal coffee maker with water from an all metal tea kettle. All metal wire basket for grounds must be used, no filter paper.

If an automatic drip system can be located with no plastic ever touching the water or coffee stream, that will be obtained and used.

The weakest links in drip coffee makers that appear to be all glass and/or metal usually lies in plastic tubing that connects the heating element to the water reservoir, the hot water application tube, and the filter basket.

Tea

No tea will be allowed. Like spices, the extensive harvest, curing, processing, and packaging offers many contamination routes.

Also like spices, the tiny fragments that compose tea increase the surface area capable of acquiring chemical contamination.

Soft drinks

Highly processed. Not allowed in the study diet.

Fruit juice

No commercial juices allowed. Highly processed. Not allowed in the study diet.

Freshly prepares using no plastic contact. In general, whole fruits are a healthier alternative to juices.

Beer and wine

No commercial products allowed. All are extensively processed using plastic.

Sourcing ingredients

All food items will be sourced from the provider. All provider locations will be personally visited and inspections made of their premises, equipment and processes.

Beef, lamb, chicken, pork, fish

Minimum standards: Organic certification, no plastic in growing, harvesting, handling, or packaging. All animals must be free-range.

Even if allowed by exceptions to organic regulations: No commercial fertilizers, pesticides, or recycled wastewater irrigation are allowed in this study. No irrigation of pasture and feeding areas is preferred. Drinking water from well or municipal water only. No PVC or other plastics.

Beef and lamb must be grass-fed and comply with AGA Statement of Best Practices.

Preference given to non-irrigated pasturing. For welfare of animals, supplemental hay is allowed but must come from non-irrigated pasture.

Possible source: Crowd Cow

Slaughter standards

Must be humane.

Solid cuts of meat only. No sausage or ground meat.

Slaughter to avoid all plastic contact unless absolutely vital for health and hygiene. Nitrile gloves.

Finished cuts to be placed in glass containers covered with aluminum foil (not in contact with meat) and finally sealed with a plastic lid.

Beef, lamb & goat

Lean cuts (minimum marbling) on beef and lamb. Lower fat content helps minimize lipophilic content.

Visible fat to be removed before cooking to minimize lipophilic concentration.

Chicken

Skin to remain on chicken, to be removed before cooking to minimize lipophilic concentration. Breasts only for chicken.

Pork, fish

Not included in the study diet.

Diet and subsequent flesh contamination are extremely hard to control or monitor.

Dairy

Same water, feed, and pasturing requirements as beef, lamb, and goat.

Udder and teat cleaning and treatments for animal welfare and human hygiene must be examined for plastic exposures and contamination minimized.

Milking must be done preferably by hand or using milk machines certified as BPA and phthalate-free. Nitrile gloves to be used. All collected milk must be in stainless steel vessels. Filtering stages cannot use polymer filters. Separation, homogenization (if any) and pasteurization must be plastic free. Glass containers must be used for bottling of milk.

Cream gathered during the separation process will either be used for cheese or discarded to minimize lipophilic contaminate concentration.

Cheese will be made using milk prepared as described above. Preference will be given to low- or moderate-butterfat cheeses.

The cheese process will use stainless steel in the initial heating processes. Curds will be gathered and drained in stainless-steel wire baskets. The whey will be discarded.

Drained curds will be pressed in stainless steel molds. Finished cheese will be packed in aluminum foil then placed in Ziploc-type airtight containers.

Note: Ziploc claims to be BPA free but has not addressed phthalates. It is also unknown whether "BPA free" means a switch to a Bisphenol analog such as BPS.

Fruits & vegetables

All vegetables and fruits must come fresh from an organically-certified source irrigated by well water or suitably filtered tap water.

Recycled municipal wastewater (increasingly used for food crops) is unacceptable.

All irrigation must also be done using metal containers. No plastic drip lines or emitters

No commercial fertilizer can be used.

No pesticide can be applied including substances that are approved for organic use unless they have been examined for -- and free of -- adjuvants, surfactants, and other auxiliary chemicals that may have endocrine-disrupting or other harmful effects.

The soil in which plants are grown cannot come from a source that uses commercial fertilizer amendments, or biosolids (sludge from municipal sewage treatment plants) which is also increasingly used on food crops.

The vegetables must be harvested and processed by hand without using polymer gloves other than nitrile. No conveyor belts, plastic tubs, or containers are allowed.

Vegetables must be placed in a glass or steel container for delivery, not in a plastic bucket or in cardboard. Phthalates are commonly used in the inks on paper and cardboard and are found in recycled paper, cardboard, and packaging materials.

Salad dressings will be made with lemon or other citrus juices, not vinegar.

Bread and cereal

Bread will be sourced directly from a baker who has ground the grain without any plastic contact including utensils, dough rising pans or wrapping. Paper for wrapping cannot be recycled because of phthalate inks commonly used in packaging printing.

Plain bread without seeds, nut, spices, or other components such as raisins may be allowed.

Corn-based foods must be from non-GMO corn raised organically and fried in oil which is similarly organic and non-GMO in origin. It is unknown at this time whether such healthier alternative is available.

Commercially produced cereals are not allowed on this diet due to extensive processing involved. Rolled oats may be allowed if as suitable source can be found.

Edible Oils

Given the lipophilic nature of BPA, phthalates and many other harmful environmental chemicals, finding an acceptable source of edible oils is one of the most difficult.

This is aggravated by the fact that producing edible oils requires many processing steps to separate the desired lipids from the pulp and aqueous portions of the source fruit, nut or seed.

Because of its local ready availability, this diet will use first cold press olive oil.

Locally produced olives will, ideally, be non-irrigated.

The Olive fruit fly is endemic in California and other wine producing regions around the world. There are a variety of methods for controlling infestations including baits, traps, attractant strips and certified organic pesticides such as Spinosad and Surround. (UC Pest Management Guidelines).

Despite their organic-certified status, both Surround and Spinosad contain toxic chemicals and proprietary chemicals whose identities are trade secrets and not disclosed. Because of this, olives treated with these are unacceptable.

Untreated olives or those produced in groves using baits, traps, or attractant strips are acceptable.

Olives undergo a washing process -- a water rinse -- before pressing. There are many other stages, some of which commonly use plastic components in the process.

Visits will be made to determine which oil press minimizes the use of plastic components.

Nuts & Spices

Almonds will either be hand-shelled or obtained from a commercial processor directly from the shelling process before encountering plastic materials in the processing and packaging processes. Slight contact with plastic may be encountered as almond nuts exit the sheller into glass or metal containers.

We will grow our own spices except for whole black/green/red peppercorns which will be ground in a glass, ceramic, or metal peppermill.

Spices will be irrigated with carbon-filtered water.

Spices will be diced with a knife on a wooded cutting board or ground in a grinder without contact with plastic.

Sugar and sweeteners

No refined sugar or sugar substitutes will be allowed in this diet. Sugar undergoes extensive processing from harvest to store and has too many possible contamination sources to be allowable.

Acceptable is raw, organic, unprocessed honey from blossom sources distant from non-agricultural regions where pesticides, fungicides, and herbicides are applied.

Candy, snacks, protein- & meal-replacement bars

Highly processed. Not allowed in the study diet.

We will avoid products known to have GMO ingredients.

While the debate on potential negative effects has not reached a scientific consensus, the debate over the significance of regulatory limits and low levels (nano-and picomolar) parallels earlier work done on endocrine disruptors.

GMO ingredients raise two issues for this study:

(1) GMO crops are designed to withstand levels of pesticides such as glyphosate which would kill non-GMO plants. As such, glyphosate is becoming common in foods sold in the marketplace

> Rubio F, Guo E, Kamp L (2014) Survey of Glyphosate Residues in Honey, Corn and Soy Products. J Environ Anal Toxicol 4: 249. doi: 10.4172/2161-0525.1000249
>
> Glyphosate residues in Swiss market foods: monitoring and risk evaluation Otmar Zoller , Peter Rhyn, Heinz Rupp, Jürg A. Zarn & Christoph Geiser Pages 83-91 |

Received 14 Sep 2017, Accepted 17 Dec 2017, Accepted author version posted online: 28 Dec 2017, Published online: 23 Jan 2018

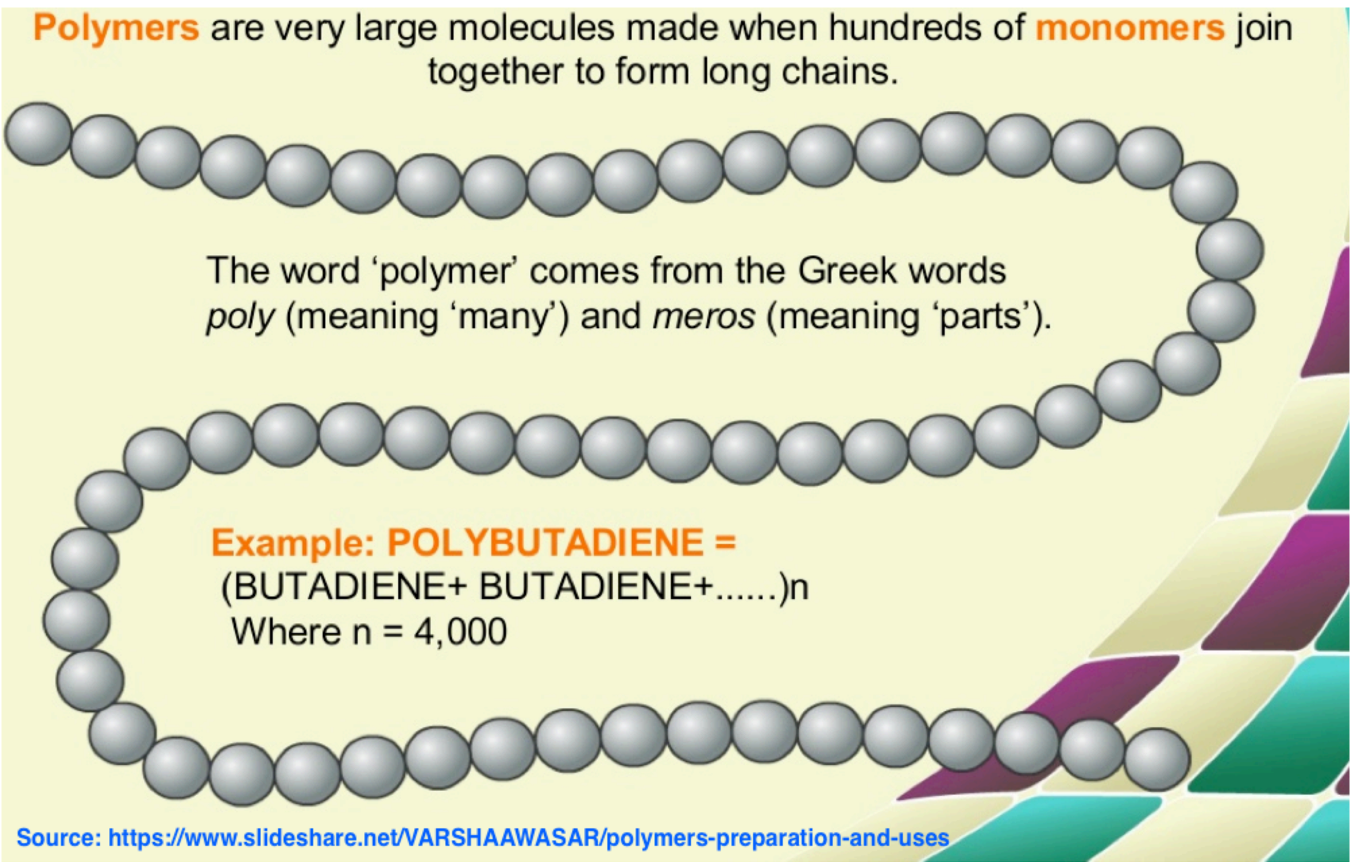
(2) Evidence is accumulating that GMO plants may not be as safe as initially warranted.
Zdziarski, I.M., Carman, J.A. and Edwards, J.W. (2018) Histopathological Investigation of the Stomach of Rats Fed a 60% Genetically Modified Corn Diet. Food and Nutrition Sciences, 9, 763-796. https://doi.org/10.4236/fns.2018.96058

