Study Application (Version 1.0)

1.0 General Information

***Enter the full title of your study:**

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

***Enter the study number or study alias**

Blood profile biomarkers, effects of environmental chemicals.
* This field allows you to enter an abbreviated version of the Study Title to quickly identify this study.

2.0 Add Department(s)

2.1 List the departments associated with this study. The Principal Investigator's department should be Primary.:

Primary Dept?	Department Name
◆	**UCSF** - *133144* - M_Psych-LPPI-Core-General

3.0 List the key study personnel: (Note: external and affiliated collaborators who are not in the UCSF directory can be identified later in the Qualifications of Key Study Personnel section at the end of the form)

3.1 *Please add a Principal Investigator for the study:

Reus, Victor I. MD

Select if applicable

☐ Department Chair ☐ Resident

☐ Fellow

If the Principal Investigator is a Fellow, the name of the Faculty Advisor must be supplied below.

3.2 If applicable, please select the Research Staff personnel:

A) Additional Investigators

Perdue, Lewis
Co-Principal Investigator

B) Research Support Staff

3.3 *Please add a Study Contact:

Perdue, Lewis
Reus, Victor I. MD

The Study Contact(s) will receive all important system notifications along with the Principal Investigator. (e.g. The project contact(s) are typically either the Study Coordinator or the Principal Investigator themselves).

3.4 If applicable, please add a Faculty Advisor/Mentor:

3.5 If applicable, please select the Designated Department Approval(s):

Add the name of the individual authorized to approve and sign off on this protocol from your Department (e.g. the Department Chair or Dean).

4.0 Qualifications of Key Study Personnel

4.1 November, 2015 - NEW Definition of Key Study Personnel and CITI Training Requirements:

UCSF Key Study Personnel include the Principal Investigator, other investigators and research personnel who are directly involved in conducting research with study participants or who are directly involved in using study participants' identifiable private information during the course of the research. Key Personnel also include faculty mentors/advisors who provide direct oversight to Postdoctoral Fellows, Residents and Clinical Fellows serving as PI on the IRB application. **The IRB requires that all Key Study Personnel complete Human Subjects Protection Training through CITI prior to approval of a new study, or a modification in which KSP are being added. More information on the CITI training requirement can be found on our website.**

List the study responsibilities and qualifications of any individuals who qualify as Key Study Personnel (KSP) at UCSF and affiliated sites ONLY by clicking the "Add a new row" button. This information is required and your application will be considered incomplete without it.

KSP Name	Description of Study Responsibilities	Qualifications
Reus, Victor I., MD	PI, No Subject Contact Study: Oversees design of project, data collection, data management, protocol adherence.	Victor I. Reus, M.D. is a Professor in the Department of Psychiatry at the University of California, San Francisco School of Medicine and an investigator in the Center for Neurobiology and Behavior. He is a former Medical Director of the Langley Porter Hospital and is Co-Principal Investigator or Co-Investigator on a number of extramural supported research grants, as well as an editor of Focus:the Journal of Life Long Learning in Psychiatry, the Journal of Depression and Anxiety, and Faculty 1000 reviews. He has received the APA/NIMH Vestermark Award for excellence as a psychiatric educator, served on the DSM-5 Oversight and Community

			and Public Health Committees, is an Emeritus Director and Vice-Chair of the American Board of Psychiatry and Neurology (ABPN) and a former Chair of the Psychiatry Residency Review Committee (RRC) for the Accreditation Council for Graduate Medical Education (ACGME), and has been listed in successive editions of The Best Doctors in America and America's Top Doctors for over twenty years. He currently serves as Vice-Chair of the Board of Directors of the Accreditation Council for Continuing Medical Education (ACCME) and is Chair of the Practice Guideline Writing Group for the American Psychiatric Association, as well as Chair of the UCSF (Parnassus) Committee on Human Research. He has published over 290 peer reviewed articles and chapters, with a particular emphasis on the biology and genetics of mood disorders, resulting in almost 8000 citations and an h index of 48. Twenty two papers have received over 100 citations each.
Perdue, Lewis	Co-PI, study coordinator - Oversees all aspects of the proposed study, including design, data collection, analysis, recruitment, informed consent, and reporting of results. In charge of recruiting, consenting, tracking and follow-up of participants, and collecting and managing study data.	Academic and vocational background in biology, organic chemistry, environmental science, high-energy physics and nuclear engineering. Graduate of Cornell University, B.S. (With Distinction), 1972. Majored in biology with an emphasis on Ecology, Evolution & Systematics. University recognition for several academic accomplishments including the discovery of 23 incorrect quantum bonding orbital diagrams and explanations contained in the required Organic Chemistry textbook. Intensive independent study of environmental chemicals (2012 to present) including two original scientific papers, one of which was the first connection between low-level exposure to Bisphenol A and the over-expression of cyclin Kinase CDK5 and its role in Medullary Thyroid Cancer. Co-founder of the Stealth Epidemics Project