APPENDIX 3 - How does the food chain get contaminated?

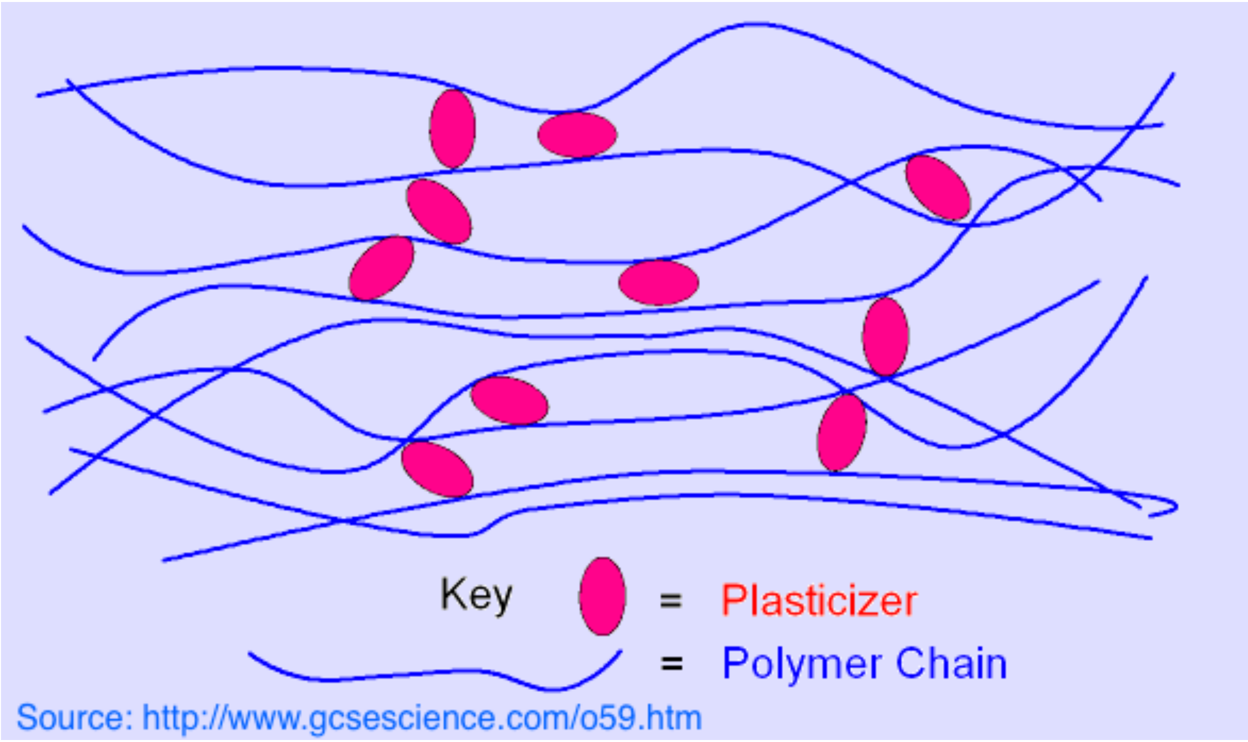
BPA & phthalates (and other plasticizers) migrate, leach and flake from plastics

BPA & phthalates migrate, leach, and flake off of plastics primarily because they are not chemically bound to the plastic.

It's important to understand that any specific plastic is a mixture of one or more polymers along with a variety of additives like BPA and phthalates that are added to provide desired characteristics such as color, strength, rigidity or flexibility and other qualities of the finished plastic.



In some ways, polymers are like dry cement. Water can be added, and a hard substance results when it cures. Aggregates like sand and stone are mixed in to provide strength. Steel rebar is added for flexibility and tensile strength. Polymer fibers offer flexibility. Dyes are added for color.



An exothermic chemical reaction takes place when water is added to cement. But the sand, stones and re-bar are not part of the chemical reaction.

Just like plasticizers added to plastics, the additives to cement and not covalently bound to the concrete. Instead, those additives -- whether to concrete or a plastic -- are physically confined when the mixture cures, but can separate under many circumstances.

Rebar, stones and even sand are massive compared with the tiny sizes of the plasticizer and additive molecules that give polymer chains the desired characteristics. Because of this, additives can migrate among the polymer chains and -- when they reach the surface of the plastic -- can easily leach or simply fall out of the plastic like pebbles from old concrete.

What helps additives escape from the plastic?

Additives escape from plastic and enter the food chain or directly into people's bodies through a combination of actions that include:

Mechanical- Scraping, friction, bending, stretching, twisting or compressing plastic promotes microfractures that speed additive particles toward a surface. Friction between plastics or other components can create fine dust particles which accelerate the release of additives.

Mechanical stressors are particularly applicable to conveyor belts, squeezable condiment containers, plastic utensils in contact with plastic bowls or paper plates (most of which have a plastic coating), plastic gloves, and plastic beverage containers.

Children frequently treat their plastic toys and other objects with less than tender loving care.

Light - Degrades plastic and accelerates the release of plastic additives.

Chemical action - Acidic foods and beverages can react with a variety of additives because those are not chemically bound (covalently) to the polymers. Some polymers may also be subject to reacting with acids or other food and beverage compounds.

Lipophilia - Promotes absorption of chemicals in oil based foods. Studies show that people can absorb BPA from touching thermal paper cash receipts. What's more, those who use hand moisturizers absorb far more BPA because of the increased lipids from the hand cream.

Heat - Adds energy to the migration process, speeds up chemical reactions that can loosen bonds.

Processing

Why food processing adds contamination

Contamination of basic foods -- even those that do not undergo extensive processing -- comes from:

- Contact with contaminated soil and water during planting, irrigation and growth.
- Exposure to plastics during harvest from conveyor belts, chutes, pipes, baffles and other equipment.
- Exposure to plastic in the washing process through the use of bins, tanks, implements and pipes.
- Exposure to plastics during the drying and packing stages including the use of recycled or coated cardboard.

Contamination through processing

This article from the British Medical Journal offers a look at many of the substances added to highly processed foods: *Consumption of ultra-processed foods and cancer risk: results from NutriNet-Santé prospective cohort*

While the BMJ article focused on the nutritional downsides to processing, it's vital to recognize that each processing operation and additive -- regardless of nutritional value -- brings with it its own unique contamination trail and chemical burdens that are incorporated into a highly processed food product for sale.

Specific contamination routes found in individual food groups are discussed elsewhere in this document.

Degree of food processing

We categorized all food and drink items of the NutriNet-Santé composition table into one of the four food groups in NOVA, a food classification system based on the extent and purpose of industrial food processing.

This study primarily focused on the "ultra-processed foods" NOVA group.

This group includes mass produced packaged breads and buns; sweet or savory packaged snacks; industrialized confectionery and desserts; sodas and sweetened drinks; meat balls, poultry and fish nuggets, and other reconstituted meat products transformed with addition of preservatives other than salt (for example, nitrites); instant noodles and soups; frozen or shelf stable ready meals; and other food products made mostly or entirely from sugar, oils and fats, and other substances not commonly used in culinary preparations such as hydrogenated oils, modified starches, and protein isolates.

Industrial processes notably include hydrogenation, hydrolysis, extruding, moulding, reshaping, and pre-processing by frying. Flavouring agents, colours, emulsifiers, humectants, non-sugar sweeteners, and other cosmetic additives are often added to these products to imitate sensorial properties of unprocessed or minimally processed foods and their culinary preparations or to disguise undesirable qualities of the final product.

The ultra-processed food group is defined by opposition to the other NOVA groups: "unprocessed or minimally processed foods" (fresh, dried, ground, chilled, frozen, pasteurized, or fermented staple foods such as fruits, vegetables, pulses, rice, pasta, eggs, meat, fish, or milk), "processed culinary ingredients" (salt, vegetable oils, butter, sugar, and other substances extracted from foods and used in kitchens to transform unprocessed or minimally processed foods into culinary preparations), and "processed foods" (canned vegetables with added salt, sugar coated dried fruits, meat products preserved only by salting, cheeses, freshly made unpackaged breads, and other products manufactured with the addition of salt, sugar, or other substances of the "processed culinary ingredients" group).

Lipophilia: for the love of fat

In the scientific world, fats and oils are known as lipids. Lipophilia means a "love of lipids." Fats tend to be solid (or relatively so) at room temperature and oils, liquid.

Significantly, BPA, phthalates and many other harmful environmental chemicals are "lipophilic" -- they are easily dissolved in fats and oils.