Other scientific work included a position with Westinghouse Electric where he helped improve spectrographic test equipment and prototyped solar flux instruments for a Mars fly-by, and calibrated neutron density measurement probes for nuclear reactors.

Inventor of several significant devices including the first demonstration of web payments (1999). Patent filed (2014) for advanced computer /online recommendation algorithm.

5.0 Initial Screening Questions - Updated 9/13

(Note: You must answer every question on this page to proceed). If you are converting to the new form, check questions 5.4, 5.6, 5.7, 5.8 and 5.10 before saving and continuing to the next section.

5.1 * Application type:

- ○ Full Committee
- ◉ Expedited
- ○ Exempt

5.2 * Risk level (Help Text updated 9/13):

- ◉ Minimal risk
- ○ Greater than minimal risk

5.3 * Subject contact:

- ◉ Yes (including phone, email or web contact)
- ○ No (limited to medical records review, biological specimen analysis, and/or data analysis)

5.4 * Funding (past or present):

- ◉ Funded or will be funded (external sponsor, gift, program or specific internal or departmental funds)
- ○ Unfunded (no specific funds earmarked for this project)
- ○ Unfunded student project

5.5 * The Principal Investigator and/or one or more of the key study personnel has financial interests related to this study:

- ○ Yes ◉ No

If **Yes**, the Conflict of Interest Advisory Committee (COIAC) office may contact you for additional information.

5.6 * This is an investigator-initiated study:

(•) Yes ( ) No

5.7 * This study ONLY involves retrospective records review and/or identifiable biospecimen analysis:

( ) Yes (•) No

5.8 * This is a clinical trial:

( ) Yes (•) No

Clinical Trial Registration
"NCT" number for this trial:

5.9 * This is a multicenter study:

( ) Yes (•) No

5.10 * This application involves the study of unapproved or approved drugs, devices, biologics or in vitro diagnostics:

( ) Yes (•) No

5.11 * This application involves a Humanitarian Use Device:

(•) No
( ) Yes, and it includes a research component
( ) Yes, and it involves clinical care ONLY

5.12 * This study involves human stem cells (including iPS cells and adult stem cells), gametes or embryos:

(•) No
( ) Yes, and requires CHR and GESCR review
( ) Yes, and requires GESCR review, but NOT CHR review

5.13 * This is a CIRB study (e.g. the NCI CIRB will be the IRB of record):

( ) Yes (•) No

5.14 * This application includes a request to rely on another IRB (other than NCI CIRB):

( ) Yes (•) No

Note: If this request is approved, the CHR will **NOT** review and approve this study. Another institution will be the IRB of record.

6.0 Expedited Review Categories

6.1 * If you think this study qualifies for expedited review, select the regulatory category(ies) that the research falls under:

- [ ] Category 1: A very limited number of studies of approved drugs and devices
- [x] Category 2: Blood sampling
- [x] Category 3: Noninvasive specimen collection (e.g. buccal swabs, urine, hair and nail clippings, etc.)
- [ ] Category 4: Noninvasive clinical procedures (e.g. physical sensors such as pulse oximeters, MRI, EKG, EEG, ultrasound, moderate exercise testing, etc.)
- [ ] Category 5: Research involving materials (data, documents, records, or specimens) that were previously collected for either nonresearch or research purposes
- [ ] Category 6: Use of recordings (voice, video, digital or image)
- [ ] Category 7: Low risk behavioral research or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies

7.0 Funding

7.1 Identify all sponsors and provide the funding details. If funding comes from a Subcontract, please list only the Prime Sponsor: **Note: we require only a P Number *OR* an A Number for funding coming through UCSF. Please avoid these common errors in funding documentation:**

- **DO NOT add the A Number if a P Number was already provided OR update the A Number field when a new funding cycle begins. The IRB does NOT use this information or want these changes made.**
- **DO NOT add a grant continuation as a new funding source.**

External Sponsor:

View Details	Sponsor Name	Sponsor Type	Awardee Institution	Contract Type:	UCSF RAS "P number" or eProposal number	UCSF RAS System Award Number ("A" + 6 digits)
No Sponsor has been added to this IRB Study						

Gift, Program, or Internal Funding (check all that apply):

- [ ] Funded by gift (specify source below)
- [ ] Funded by UCSF or UC-wide program (specify source below)
- [ ] Specific departmental funding (specify source below, if applicable)

List the gift, program, or departmental funding source:

7.2 If you tried to add a sponsor in the question above and it was not in the list, follow these steps:

- **If funding has already been awarded or the contract is being processed by the Office of Sponsored Research (OSR) or Industry Contracts Division (ICD), your sponsor is already in the system and the project has an eProposal Proposal or Award number. Check with your department's OSR Staff or ICD Officer to ask how the sponsor is listed in the UC sponsor list and what the Proposal or Award number is. Click here to find your OSR staff and here to find your ICD staff.**

- **If your sponsor is not yet in the list, enter it in the box below.**

(•) Sponsor not in list

Only if your sponsor is not yet in the list, type the sponsor's name:

Stealth Syndromes Project

If the funding is administered by the UCSF Office of Sponsored Research, your study will not receive CHR approval until the sponsor and funding details have been added to your application.

7.3 * This study is currently supported in whole or in part by Federal funding OR has received ANY Federal funding in the past (Help Text updated 9/13):

( ) Yes (•) No

If **yes**, indicate which portion of your grant you will be attaching:

- [ ] The Research Plan, including the Human Subjects Section of your NIH grant or subcontract
- [ ] For other federal proposals (contracts or grants), the section of the proposal describing human subjects work
- [ ] The section of your progress report if it provides the most current information about your human subjects work
- [ ] The grant is not attached. The study is funded by an award that does not describe specific plans for human subjects, such as career development awards (K awards), cooperative agreements, program projects, and training grants (T32 awards) OR UCSF (or the affiliate institution) is not the prime recipient of the award

8.0 Sites

8.1 Institutions (check all that apply):

- [ ] UCSF
- [ ] China Basin
- [ ] Helen Diller Family Comprehensive Cancer Center
- [ ] Mission Bay
- [ ] Mount Zion
- [ ] San Francisco General Hospital (SFGH)
- [ ] SF VA Medical Center (SF VAMC)
- [ ] Blood Centers of the Pacific (BCP)
- [ ] Blood Systems Research Institute (BSRI)
- [ ] Fresno (Community Medical Center)
- [ ] Gallo
- [ ] Gladstone
- [ ] Institute on Aging (IOA)
- [ ] Jewish Home
- [ ] SF Dept of Public Health (DPH)

8.2 Check all the other types of sites not affiliated with UCSF with which you are cooperating or collaborating on this project (Help Text updated 9/13):

- [ ] Other UC Campus
- [ ] Other institution

☑ Other community-based site

☐ Foreign Country

List the foreign country/ies:

8.3 Check any research programs this study is associated with:

☐ Cancer Center
☐ Center for AIDS Prevention Sciences (CAPS)
☐ Global Health Sciences
☐ Immune Tolerance Network (ITN)
☐ Neurosciences Clinical Research Unit (NCRU)
☐ Osher Center
☐ Positive Health Program

9.0 Studies Involving Other Sites

9.1 UCSF is the coordinating center:

○ Yes ◉ No

If **Yes**, describe the plan for communicating safety updates, interim results, and other information that may impact risks to the subject or others among sites:

If **Yes**, describe the plan for sharing modification(s) to the protocol or consent document(s) among sites:

9.2 Check any other UC campuses with which you are collaborating on this research study:

☐ UC Berkeley
☐ UC Davis
☐ Lawrence Berkeley National Laboratory (LBNL)
☐ UC Irvine
☐ UC Los Angeles
☐ UC Merced
☐ UC Riverside
☐ UC San Diego
☐ UC Santa Barbara
☐ UC Santa Cruz

9.3 Are the above UC campuses requesting to rely on UCSF's IRB (check all that apply):

☐ Yes (Submit a reliance request through the UC IRB Reliance Registry)
☐ No (Complete IRB Approval Certification section)

10.0 Outside Site Information

10.1 Outside Site Information

Click "Add a new row" to enter information for a site. Click it again to add a second site again to add a third site, a fourth site, etc.

Outside Site Information

Non-UCSF affiliated site information:

Site name:

Stealth Syndromes investigation site

Contact name:

Lewis Perdue

Email:

lperdue@ideaworx.com

Phone:

707-326-4503

For Federally-funded studies only, corresponding FWA#:

*** The research at this site will be reviewed by:**

- ○ The non-affiliated site's IRB or a private IRB
- ○ The non-affiliated site is requesting UCSF to be the IRB of record for this study
- ◉ The non-affiliated site is not engaged in the human subjects research and has provided a letter of support

If the other site's IRB approval letter is available now, attach it to the application. If the IRB approval letter is not yet available, submit it once you receive it.

Or, if the other site is **not engaged** in human subjects research, attach the letter of support to your application.

11.0 Study Design

11.1 * Study design (Help Text updated 9/13):

This is an interventional dietary study to determine the usefulness of carefully selected tests from standard medical blood profiles to indicate health effects which may result from the staged reduction of specific foods and substances found by published, peer-reviewed investigations to contain certain environmental chemicals.
This study is the first to use easily accessed and medically accepted laboratory methods to directly measure health effects of dietary intervention on the reduction of persistent and ubiquitous environmental chemicals. While this is an n=1, proof-of-concept study using co-Principal Investigator Lewis Perdue as the test subject, it expands upon previous studies with a longer observation period, and by designating specific substances (packaged in glass vs plastic or cans, elimination of dermal contact) for intervention instead of general parameters (fresh versus prepared foods).

11.2 If this is a clinical trial, check the applicable phase(s) (Help Text updated 9/13):

- ☐ Phase I
- ☐ Phase II
- ☐ Phase III
- ☐ Phase IV

12.0 Scientific Considerations

12.1 Hypothesis (Help Text updated 9/13):

This study has a hypothesis:

◉ Yes ○ No

If yes, state the hypothesis or hypotheses:

The controlled and stepwise elimination of environmerntal chemicals known as Chemicals of Emerging Concern (CECs) from the test subject environment will result in measurable changes in serum and urine concentrations of specific chemicals and standard clinical health biomarkers attributable to each class of CEC-containing product.

12.2 * List the specific aims:

Determine whether a positive correlation exists between CEC intevention and test subject blood profiles and CEC levels in serum and urine. Because the significance of CEC urine and serum levels is controversial, the primary aim of this study is to provide a measurement of direct CEC health effects (or lack thereof) using widely available laboratory blood profile indicators.
A secondary aim of this study is to provide a method to correlate potential health effects of CECs with their observed human levels as previously measured by NHANES and other investigations.