This should not be surprising because most environmental chemicals -- including endocrine disruptors and pesticides -- are derived from petroleum. The same goes for artificial fragrances, flavor enhancers and food coloring as well as plastics in general, and the printing inks used on them.

What this means is that contact between plastic and any form of food-based oil or fat results in increased migration of BPA, phthalates and other from the plastic and into the edible portions of the food.

While there is no valid science yet, there is a logical possibility that the health stigma of fat in the diet and its role in obesity may be due more to the presence of harmful environmental chemicals in the fat, rather than its metabolism and actual calorie count.

Scores of well-designed, peer-reviewed, published studies have shown that BPA and phthalates act as "obesogens" -- substances that disrupt the metabolic process and result in the preferential storage of fat rather than its use as energy.

Why does lipophilia matter?

The opposite of lipophilic is hydrophobic -- the fear of water. This means that harmful environmental chemicals are somewhat less likely to leach into foods and beverages that are water based.

Despite that, BPA (hydrophobic) still leaches into the water of plastic bottles.

The migration of BPA, phthalates and other lipophilic chemicals is preferentially accelerated when placed in contact with lipids -- fats and oils -- whether from foods like bacon or cooking oils.

This means that even very heart-healthy foods like olive oil packed in plastic bottles will contain higher concentrations of BPA and phthalates than those in glass bottles.

Impacts cooking and processing

Lipophilia impacts both cooking and processing.

In cooking, the BPA and phthalates in plastic mixing bowls, utensils and other items can migration into the foods themselves.

Heat will further encourage migration of chemicals from plastics. This includes microwaving food in plastic, allowing warm or hot foods to come into contact with plastic bowls, dishes or cooking with plastic utensils.

The spice lipo-paradox

Spices have evolved over the centuries as effective ways to preserve foods from spoiling and to disguise the taste of items that have started to decompose.

By themselves, many spices also have beneficial health properties, as evidenced most recently by studies showing turmeric's potential cancer-fighting properties. (Spices for Prevention and Treatment of Cancers).

On the other hand, a number of studies have found that spices often have very high and variable concentrations of phthalates. Those studies have posited that the contamination comes from extensive handling and processing.

While the flavor ingredients in spices are sometimes water-soluble, most spice flavors come from lipid soluble compounds. This is why cooks will often sauté spices in oil before adding aqueous ingredients. This process, known as "blooming," intensifies the flavor because the oil extracts the lipid components at a temperature hotter than that of the boiling point of water.

Blooming is useful when cooking at high altitudes where the boiling point of water is lower than at sea level. This means the extraction of spice flavors drops, resulting in blander foods. At Lake Tahoe, for example, water boils at 94°C, something that prevents full flavor extraction, even with longer cook times.

Water & fertilizers: Ubiquitous contamination sources.

Irrigation water: farm ponds, biosolids and recycled municipal wastewater.

With rare exceptions, irrigation involves plastic pipes, tanks, tubing, drip devices, and valves which leach varying amounts of plastic chemical contaminants.

Well water may be the purest source, but is less available as water tables drop from drought and over-pumping. The distribution lines of a well are usually plastic.

Municipal water may be the second best source depending upon the treatment methods, filtering and added chemicals. However, municipal water distribution is increasingly using plastic pipes for mains and secondary distribution lines.

Farm ponds are questionable for direct use because of wildlife, livestock and other uses in the upstream drainage area.

In addition to BPA and phthalates, recycled municipal wastewater contains scores of harmful chemicals including pharmaceuticals, illegal narcotics and other undesirable compounds that can find their way into animal flesh and meat.

- Contaminants of Emerging Concern in the Environment
- Nationwide reconnaissance of contaminants of emerging concern in source and treated drinking waters of the United States
- Simultaneous determination of 148 pharmaceuticals and illicit drugs in sewage sludge
- Wastewater Treatment Plants as Chemical Observatories to Forecast Ecological and Human Health Risks of Manmade Chemicals
- Risks associated with the environmental release of pharmaceuticals on the U.S. Food and Drug Administration “flush list
- Pharmaceuticals occurrence in a WWTP with significant industrial contribution and its input into the river system

- A review on emerging contaminants in wastewaters and the environment: Current knowledge, understudied areas and recommendations for future monitoring
- Risks and Benefits of Tertiary Sewage Effluent as Drinking Water
- Prioritization of Contaminants of Emerging Concern in Wastewater Treatment Plant Discharges Using Chemical:Gene Interactions in Caged Fish
- Drug residues in urban water: A database for ecotoxicological risk management
- Veterinary pharmaceutical contamination in mixed land use watersheds: from agricultural headwater to water monitoring watershed

Reviews of the use of recycled municipal wastewater indicate that contaminates remain in the water and can be absorbed the tissues of growing plants.

- Major Study Indicts Chemicals Found in Recycled Wastewater Used For Vineyards And Other Crops
- Recycled Wastewater In The Wine Vineyard: Unknowns, Health Hazards, Brand Issues
- Wastewater Recycling Controversy

Significantly, commercial hay fields are frequently fertilized to increase production. That fertilizer may be a commercial product, or biosolids -- sludge from sewage treatment plants which frequently contain heavy metals.

Assessment of endocrine disruption and oxidative potential of bisphenol-A, triclosan, nonylphenol, diethylhexyl phthalate, galaxolide, and carbamazepine, common contaminants of municipal biosolids

Highlights

•Relative potency determined for six individual contaminants in a suite of bioassays

•Multiple-modes of action of individual contaminants demonstrated in different in vitro assays

•Comprehensive assessment of potential in vitro effects associated with carbamazepine

Abstract

The use of biosolids as a soil conditioner and fertiliser is hindered by the limited knowledge on the risks of micro-contaminants they contain. This study investigated the binding of six organic contaminants commonly found in biosolids, to the estrogen (ER), androgen (AR), aryl hydrocarbon (AhR), and transthyretin (TTR) receptors and their redox activity. Triclosan (TCS), bisphenol-A (BPA), and technical nonylphenol (TNP) had affinity for the TTR with relative potencies of 0.3, 0.03, and 0.076 respectively. Further, binding to TTR was the only toxicological response observed for carbamazepine, which induced sub-maximal response and relative potency of 0.0017. Estrogenic activity was induced by BPA, galaxolide (HHCB), diethylhexyl phthalate (DEHP) and TNP with BPA having the strongest potency of 5.1×10^{-6} relative to estradiol. Only BPA showed androgenic activity but it was not quantifiable. BPA also showed anti-androgenic activity along with TCS, HHCB, and TNP in the order of

TNP > HHCB > TCS ~ BPA (relative potencies 0.126, 0.042, 0.032, 0.03). No compounds exhibited anti-estrogenic or AhR activity, or were redox-active in the dithiothreitol assay. The results highlight the multiple modes of action through which these compounds may impact exposed organisms, and the concentrations at which effects may occur. This allows assessment of the likelihood of effects being observed at environmental concentrations, and the potential contribution of these compounds.

Biosolid Risks

Unfortunately, papers in the last couple of years are pointing toward biosolids as a source of microplastics, drug-resistant bacterial and genes, as well as artificial estrogens and other endocrine disruptors.

The safe and environmentally responsible use of biosolids is a goal worth striving for. However, biosolids are not — yet — ready for prime time. Below is a small sample of recent published studies which point to the need for more caution and the need for further research to protect the public health.

Contamination by E. Coli and other pathogens

Rainfall-runoff of anthropogenic waste indicators from agricultural fields applied with municipal biosolids

Highlights

•Biosolids-derived emerging contaminants found in simulated rainfall runoff.

•Biosolids are a potential source of anthropogenic contaminants to surface waters.

•Runoff contaminant concentrations relatively constant across multiple rain events.

•Intense and frequent precipitation dramatically increases contaminant load.

•Some contaminants undergo in situ attenuation unrelated to precipitation events.

Abstract

The presence of anthropogenic contaminants such as antimicrobials, flame-retardants, and plasticizers in runoff from agricultural fields applied with municipal biosolids may pose a potential threat to the environment. This study assesses the potential for rainfall-induced runoff of 69 anthropogenic waste indicators (AWIs), widely found in household and industrial products, from biosolids amended field plots. The agricultural field containing the test plots was treated with biosolids for the first time immediately prior to this study. AWIs present in soil and biosolids were isolated by continuous liquid-liquid extraction and analyzed by full-scan gas chromatography/mass spectrometry. Results for 18 AWIs were not evaluated due to their presence in field blank QC samples, and another 34 did not have sufficient detection frequency

in samples to analyze trends in data. A total of 17 AWIs, including 4-nonylphenol, triclosan, and tris(2-butoxyethyl)phosphate, were present in runoff with acceptable data quality and frequency for subsequent interpretation. Runoff samples were collected 5 days prior to and 1, 9, and 35 days after biosolids application. Of the 17 AWIs considered, 14 were not detected in pre-application samples, or their concentrations were much smaller than in the sample collected one day after application. A range of trends was observed for individual AWI concentrations (typically from 0.1 to 10 µg/L) over the course of the study, depending on the combination of partitioning and degradation mechanisms affecting each compound most strongly. Overall, these results indicate that rainfall can mobilize anthropogenic contaminants from biosolids-amended agricultural fields, directly to surface waters and redistribute them to terrestrial sites away from the point of application *via* runoff. For 14 of 17 compounds examined, the potential for runoff remobilization during rainstorms persists even after three 100-year rainstorm-equivalent simulations and the passage of a month.

Antibiotic Resistance

Novel Antibiotic Resistance Determinants From Agricultural Soil Exposed To Antibiotics Widely Used In Human Medicine And Animal Farming

ABSTRACT

Antibiotic resistance has emerged globally as one of the biggest threats to human and animal health. Although the excessive use of antibiotics is recognized for accelerating the selection for resistance, there is a growing body of evidence suggesting that natural environments are “hotspots” for the development of both ancient and contemporary resistance mechanisms. Given that pharmaceuticals can be entrained onto agricultural land through anthropogenic activities, this could be a potential driver for the emergence and dissemination of resistance in soil bacteria. Using functional metagenomics, we interrogated the “resistome” of bacterial communities found in a collection of Canadian agricultural soil, some of which had been receiving antibiotics widely used in human medicine (macrolides) or food animal production (sulfamethazine, chlortetracycline and tylosin) for up to 16 years. Of the 34 new antibiotic resistance genes (ARGs) recovered, the majority were predicted to encode for (multi)drug efflux systems, while a few share little to no homology with established resistance determinants. We characterized several novel gene products, including putative enzymes that can confer high-level resistance against aminoglycosides, sulfonamides, and broad range of beta-lactams, with respect to their resistance mechanisms and clinical significance. By coupling high-resolution proteomics analysis with functional metagenomics, we discovered an unusual peptide, $PPP^{AZI\,4}$, encoded within an alternative open-reading frame not predicted by bioinformatics tools. Expression of the proline-rich $PPP^{AZI\,4}$ can promote resistance against different macrolides but not other ribosomal-targeting antibiotics, implicating a new macrolide-specific resistance mechanism that could be fundamentally linked to the evolutionary design of this peptide.