12.3 Statistical analysis:

12.4 If this study has undergone scientific or scholarly review, please indicate which entity performed the review:

- ☐ Cancer Center Protocol Review Committee (PRC) (Full approval is required prior to final CHR approval for cancer-related protocols.)
- ☐ CTSI Clinical Research Center (CRC) advisory committee
- ☐ Departmental scientific review
- ☐ Other:

Specify **Other**:

13.0 Background

13.1 Background:

INTRODUCTION
The human health effects of low-level concentrations of certain Chemicals of Emerging Concern (CECs) has stirred immense controversy between traditional toxicologists and a more recent, emerging body of

scientists grounded in epigenetics and molecular-level effects. Traditional toxicologists insist that current risk evaluations at high concentration levels can be monotonically extrapolated to low concentrations and that a firm No Observed Adverse Effects Level (NOAEL) of safety can be established.
On the other hand, a more recent and growing body of peer-reviewed, published data indicates that many CECs exhibit non-monotonic behavior and present risks to humans at low concentrations. That controversy continues partly because of the lack of controlled human studies and the almost complete absence of investigations into effects of combinations of CECs.
BACKGROUND
Exposure to environmental chemicals in the U.S. is widespread[20].
More than 84,000 chemicals are approved for use in the United States today[1]. And at least 4,000 of those are present in food contact materials[2,3,4]. The health effects of most of those chemicals is unknown and/or incomplete[5].
While controversial by some, many of these chemicals in low-level concentrations are increasingly classified as endocrine disruptors[22,23].
Among chemicals of emerging concern (CEC) are Bisphenol A (BPA) and phthalates, both of which are present in approximately 97% of the U.S. population.[6,8] Public concern over the risks from these chemicals have resulted in the reduction of concentrations of some[7] but also increases in concentrations of substitutes which are also of concern. [39]
BPA is used to strengthen and offer heat resistance to common plastics such as polycarbonate. Phthalates are added to plastics for flexibility. Those two compounds are among the most common and widely studied chemicals of emerging concern. For that reason, this study will use them as proxies for overall chemical contamination.

Exposure

Bisphenol A (BPA) and phthalates have become nearly ubiquitous in our environment and can be found in many different products, including the plastic in water bottles and baby bottles, thermal paper for printers, and even in dental sealants and medical devices including intravenous fluid and chemotherapy bags and tubing [8,9,10,1,12,13,14].
In addition food and beverage packaging are substantial contributors to the CEC Burden[8,15,16,17,25,26].
Consumers are exposed to many chemicals of concern from leaching and migration of chemicals from plastics and other food contact materials.[8,14,15,16, 30-37]
Other chemicals of concern are deliberately added to consumer and household products such as detergents, cosmetics, lotions, and fragrances[38].
Still other contamination may result from the harvest and processing of food products[17].

Causes For Concern

Human and animal studies have identified those compounds as contributors to cancer[24,40-52], cardiovascular disorders[53-61], obesity[62-68], type 2 diabetes[69-72], metabolic syndrome[73-77], neurological and behavioral disorders including Alzheimer's Disease[78-84], as well as reproductive[85-94], and developmental[95-102] disorders and allergies[103-110].

Specific Exposure Routes

All products:

1. Migration/leaching of chemicals from packaging materials,
2. Deliberate addition of chemicals used as preservatives, flavorings, scents, texture enhancers, coloring agents etc.[4],
3. Contamination by unknown compounds formed by chemical reactions among multiple intentionally used constituent chemicals[18].

Food and beverages specifically:

1. Incidental contamination via migration/leaching of chemicals from harvesting and processing[17].
2. Home food-handling can also accelerate migration through heating, microwaving, ultraviolet light exposure (including fluorescent lighting) and the contact of oils and alcohols with plastics.

13.2 Preliminary studies:

All studies so far that evaluate potential adverse health effects of CECs by controlled exposure have been done *in vitro* or *in vivo* using murine or other non-human models. Despite the fact that that all of the CECs in question are nearly ubiquitous in the human environment, ethical concerns have prevented controlled exposure studies. Practical concerns also complicate controlled human exposure studies because ubiquitous exposure to mixtures of CECs make it impossible to create an adequate control population. Because of that,a small number of interventional dietary studies have been done. These studies have focused on foods and beverages because thet constitute major sources of CECs. Dietary interventions are easier to control and offer opportunities to reduce health risks[24,27].

Recent dietary interventions[16, 17,28] have found significant reductions in the targeted chemicals measured concurrent with study designs to replace pre-prepared meals and other foods with known levels of endocrine disruptors with a fresh, home-prepared diet.
Those interventional studies have been:

1. time-limited (3 -16 days),
2. involved relatively small numbers of test subjects (20 - 40)′,
3. imposed very general dietary restrictions (whole diet, fresh foods)

The most significant failing, however, is the failure to connect the reduced levels of CECs to any measurable indication of health benefits.

13.3 References:

PARTIAL BIBLIOGRAPHY
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If you have a separate bibliography, attach it to the submission with your other study documents.

14.0 Sample Size and Eligibility

14.1 Number of subjects that will be enrolled at UCSF and affiliated institutions:

0

14.2 Total number of subjects that will be enrolled at all sites (Help Text updated 9/13):

1

14.3 Estimated number of people that you will need to consent and screen here (but not necessarily enroll) to get the needed subjects:

1

14.4 Explain how and why the number of subjects was chosen (Help Text updated 9/13):

Willingness, availability, and long-established tradition of scientists using themselves as test subjects.

14.5 * Eligible age range(s):

- [ ] 0-6 years
- [ ] 7-12 years
- [ ] 13-17 years
- [x] 18+ years

14.6 Inclusion criteria:

Co-Principal Investigator is a willing subject

14.7 Exclusion criteria:

14.8 There are inclusion or exclusion criteria based on gender, race or ethnicity:

- ( ) Yes
- (•) No

If **yes**, please explain the nature and rationale for the restrictions:

15.0 Other Approvals and Registrations

15.1 * Do any study activities take place on patient care units:

○ Yes ◉ No

If **Yes**, attach a letter of support for the study from the involved patient care manager(s).

15.2 * Does your protocol involve any radiation exposure to patients/subjects? The UCSF Radiation Safety Committee requires review of your protocol if it includes administration of radiation as part of standard of care OR research exposures:

○ Yes ◉ No

15.3 * This study may generate genetic data that may be broadly shared (e.g. submitted to NIH for Genome-Wide Association Studies (GWAS) in dbGaP, TCGA, etc):

○ Yes ◉ No

15.4 * This study involves administration of vaccines produced using recombinant DNA technologies to human subjects:

○ Yes ◉ No

15.5 * This study involves human gene transfer (NOTE: Requires NIH Recombinant DNA Advisory Committee (RAC) review prior to CHR approval):

○ Yes ◉ No

15.6 This study involves other regulated materials and requires approval and/or authorization from the following regulatory committees:

☐ Institutional Biological Safety Committee (IBC)

Specify BUA #:

☐ Institutional Animal Care and Use Committee (IACUC)

Specify IACUC #:

☐ Radiation Safety Committee

Specify RUA #:

☐ Radioactive Drug Research Committee (RDRC)

Specify RDRC #:

☐ Controlled Substances

16.0 Procedures

16.1 * Procedures/Methods (Help Text updated 9/13) For clinical research list all study procedures, test and treatments required for this study, including when and how often they will be performed. If there are no clinical procedures, describe the Methods:

1. Weekly blood profile as direct clinical health-linked proxies for CEC body burden.
2. Weekly blood profile and urine measurements of Bisphenol A and phthlates for correlation with blood biomarkers.
3. Monthly double-stranded DNA break levels.
4. Monthly epigenetic profiles of specific methylation locations known to be associated with cancer, obesity, aging, infertility, or Alzheimer's disease.

We propose using specific elements of standard blood profiles that can provide direct health assessments of inflammation, glucose tolerance, lipid and cholesterol levels and similar well-established indicators.

Rationale For Selection of Specific Clinical Blood Tests

Preliminary universe of tests based on known cellular and biological mechanisms of BPA, phthalates and other CECs. To be narrowed down in consultation with a qualified hematologist.