IMPORTANCE

Antibiotic resistance is a clinical phenomenon with an evolutionary link to the microbial pangenome. Genes and protogenes encoding for specialized and potential resistance mechanisms are abundant in natural environments, but understanding of their identity and genomic context remain limited. Our discovery of several previously-unknown antibiotic resistance genes from uncultured soil microorganisms indicates that soil is a significant reservoir of resistance determinants, which, once acquired and "re-purposed" by pathogenic bacteria, can have serious impacts on therapeutic outcomes. This study provides valuable insights into the diversity and identity of resistance within the soil microbiome. The finding of a novel peptide-mediated resistance mechanism involving an unpredicted gene product also highlights the usefulness of integrating proteomics analysis into metagenomics-driven gene discovery.

Plastic Pollution

The growing evidence of an environmental crisis caused by plastics in both fresh and seawater offers further reasons for concern.

While vast floating islands of plastic afflict parts of the oceans, the larger danger to humans may be due to the vast qualities of wastewater entering rivers, streams, and estuaries.

That wastewater carries significant concentrations of hundreds of dangerous chemicals, pharmaceuticals, illegal drugs, BPA, phthalates, pesticides, household chemicals and more.

These are in addition to microfibers which are already building up on land irrigated with recycled wastewater.

Organic fertilizer as a vehicle for the entry of microplastic into the environment

Abstract

The contamination of the environment with microplastic, defined as particles smaller than 5 mm, has emerged as a global challenge because it may pose risks to biota and public health. Current research focuses predominantly on aquatic systems, whereas comparatively little is known regarding the sources, pathways, and possible accumulation of plastic particles in terrestrial ecosystems. We investigated the potential of organic fertilizers from biowaste fermentation and composting as an entry path for microplastic particles into the environment. Particles were classified by size and identified by attenuated total reflection-Fourier transform infrared spectroscopy. All fertilizer samples from plants converting biowaste contained plastic particles, but amounts differed significantly with substrate pretreatment, plant, and waste (for example, household versus commerce) type. In contrast, digestates from agricultural energy crop digesters tested for comparison contained only isolated particles, if any. Among the most abundant synthetic polymers observed were those used for common consumer products. Our results indicate that depending on pretreatment, organic fertilizers from biowaste fermentation and composting, as applied in agriculture and gardening worldwide, are a neglected source of microplastic in the environment.

Nano-Contamination

The increased use of nanoparticles in clothing, toothpaste, personal care products and other items are finding their way into the municipal wastewater stream. In addition to chemical leaching, some nanoparticles may be small enough to be absorbed directly into the blood streams of fish and other animals.

- Soil microbial community responses to contamination with silver, aluminium oxide and silicon dioxide nanoparticles
- TiO2 nanoparticles and sludge from wastewater treatment plants: a new concern for crops?

Whole Foods, in 2014, banned vegetables fertilized with biosolids, but the practice remains controversial:

- Whole Foods Bans Sludge Fertilizer
- Whole Foods Bans Produce Grown With Sludge. But Who Wins?
- Health risks associated with wastewater use
- Wastewater Reuse in Agriculture and Potential Risks to Human Health
- Standards for Irrigation and Foliar Contact Water - The Pew Charitable ...
- High levels of microbial contamination of vegetables irrigated with wastewater by the drip method.
- Effect of biofilm in irrigation pipes on microbial quality of irrigation water.
- Microbial contamination of vegetable crop and soil profile in arid regions under controlled application of domestic wastewater.
- Escherichia coli contamination and health aspects of soil and tomatoes (Solanum lycopersicum L.) subsurface drip irrigated with on-site treated domestic wastewater.
- Monitoring the occurrence of pharmaceuticals in soils irrigated with reclaimed wastewater

Sourcing the Menu: Standards and Choice Limitations

Meat the enemy

Animal flesh presents an especially tough issue when it comes to systematic contamination by endocrine disruptors and other harmful environmental chemicals. Dairy (to be dealt with in the next section) presents even more opportunities for contamination.

While plastic food contact materials present one of the the most visible contamination sources, human contamination from consuming meat begins with animals consuming contaminated food and water.

The following emphasizes cattle, but the contamination sources are mostly analogous for sheep, poultry and pigs. Variations among species will be noted after common contamination pathways are described.

Commercial cattle and other farm animal feed suffers from the same plastic contamination as other highly processed products involving conveyor belts, plastic pipes, tubing and contact with other polymer-based machinery.

In addition, the "finishing" process by which cattle and livestock are fattened before slaughter involves numerous undesirable chemicals, but also involves grain which is another category of food with contamination problems from farm to table.

Cattle and livestock that forage in pastures or which are fed hay might seem to offer a lower burden of environmental chemicals. This would be the case if the fields from which the hay is harvested has not been irrigated.

Because of the expense of installing permanent irrigation sprinklers, pasture irrigation is often accomplished through the use of mobile sprinkler heads connected to a water source by means of plastic hoses that are frequently 100 yards long or greater.

(Example: K-Line irrigation)

Contaminates leaching from the long irrigation hoses are compounded if the water source is highly treated recycled municipal wastewater.

Cattle grazing on wastewater-irrigated fields contaminate themselves by eating moist, recently irrigated grass, or grass that is dry but which is coated with wastewater chemical residues.

Searches for studies on concentrations of chemicals of concern in livestock and their flesh could find little other than one which showed severe health effects in sheep that grazed on pasture fertilized with biosolids.

Grass-fed healthy alternative, but often abused

Grass-fed beef and other livestock offer relief from the excessive chemical, pharmaceutical and dietary practices used by industrial producers to produce maximum meat in minimum time and less money. Such factory farming has seen many health abuses in both the livestock and meat consumers.

However, even the grass-fed process has been abused (Grass-Fed Beef Loses Its Luster) by operators who employ factory-style, crowded feedlot practices.

An entire industry has developed where hay or other grass products are formed into feed pellets along with growth enhancers which are fed to cattle subsequently marketed as "grass-fed."

From: *Grass-Fed Beef Loses Its Luster*

"A growing number of consumers began turning to grass-fed beef in order to avoid buying meat from feedlot cattle and factory farms. "But as grass-fed beef skyrocketed in popularity," Lowry points out, "these same large producers have jumped on the bandwagon to offer a product that meets the letter of the law without a lot of respect for the spirit."

Lowry explains that beef-- technically grass-fed and grass-finished--is in fact coming from concentrated feedlots where the cattle are fed from troughs of manufactured grass pellets. "Large scale farms are talking about how to dope their grass with nitrogen," Lowry says,
and undernourished cattle are getting sold to the consumer at a premium because they have the "grass fed" label.

The American Grassfed Association has issued a set of guidelines outlawing the pellets, crowded conditions and other animal welfare abuses.

While true grass-fed beef offers a healthier alternative when done to standards, (Membership and Certification Submission Checklist), even those operations need to be certain that pastures and any supplemental hay and feedings done when pasturing is impossible, are free of irrigation and other harmful environmental chemical contamination.

This probably isn't what most people think they're signing up for. But if you're buying "grass-fed" beef and you can't name the farmer or locate the farm on a map, it's a good bet you're getting pellets, not pasture."

Chicken & pork

Factory farming for chicken and pork have paralleled beef in intensity and opportunities for contamination in animal concentration, feeding for swift, maximum growth and processing after slaughter.

Organic regulations requiring space for animal welfare and feed ameliorate some of the contamination issues of mainstream husbandry. Potential issues remain with water sourcing as well as irrigation and growing conditions for feed which is seasonally required even for free-range animals.

The EU found environmental chemicals in feed and chicken coop construction materials in flesh and eggs. This was confirmed by a Belgian study and others.

Sausage: the original processed food (Now in plastic casings!)

Sausage of various sorts has been used for centuries to stuff animal intestines with various bits and pieces of meat, organs and offal that are unsuitable, unpalatable, or impractical to serve in their natural state.

Over the centuries, various fillers, spices, preservatives, emulsifiers, and other substances have been added to the meat bits. Modern sausage -- especially the ubiquitous hot dog -- is more often than not in a manufactured synthetic casing usually made of polymers and packed with meat of various origins ground into a paste with fillers and binders.

Spices, which have a lipophilic effect in attracting BPA and phthalates, are often used to cover up the off-tastes in sausages and other manufactured foods.

Replicant meat

Frozen and pre-prepared meals as well as sliced cold-cuts are usually replicant meat -- created from manufacturing processes designed to be made mostly of meat, binders and other substances which are then molded to look resemble the real thing.

The associated use of "mechanical fingers" and chemical solutions designed to strip every last shred of meat from bones have introduced a new category of semi-fake meat that is artificially formed from meat fragments, glued together with a host of mostly un-disclosed substances, and re-formed either into "nuggets" or shaped to look like a whole, natural piece of meat -- sometimes with fake painted/printed-on "grill" marks made of yet another chemical composition.

Many of the ingredients in these are not publicly available because the companies have classified them as trade secrets, something allowed by regulators.

Burgers

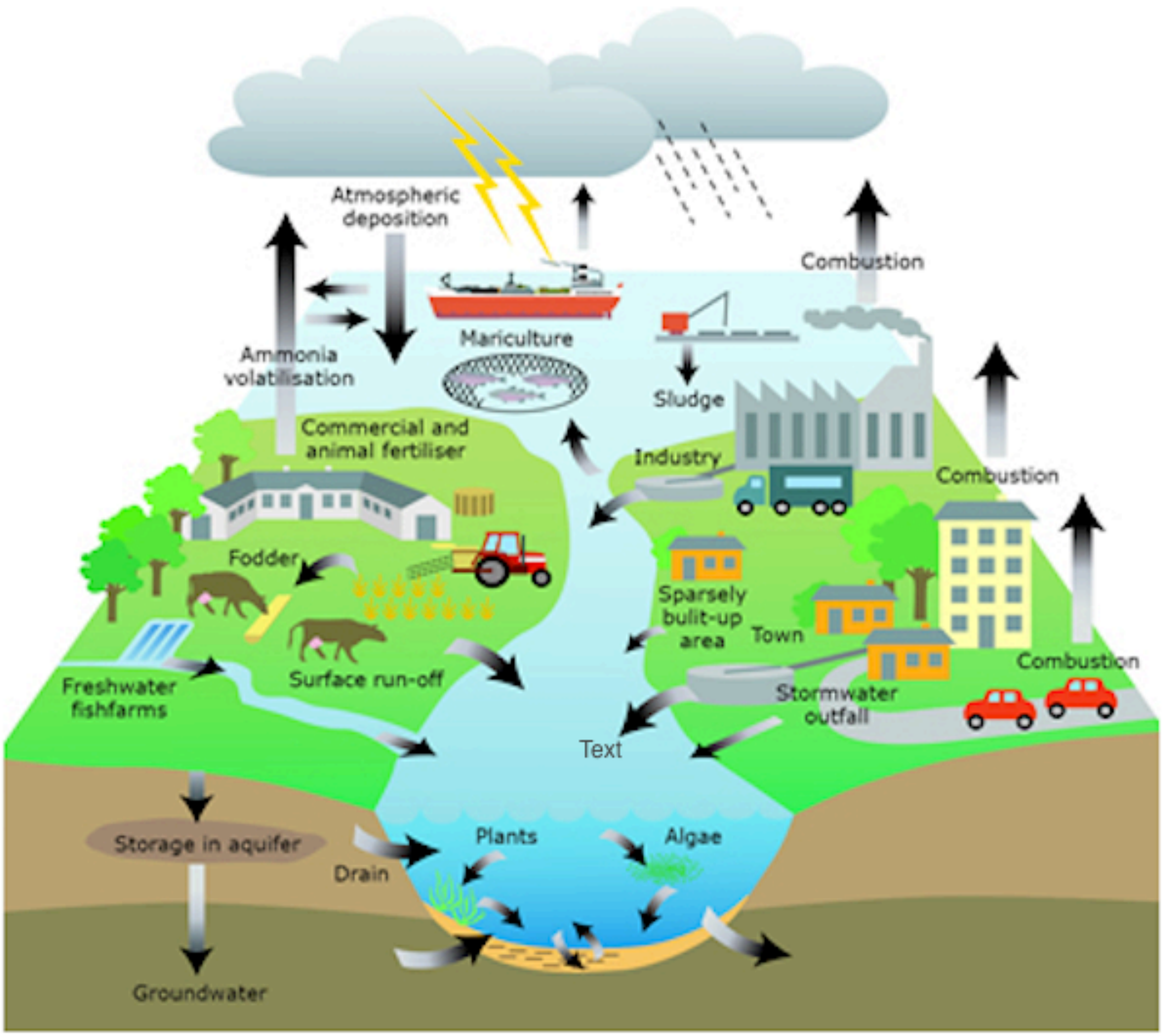
In their own way, burgers resemble sausage without a casing. And, like sausage, burgers -- whether beef, chicken, fish, or veggie are fertile ground for undisclosed additives. One of the most notorious of the additives in hamburgers, as well as chicken nuggets, and manufactured meat designed to look like the real thing is the notorious "Pink Slime.

The chicken AND the egg? A fowl situation

Both the flesh and the eggs of chickens and other edible fowl have the same issues with opportunities for contamination from feed and water as other farm animals.

Fishy business

Fish contamination occurs in growth, harvest, processing, and sales. But because edible fish grow in polluted oceans and freshwater lakes, rivers and streams, they can accumulate contaminates from many sources in their natural environment.



Pollution comes from a variety of sources: legacy pollutants that persist in the sentiment, industrial discharge, treated and untreated wastewater, and fertilizers. We are also culpable: chemicals in lawn pesticides and car exhaust accumulate in storm runoff that flows into nearby streams and rivers. Illustration: Ærtebjerg et al. National Environmental Research Institute, Denmark

Source: http://deohs.washington.edu/environmental-health-news/fish-we-eat

Auto-correct typo in original graphic: “sentiment” should read, “sediment.”

- U.S. Agency Study Finds Toxic Chemicals in Fish is Widespread
- Chemicals in Fish

- Bioaccumulation of super-lipophilic chemicals in fish

Because chemical contamination grows with time, this set of recommendations from the state of Washington recommends eating smaller, younger fish. It also recommends cutting away the fatty portions of fish such as salmon because some chemicals are lipophilic. Other contaminates such as methyl mercury, are water soluble.

Beware of farmed fish

Studies have determined that farmed fish are subject to contamination by multiple chemicals (Friends Don't Let Friends Eat Farmed Salmon). Feed is one suspect as are chemicals and pharmaceuticals added to keep fish as healthy as possible in crowded pens.

Plastic Pollution

The growing evidence of an environmental crisis caused by plastics in both fresh and seawater offers further reasons for concern.

While vast floating islands of plastic afflict parts of the oceans, the larger danger to humans may be due to vast qualities of wastewater entering rivers, streams, and estuaries which are used for irrigation and other agricultural uses.

Dairy: Milk & Cheese

The contamination of the dairy chain starts with what the female mammal -- aka "cow" -- consumes. This is most often a bovine cow in America, but globally includes goats, sheep and other mammals. (see "Meat the enemy")

The milk from cows -- like its flesh and that of its male counterparts -- can be contaminated with environmental chemicals from its food and water.

But the milk produced will be further contaminated by many additional processes before milk, cheese, yogurt and the whey for dietary supplements reaches a human consumer.

The introduction of plastic chemicals into the dairy food chain begins with the milking process and continues to increase at each step before reaching the consumer.

Milking machines

Other than the rare artisan-produced cheese, the hand-milking of cows, goats and other livestock has mostly vanished. Milking machines make the first step of production more cost effective, time-efficient, and sanitary -- all benefits to the consumer.

Before milking begins, the udder and teats undergo a number of hygiene steps that include cleaning with anti-bacterial solutions (Hygiene in milk production).

This helps insure the cleanliness of the milk and starts a process to extend the length of time before milk can sour. This also helps prevent injuries to the cow, including mastitis, a serious inflammation of the udder and mammary gland.

- Mastitis is most often transmitted by contact with the milking machine, and through contaminated hands or other materials.
- The Milking Machine and Mastitis

Another anti-bacterial cleaning occurs after milking. All of the cleaning and irritation from the milking machine results in the application of salves.

No research can be found so far on whether antibiotics, salves and cleaning agents may contaminate the collected milk.

It's also notable that plastic gloves worn by handlers through the milking process can result in phthalate transfer to the teat. This extent of this transfer is unknown.

In addition, the phthalates and other EDCs in the gloves can leach out and be absorbed through the skin of the wearer. The leaching and transfer is encouraged by people who use hand creams.

Plastic contamination and the milking machine

Milking machines use a pulsating vacuum to draw raw milk from the udder.

https://hoards.com/images/udder.111.widea.0.gif

The teatcup that attaches to each teat is lined with a flexible plastic (phthalate soft) that alternately compresses and relaxes as the vacuum pump operates.

The milk is drawn into a one-way plastic chamber (known as "the claw") which allows the milk to be drawn off and transferred into a collection tank that is sometimes plastic, sometimes stainless steel. From the collection tank, milk flows to a bulk tank, frequently via plastic piping or tubing. (How the milking system works)

From the bulk tank at the dairy, milk is transferred via plastic hoses to a tanker truck which reverses the process through plastic hoses to larger tanks at the creamery. All of the processing involves plastic hoses, pipes, fixtures, pumps, valves, vats, vessels and other equipment that often contain or are made of plastic.

At the creamery, plastic hoses dominate the processes of separating cream from the whole milk. The skimmed milk and cream are usually pasteurized separately.

Some cream is returned to the skimmed milk to create a range of butterfat levels, some is made into butter. Cheese can be made from milk at a variety of stages in this process.

Lipophilia

Significantly, BPA, phthalates and many other harmful environmental chemicals are "lipophilic" -- they are easily dissolved in fats.

This means that the cream separation process creates a high-fat environment that encourages leaching of these environmental chemicals into dairy products.

Cheese & Whey

Cheese made from whole milk contains more fat. More fat offers contamination opportunities for lipophilic chemicals like BPA and phthalates.

The cheesemaking process can use plastics at various points, but most likely as utensils, filtering materials, molds for curds and the process for draining off whey. Further contamination can occur in the processing that cuts large blocks then wraps individual blocks, wheels, and other large shapes. Sliced and grated cheeses expose cheese to contamination as well as the plastic pouches and bags they are packed in.

Most organic cheeses use plastic in their final packaging. The most highly contaminated will be blocks which have been shrink-wrapped. This is because the film is warm/hot when it comes into contact with the cheese. The heat encourages migration of contamination from the plastic into the cheese.

Whey is a mostly water-loving substance left over from the cheesemaking process. However, studies have shown that many organic contaminates can be bound to the milk proteins.

Fruit & veggies

Vegetables in both the exposure and decontamination phases will be coordinated to accommodate seasonally available local products obtained from USDA-certified organic farms which do not use recycled wastewater for irrigation.

Most fruits and vegetables receive substantial exposure to plastics before they reach the supermarket. This contamination, which also applies to grains for bread, cereal and pasta, results from the use of plastics during harvest, processing, and packaging for sale.

Most supermarket fruits and vegetables are grown with commercial fertilizers and an increasing percentage are fertilized with biosolids -- a euphemism for the sludge from municipal sewage treatment plants.

Due to loosening standards and a lengthening list of "exceptions" to the USDA rules, even certified organic fruits and vegetables can be fertilized and treated with a growing number of commercial chemicals.

Exceptions to the regulations have been made by the USDA without extensive study of the substances involved. Also overlooked are additives, surfactants, and other auxiliary chemicals added to enhance the active ingredients. Those added substances often have endocrine-disrupting or other harmful effects.

From sewer to table

Most American supermarket produce aisles will feature fruits and vegetables irrigated with recycled municipal sewer and wastewater and fertilized with biosolids - sewage sludge.