Estrogenic activity
Anti-androgenic activity
Oxidative stress / inflammation
Glucose metabolism
Insulin resistance
Adipocyte functioning
Epigenetic alterations
Interference with Mitosis (centrioles)
CDK5 effects (thyroid cancer)
Prostate cancer (PSA levels)
Accelerated cell proliferation and decreased apoptosis
Affects on G-Protein Coupled Receptors
WBC
Cytokines:Il-1,6,8,10
TNF alpha
CRP
BDNF, VEGF,IGF-BP#3,EGF,FGF,FGF-2?,NGF
ESR
F2 isoprostanes
Cholesterol/HDL/triglycerides
Hormones:cortisol,prolactin,GH,adiponectin,ghrelin,leptin,insulin, fasting glucose,NPY
Vit E,C,D
Fibrinogen
Cell adhesion molecules:VCAM-1,ICAM
Oxidative stress markers:glutthione peroxidase,superoxide dismutase,nitric oxide,
Human methylation 450 bead chip
telomere length; telomerase

Bisphenol A & Phthlates As Markers For Chemicals Of Concern

Any given product may contain multiple compounds which makes the task of identifying which compounds (or synergistic combinations) are responsible for a given health effect impractical for this study.

Indeed, given the lack of health effects data on most chemicals involved, the task would be impossible for the budgets and technical abilities of the most advanced laboratories. Significantly, even less data is known about combined health effects of the everyday mixtures to which consumers are exposed.

To make this study possible and yield the best possible data, the products chosen for stepwise abstention have been categorized primarily with an eye towards those with established and previously measured levels of BPA and phthalates.

Given that the now-well-studied BPA and phthalate compounds are often used together -- and always used in combination with other polymers, resins, and product enhancement chemicals -- we theorize that they are suitable markers for the presence of other "bad actors."

Significantly, any health effects that may be observed from our study will clearly reflect possible synergistic effects from combinations of chemicals since it is impossible for us to know exactly which compounds are in a given product.

Study Product Category Rationale

In addition to selecting products with BPA and phthalate markers, we have also categorized products by their method of exposure:

- Consumption - migration and leaching from packaging[8],
- Consumption - migration and leaching from preparation stressors: heat, microwaving, ultraviolet /sunlight exposure, use of suspected utensils, preparation and eating surfaces

- Skin contact, inhalation
- Consumption - inherent content as purchased - resulting from harvest and processing

Product Category 1: Food (migration and leaching from packaging)

- Eliminating all products packaged in cans and plastic.
- Use of fresh products when possible.
- Products packed in glass may be substituted.
- Plastic-wrapped dry foods (bread, pasta etc)
- Plastic-wrapped wet fresh foods (veggies, cheese, meat)
- Plastic storage bags
- Milk, Cheese, dairy products
- Cutting boards

Product Category 2: Food (migration and leaching from preparation stressors)

- Foods with metalized plastic "crisping" surfaces (Hot Pockets, frozen pizza)
- Paper or plastic plates, glasses and cups
- Take-out and deli plastic containers of all sorts.
- Restaurant and fast food
- Frozen and similar convenience foods

Product Category 3 (Non-alcoholic beverages, migration and leaching from packaging)

- Filtered tap water versus unfiltered.
- Homes/Offices where the water supply comes via PVC or Pex plastics.
- Beverages in pouches, boxes and "paper bottles'
- Water in hydration bladders like Camelbak
- Drip coffee maker and Keurig (plastic) as well as the Sodastream

Product Category 4 (skin contact/inhalation)

- Laundry detergents (phthalates, fragrances, surfactants)
- Dish and dishwasher soaps (same as laundry)
- Toothpaste (plastic tube) … alternative?
- Toothbrush … what are the bristles made of?
- Floss?
- Fitbits, plastic watch bands
- Gore-Tex and other waterproof coatings
- Paper currency
- Receipts

Product Category 5 (Alcoholic Beverages - Non-alcoholic beverages, migration and leaching from packaging, Ethanol known solvent for chemicals)
Alcohol consumption limited to two five-ounce pours of 14% wine or the equivalent.

- Wine in plastic pouches/bottles/boxes
- Distilled spirits in glass versus plastic bottles.
- Wine and beer "on tap"

Product Category 6 (Alcoholic Beverages in glass bottles).
Alcohol consumption limited to two five-ounce pours of 14% wine or the equivalent.