Published scientific studies have demonstrated that chemicals in recycled wastewater can be absorbed by the edible portions of some fruits & vegetables or remain on the surface after water contact.

Tree-born fruit may have contact contamination, but the distance from the ground to the fruit makes it less likely that contamination will reach edible interior parts.

See: Recycled Wastewater In The Wine Vineyard for more.

Supermarkets okay with sewer-to-store veggies (all but one)

As far as can be determined, Whole Foods is the only grocery chain to ban fruits and vegetables fertilized with sewer sludge: Whole Foods Bans Sludge Fertilizer.

Organic Standards in Brief

- No toxic or persistent pesticides or herbicides
- No sewer sludge or synthetic fertilizers
- No GMOs (genetically modified organisms)
- No antibiotics
- No synthetic growth hormones
- No irradiation

See the full USDA Organic standards

http://www.wholefoodsmarket.com/organic

Recycled municipal wastewater (increasingly used for food crops) is currently not prohibited by USDA Organic Standards and is not addressed even by Whole Foods.

Harvesting and processing involve extensive contact with conveyor belts containing phthalates for flexibility and hard plastic rollers whose durability usually results from BPA-containing polycarbonates.

Food contact materials also contribute to contamination since many whole fresh vegetable are wrapped in plastic for sale.

Frozen vegetables

Frozen vegetables receive additional plastic contact in processing and are packaged in plastic. Some are packaged with directions for the contents to be heated or microwaved while in in the plastic bags and containers. Heating in the bag increases the release of environmental chemicals into the food.

Fruit and vegetable juice

The commercial processing of fruit and vegetable juice offer numerous exposure opportunities for contamination. Plastics are extensively present in peeling, crushing, filtering, transport and in the plastic bottles, pouches, and epoxy can linings.

Going against the grain: Bread and cereal killers

The domestication of grains nearly 11,000 years ago accelerated civilization from hunter-gatherer to the agriculturally based world of today (Ancient Waves of (Wild) Grain).

While bread and cereal products are among the most basic and valuable foodstuffs modern commercial grains are subject to the same the irrigation and fertilization problems associated with fruits and vegetables.

This includes harvest and processing contamination occurrences including the use of questionable irrigation water, commercial fertilizer, and the use of recycled municipal wastewater and sewage sludge biosolids. In addition, wheat is extensively applied with glyphosate and other pesticides.

The issue of irrigation is not as critical because a substantial portion of wheat matures during the winter when rains are more prevalent. A warming climate is expected to affect this.

Table 1. U.S. Wheat Classes.

Class	2016 Production, in Bushels	Location Produced	Uses
Hard Red Winter	1 billion	Great Plains (TX to MT)	Bread flour
Hard Red Spring	493 million	Northern Plains (ND, MT, MN, SD)	High-protein blending
Soft Red Winter	345 million	Eastern States	Cakes, cookies, crackers
White	314 million	WA, OR, ID, MI, NY	Flour for noodles, crackers, cereals
Durum	50 million	ND, MT	Pasta

Source: https://www.agmrc.org/commodities-products/grains-oilseeds/wheat/

In addition, the transportation of wheat is a massive bulk operation using barges, ships and railroad bulk carriers all of which offer ample opportunities for plastic contact with conveyor belts, augers and other plastic apparatus, and storage. Because of the size of the operation, there is little oversight of transportation.

Flour production involves extensive contact with plastic-based apparatus, conveyor belts and transport.

Commercial baking: a wonder of automation and processing contamination

The actual making and baking of commercially produced bread, again, involves conveyor belts but also plastic bins used for ingredients, mixing, and preparation for dough. Plastic loaf pans are used for dough in the rising stages.

The baking process usually employs metal conveyor surfaces with the warm loaves going into plastic bags when still warm.

This paper from the British Medical Journal defines commercial bread as a highly processed food: Consumption of ultra-processed foods and cancer risk: results from NutriNet-Santé prospective cohort.

Small batch regional bakeries

Most small-batch regional bread bakeries still use commercially available flour with its inherent contamination opportunities.

However, some very small artisan operations -- such as those associated with the California Grain Campaign -- have reduced their dependence on plastics and pack their product in brown paper bags.

- Evolution of Domesticated Bread Wheat
- Re-discovering ancient wheat varieties as functional foods

It's important to recognize that recycled paper carries high concentrations of phthalates because a high percentage of ink used in packaging gets recycled along with the paper.

Corn-based breads and cooking ingredients

Corn is a basic ingredient in many favorite American ethnic foods such as tacos, enchiladas, tamales and more.

Unfortunately, most corn available in the U.S. comes from cultivars that are genetically modified to be resistant to pesticides like glyphosate which is extensively applied.

Cereals

Breakfast cereals are among the most extensively processed grain foods. Processing includes the shaping of flakes and other forms needed to satisfy marketing and consumer demands and expectations.

Preservatives, artificial colors, and other chemicals are added in addition to the conveyor, piping, tubing and other opportunities for contamination by BPA and phthalates.

Edible Oils

Edible oils are often chosen for their flavors (such as in salads), or their behavior in a frying pan, baking or other forms of cooking.

The standard oil-producing processes involves plastic pipes, tubing, pump components, bins, tanks, conveyor belts and associated sources of contamination. Contamination increases with each additional processing step.

Producing edible oils from seeds, nuts and fruits begins with mechanical extraction by crushing or pressing the raw stock. That recovers a portion of the oil.

Once pressed or crushed, additional oil can be produced by heating the pomace.

In many cases heating is followed by solvent extraction using various petroleum distillates such as hexane to dissolve the remaining oil from the pomace.

Because the solvent has a much lower boiling point than the oil, most of the solvent is removed by a distillation process that recovers most of the solvent for reuse. Small but detectable amounts of the solvent are impossible to remove and will remain in the finished oil.

No government regulations exist to require disclosure of the process.

Harvest & Processing

High-production edible oils such as soy, canola and corn involve mechanical harvesting that involve the plastic contamination sources common to other fruits and vegetables: conveyor belts, plastic chutes, bins, gloves, processing vessels and associated components.

Olive Oil

First. avoid the "organic" pesticides.

The Olive fruit fly is endemic in California and other wine producing regions around the world. There are a variety of methods for controlling infestations including baits, traps, attractant strips and certified organic pesticides such as Spinosad and Surround. (UC Pest Management Guidelines).

Despite their organic-certified status, both Surround and Spinosad contain toxic chemicals and proprietary chemicals whose identities are trade secrets and not disclosed. Because of this, olives treated with these are unacceptable.

Untreated olives or those produced in groves using baits, traps, or attractant strips are acceptable.

Olives undergo a washing process -- a water rinse -- before pressing. There are many other stages, some of which commonly use plastic components in the process.

Visits will be made to determine which oil press minimizes the use of plastic components.

Pressing

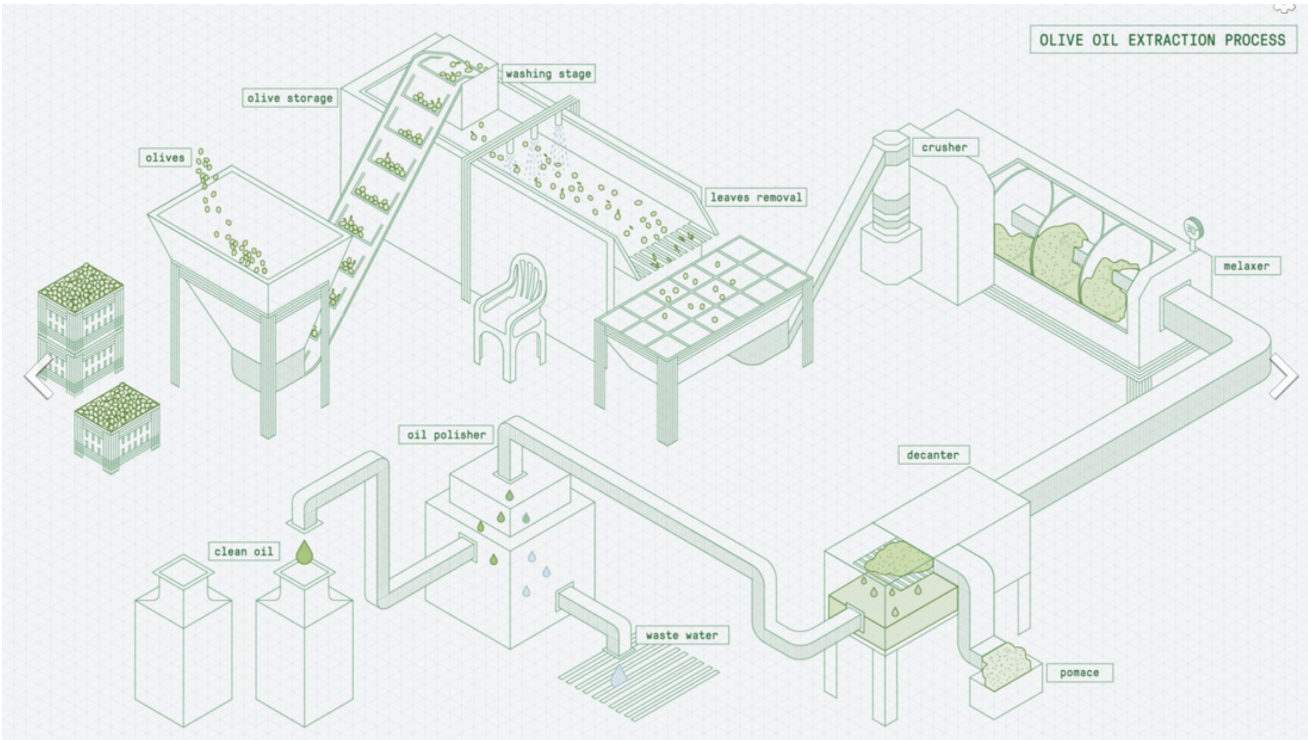
In the case of olive oil, the "first cold press" that takes place without heating produces maximum flavor.

Internationally, there is great confusion -- and often scandal -- over the regulation of grades and quality of olive oil that follow first cold press. Heating and solvent extraction are used in cheaper grades. Regulation is inconsistent and unreliable.

Significantly, heating drives off many of the aromatic compounds and reduces the healthy polyphenols in olive oil.

First cold press offers a consumer the best assurance of purchasing the healthiest edible oil product while minimizing plastic chemical contamination.

However, as healthy a first cold press is, harvest involves plastic bins, rakes and, synthetic fiber netting. What's more, the production process involves plastic bins, conveyor belts, pipes, tubing, pump components, filters, and more.



Modern method of olive oil extraction

More details

This image has been created during "DensityDesign Integrated Course Final Synthesis Studio" at Polytechnic University of Milan, organized by DensityDesign Research Lab. Image is released under CC-BY-SA licence. Attribution goes to **"Cecilia Della Longa, DensityDesign Research Lab"**. - Own work

Source: https://en.wikipedia.org/wiki/Olive_oil_extraction#/media/File:OliveOilExtractionProcess.png

CC BY-SA 4.0

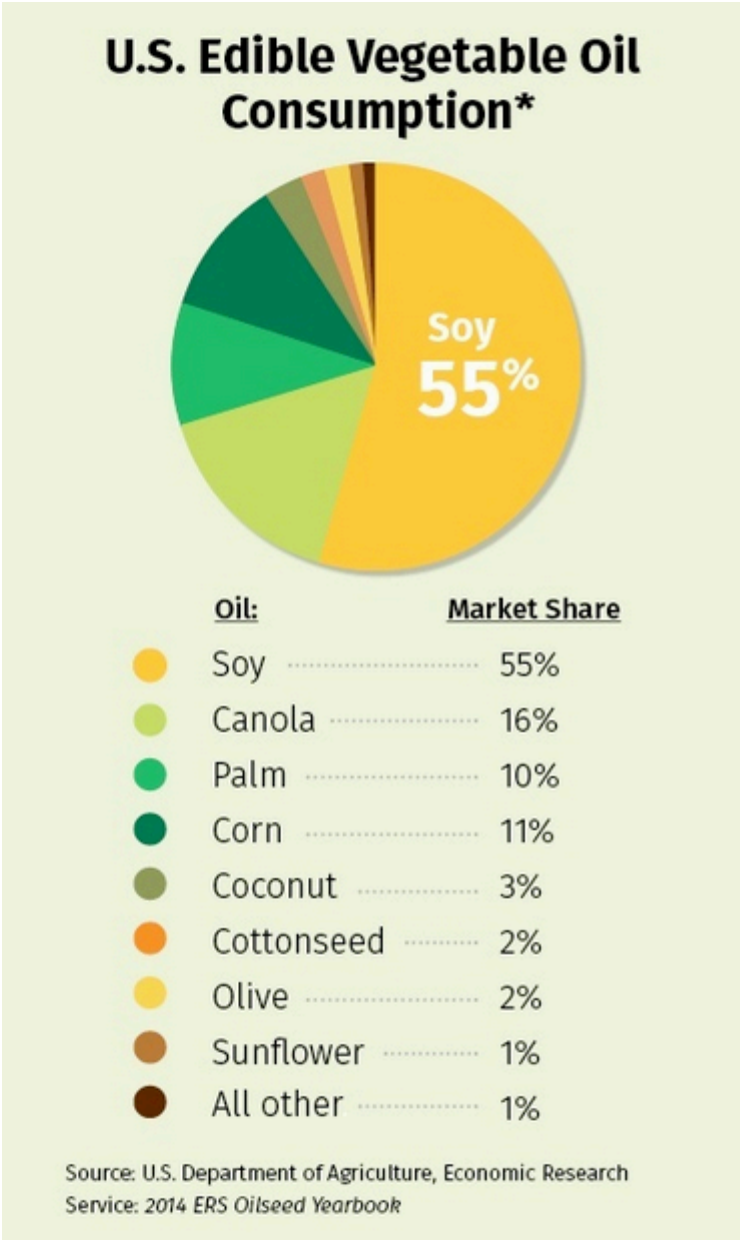
File: OliveOilExtractionProcess.png

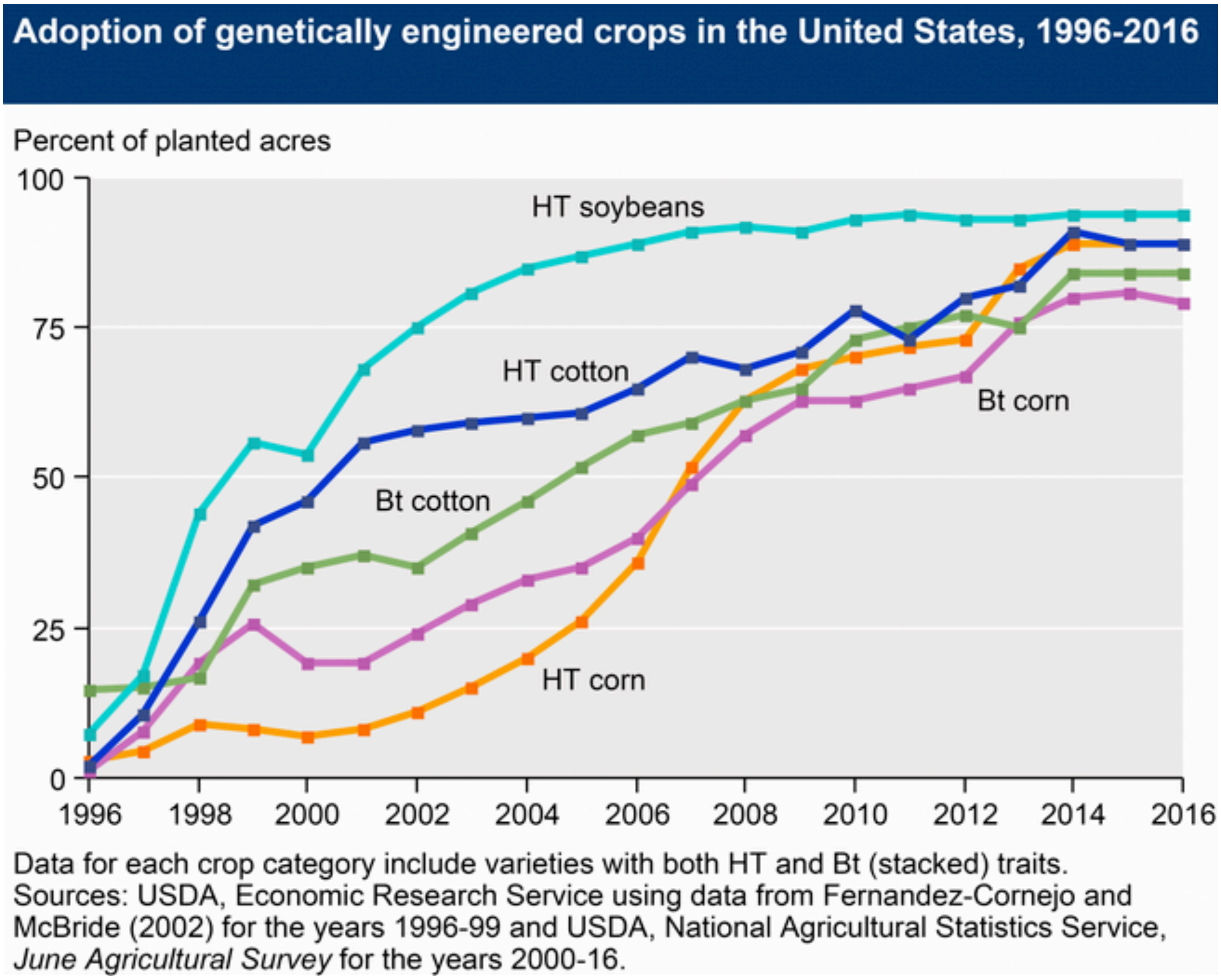
Created: 5 December 2014

Edible oil & genetic engineering (Hard for some people to swallow)

At least half of all vegetable oil consumed in the United State comes from genetically engineered crops. The genetic modifications are usually made to make the crop plant resistant to herbicides which are copiously used. In addition to the controversy concerning effects of glyphosate and other active ingredients, no research is available on adjuvants and/or other chemicals that are undisclosed or are trade secrets.

The scientific evidence concerning the safety of GMO organisms is hotly disputed. We have no evidence that GMO foods would affect our test results in any way. However, out of an abundance of caution and for the sake of reproducibility, the study will not choose those foods for the diet.


U.S. Edible Vegetable Oil Consumption*
Soy 55%
Oil:
Market Share
Soy 55%
Canola 16%
Palm 10%
Corn 11%
Coconut 3%
Cottonseed 2%
Olive 2%
Sunflower 1%
All other 1%
Source: U.S. Department of Agriculture, Economic Research Service: 2014 ERS Oilseed Yearbook



Adoption of genetically engineered crops in the United States, 1996-2016

Data for each crop category include varieties with both HT and Bt (stacked) traits.
Sources: USDA, Economic Research Service using data from Fernandez-Cornejo and McBride (2002) for the years 1996-99 and USDA, National Agricultural Statistics Service, *June Agricultural Survey* for the years 2000-16.

Candy, snacks, protein and meal-replacement bars

Candy, snacks, protein and meal-replacement bars are among the most extensively processed foods available.

Candy and snacks tend to be ultra-high fat and/or sugar products. The fat content offers a significant opportunity for the concentration of lipophilic chemicals such as BPA and phthalates.

Chips made from non-GMO corn raised organically and fried in oil which is similarly organic and non-GMO in origin would be acceptable if available.

Nutrition bar contamination

Bodybuilders, people in a hurry and those who opt for a balanced nutrition bar instead of candy bar are, however, getting extra doses of harmful environmental chemicals because these are among the most highly processed foods available.

In addition to the BPA and phthalate exposures inherent in the processing regime, the protein in these bars comes primarily from either soy or whey.

Soy presents a dual concern because it adds compounds that exert estrogen-like effects. I addition, almost all soybean crops are composed of genetically modified cultivars engineered to be immune to the application of pesticides including glyphosate.

Because of soy's estrogenic effects, many people currently buy bars fortified with whey protein left over from cheesemaking. However, whey presents the same environmental chemical concerns as dairy.

APPENDIX 4 - Additional references: Non-food contamination sources

Xenobiotic Organic Compounds in Greywater and Environmental Health Impacts

Phthalates in Indoor Dust and Their Association with Building Characteristics

Green Chemistry and the Search for New Plasticizers

Overview of air pollution and endocrine disorders

Neurotoxicity of fragrance compounds: A review

Poly(Vinyl Chloride)

Green Chemistry in Textiles

Formaldehyde in your fabrics

Toxic Free Supply Chain for Textiles and Clothing

Bisphenols, Benzophenones, and Bisphenol A Diglycidyl Ethers in Textiles and Infant Clothing

Eco-testing of textiles By K. Amutha, K. Saranya

Phthalates in cosmetic and personal care products: Concentrations and possible dermal exposure

Hazardous substances in plastics: – ways to increase recycling

Green Chemistry and the Search for New Plasticizers

Characterization of phthalates exposure and risk for cosmetics and perfume sales clerks

Risk assessment to human health: Consumer exposure to ingredients in air fresheners

Xenobiotic Organic Compounds in Greywater and Environmental Health Impacts

Overview of air pollution and endocrine disorders

Personal care product use as a predictor of urinary concentrations of certain phthalates, parabens, and phenols in the HERMOSA study

Possible endocrine disrupting effects of parabens and their metabolites

Phthalates in Indoor Dust and Their Association with Building Characteristics

Fragrance compounds: The wolves in sheep's clothings

Development of an Endocrine Disrupting Compounds Footprint Calculator

Determination of phthalate esters in cleaning and personal care products by dispersive liquid–liquid microextraction and liquid chromatography–tandem mass spectrometry

Characterization of phthalates exposure and risk for cosmetics and perfume sales clerks

Risk assessment to human health: Consumer exposure to ingredients in air fresheners

*PDF: FINAL REPORT -- Study on the Link Between Allergic Reactions and Chemicals in Textile Products Principal European Commission, DG Enterprise and Industry

*PDF: Phthalates and Their Alternatives: Health and Environmental Concerns - VALUABLE FOR LIST

Can That New Car Smell Harm You? Or Someone Else?

Reprinted by permission from the Feb. 9, 2014 issue of Nano Active

By Lewis Perdue

Driving with the windows down when you are tired may keep you awake in more ways than just the sounds and tactile effects of air currents. It could also keep you from being poisoned and, perhaps, prevent you from killing someone.

Take, for instance, Navindra Kumar Jain, a 63-year-old retired Silicon Valley tech executive who told police that the intense new car smell of his Tesla S made him drowsy enough to fall asleep at the wheel.

When Jain lost control of the Tesla on Nov. 2, 2013, he killed 40-year-old librarian Joshua Alper who had been riding a bicycle in a wide shoulder lane on Highway 1 north of Santa Cruz.

Most public reactions to Jain's claim have been met with derision and disbelief.

But scientific evidence, including a major one by Australia's CSIRO[14], indicate that many of the chemicals given off by automotive dashboards, upholstery, wiring, adhesives and interior trim can offer the same consciousness-impairing and mind-altering effects as sniffing glue.

The CSIRO study and others have found that -- in addition to toluene, xylene, benzene and other Volatile Organic Counpounds (VOCs)[(1-4)] , there are phthalates [(5-7)], flame-retardants[(11,12)] and other Endocrine Disrupting Compounds that are outgassed from car interior materials and form the scummy film on windshields and windows.[5-7].

And, in a contra-Darwinian sense, people love the fragrance of these VOCs so much that they support an entire industry of sprays and air fresheners containing many of the same petrochemicals and EDCs. (See: shop on Google for new car smell)

The National Highway Traffic Safety Administration considers toluene (a key compound in "sniffing glue") to be a Central Nervous System depressant[8] with symptoms that include: "Dizziness, euphoria, grandiosity, floating sensation, drowsiness, reduced ability to concentrate, slowed reaction time, distorted perception of time and distance, confusion, weakness, fatigue, memory loss, delusions, and hallucinations."

The California Department of Public Health says in an official statement that, "Toluene, like most organic solvents, can affect your brain the same way drinking alcohol does."

Significantly, in addition to VOCs like toluene, xylene, and benzene -- all of which can cause leukemia[10] -- we found studies that detected more than 100 compounds -- many of which are petrochemicals and fit into the California Department of Public Health's definition of "organic solvents."

The CSIRO study stated that, "Controlled exposures of human subjects to a 22-compound mixture at TVOC [Total VOC] concentrations of 7,000–33,000 $\mu g/m^3$ have observed effects within minutes, such as subjective reactions (odour, discomfort, drowsiness, fatigue/confusion), eye/nose/throat irritation, headache, and (in symptomatic subjects) neurobehavioural impairment"

Further, the CSIRO study noted conditions which suggest that it is altogether possible that Tesla driver Jain had been impaired, as he has stated, by the sedan's new car smell.

"Investigation into VOCs in new cars has been limited. Bauhof and Wensing (1999) described a standardised test procedure used in Germany in which VOC concentrations were measured at car interior temperatures of 23–65°C and an unspecified ventilation rate.

"TVOC concentrations of 35,000–120,000 $\mu g/m^3$ were reported for six new cars (test temperature not specified), these concentrations decreasing exponentially over a 40-day period to about 10,000–30,000 $\mu g/m^3$. VOCs consisted of aromatics, glycol ethers and esters, aldehydes, ketones and amines.

"Grabbs et al. (1999) screened four new cars in the USA, all after being closed for one hour and without temperature control. Three exhibited initial TVOC concentrations of 300–600 $\mu g/m^3$ and the fourth 7500 $\mu g/m^3$. The latter decreased exponentially by about 90% within three weeks."

Click here for a chart of chemicals from Grabbs, et. al.

Click here for a chart of chemicals from Faber, et. al.

A sampling of the top 10 petrochemicals found were:

Methylcyclohexane is also used in perfumes for its minty fragrance. This compound is closely related to 4-Methylcyclohexanemethanol, MCHM, spilled in the vast West Virginia chemical spill in January 2014. Ironically, MCHM has been patented for use in air fresheners. (13)

Undecane, the National Toxicological Program says, is an organic solvent and Central Nervous System depressant.

Ethylbenzene, is classified by the EPA as the same sort of organic solvent with Central Nervous System effects. Used as a perfuming agent in cosmetics.

As time allows, we'll work our way through those lists above, and draw a few more connections and contextual touchpoints.

Many of the compounds mentioned above have not been studied in enough detail to assess their human health effects. In addition, no studies have been located that assess the effects on humans of possible interactions among the various chemicals.

The windshield scum of phthalates and flame retardants will be examined in a future post.

The footnotes in this post will also be re-arranged and cleaned up as time and the location of more original source documents allow.

How can you protect yourself?

Tech Exec Jain's case may turn on whether his attorney's can establish that he was affected by the chemicals from his Tesla's new car smell.

Regardless, there are some cautions you should know about and actions you can take.

According to Toshiaki Yoshida, chief researcher at the Osaka Prefectural Institute of Public Health, it takes more than three years for a vehicle's inside air to drop to levels considered safe to breathe.

The CSIRO study indicated a decrease of about 20% per week. But remember if amounts decreased by 20% the first week, then the second week would see a decrease from 80% to overall 64% the second week, then to 51% of the initial value the third, 41% the fourth and so forth.

The tests done by Overton & Manura(1) indicated that the levels of interior pollutants decreased after two months, but that they remained temperature dependent.

In light of those issues the following could help you and your passengers decrease exposure to the chemicals detected:

1. After your car has been sitting unused and closed even overnight, when possible roll down all the windows and drive for several minutes with the windows open. This is especially important in warm or hot weather.
2. Drive as much as possible with the windows open.
3. Avoid using your ventilation system's recirculate functions except in heavy traffic where the outside air may be more unhealthy than that inside your car.
4. Don't use air fresheners.
5. Don't use plastic upholstery, floor mat or other interior treatments, especially those with the "new car smell." Make sure to tell your carwash you don't want those.
6. While you should not let your guard down, the levels inside your vehicle may be safest at the point when your windows no longer get scummed up from the chemical outgassing.

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(7) Determination of the Fogging Characteristics of Interior Automotive Materials, Society of Automotive Engineers, Standard SAE J1756,http://standards.sae.org/j1756_200608/ (Web site accessed Feb 9, 2014)
(8) http://www.nhtsa.gov/people/injury/research/job185drugs/toluene.htm
(9) http://www.epa.gov/ttn/atw/hlthef/toluene.html
(10) Am J Ind Med. 2008 Nov;51(11):803-11. doi: 10.1002/ajim.20592. Risk of leukemia and multiple myeloma associated with exposure to benzene and other organic solvents: evidence from the Italian Multicenter Case-control study. Costantini AS, Benvenuti A, Vineis P, Kriebel D, Tumino R, Ramazzotti V, Rodella S, Stagnaro E, Crosignani P, Amadori D, Mirabelli D, Sommani L, Belletti I, Troschel L, Romeo L, Miceli G, Tozzi GA, Mendico I, Maltoni SA, Miligi L. Risk of leukemia and multiple myeloma associated with exposure to benzene and other organic solvents: evidence from the Italian Multicenter Case-control study. Costantini AS, Benvenuti A, Vineis P, Kriebel D, Tumino R, Ramazzotti V, Rodella S, Stagnaro E, Crosignani P, Amadori D, Mirabelli D, Sommani L, Belletti I, Troschel L, Romeo L, Miceli G, Tozzi GA, Mendico I, Maltoni SA, Miligi L.
(11) Environmental Profiles of Chemical Flame-Retardant Alternatives for Low-Density Polyurethane Foam | Design for the Environment (DfE) | US EPA, (http://www.epa.gov/dfe/pubs/flameret/ffr-alt.htm Web site accessed Feb 9, 2014),

(12) Section 3 of Environmentally Preferable Options for Furniture Fire Saftey: Low-Density Furniture Foam, Volume 1 (http://www.epa.gov/dfe/pubs/flameret/altrep-v1/altrep-v1a-sec3.pdf Web site accessed Feb 9, 2014)
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(14) Volatile organic compounds (VOCs) in new car interiors, Brown, S. K.; Cheng, Min, CSIRO Fifteenth International Clean Air & Environment Conference, 26-30 November, 2000, Vol 1, Pages: 464-468, procite:bae3deda-6166-4e69-8887-22f64ed05e14
Additional links:

- DA: Santa Cruz Tesla driver to face misdemeanor in fatal bike crash
- Enjoying the smell of a new car 'is like glue-sniffing'
- Identification Of Volatile Organic Compounds In a New Automobile
- Inhalation toxicokinetics of p-dichlorobenzene and daily absorption and internal accumulation in chronic low-level exposure to humans
- 1,4-Dichlorobenzene