Product Category 7: dairy products Consumption - inherent content as purchased - resulting from harvest and processing
The present study will focus on dairy products as a category for its own abstain/intervention. This is because a recent study found an unexpected increase in phthalates especially in children. That study theorized this increase was due to their greater consumption of milk than adults. Investigators in that study theorize that the extensive use of plastics in the milk-production process was responsible for the phthalates increase despite the fact that milk was delivered in glass bottles. In fact, that study calculated that children were exposed to 183 micrograms/kg/day and noted that level was more than 9X higher than, the EPA oral reference dose of 20 micrograms/kg/day.

ACTIVITY	Week									
	0	1	2	3	4	5	6	7	8	9
Usual diet/lifestyle										
Blood/urine sample - Baseline1										
Epigenetic Profile & Double-stranded DNA testing - baseline										
Intentional EDC Exposure - "Normal American " diet										
Blood/urine sample - Baseline2										
Abstain Product Category 1										
Blood/urine sample - After P-1 Abstain										
Abstain Product Category 2										
Blood/urine sample - After P-2 Abstain										
Abstain Product Category 3										
Epigenetic Profile & Double-stranded DNA testing - mid-point										
Blood/urine sample- After P-3 Abstain										
Abstain Product Category 4										
Blood/urine sample- After P-4 Abstain										
Abstain Product Category 5										
Blood/urine sample - After P5 Abstain										
Abstain Product Category 6										
Blood/urine sample- After P-6 Abstain										
Abstain Product Category 7										
Blood/urine sample- After P-7 Abstain										
Resume Normal Diet										
Blood/urine sample - After Return to usual diet/lifestyle										
Epigenetic Profile & Double-stranded DNA testing -final										

If you have a procedure table, attach it to the submission with your other study documents.

16.2 Interviews, questionnaires, and/or surveys will be administered or focus groups will be conducted:

(•) Yes ( ) No

List any standard instruments used for this study:

Test subjects will engage in real-time, daily logging of everything they eat, drink use, or apply to their bodies and will involve the removal of one item category per week.
Because BPA and phthalates are cleared within 24 hours[8,17,21,22], a weekly schedule should provide adequate time for clearance of BPA and phthalates
However, given the certainty of unknown chemicals and their uncertain clearance rates from the body, this period is uncertain.
Items chosen for removal will be selected according to peer-reviewed, published data measuring CECs in consumer products.
We theorize that removal of items known to contain or leach chemicals of concern will result in improvement of test subjects' blood profiles as well as epigenetic profiles and double-stranded DNA break analysis
If that is confirmed, then it may be reasonable to conclude that the removal of those items was responsible.
It is possible that the change of chemical levels measured may fall beneath the noise level or the margins of error for an individual test. In those cases, we anticipate that the longer term levels will show a decrease.

Attach any non-standard instruments at the end of the application.

16.3 Conduct of study procedures or tests off-site by non-UCSF personnel:

(•) Yes ( ) No

If yes, explain:

Procedures conducted by Co-Principal Investigator in personal environment.
Urine, serum, double-stranded DNA break and epigenetic testing to be peformed by contractors as yet unseselected.

16.4 Sharing of experimental research test results with subjects or their care providers:

(•) Yes ( ) No

If yes, explain:

Procedures conducted by Co-Principal Investigator

16.5 * Specimen collection for future research and/or specimen repository/bank administration:

( ) Yes (•) No

16.6 Time commitment (per visit and in total):

Two hours per day average, 150 hours total

16.7 Locations:

19100 Ola Ct., Sonoma, CA + external locations as dictated by lifestyle, vocation and personal duties.

16.8 Describe the resources in place to conduct this study in a way that assures protection of the rights and welfare of participants:

No change in environment for test subject.

17.0 Risks and Benefits

17.1 * Risks and discomforts:

none

17.2 Steps taken to minimize risks to subjects:

none neded

17.3 Benefits to subjects:

(•) Yes ( ) No

If yes, describe:

potential increase in health indicators

17.4 Benefits to society:

1. First connection established between dietary intervention and health indicators.

2. Establishment of a framework to move risk assessment of low-level Chemicals of Emerging Concern beyond traditional toxicological ervaluations and toward molecular and epigenetic evaluations.
3. Development of techniques to reduce exposure to CECs
4. Emphasis on techniques (#2, above) that can easily and economically be implemented by the average person without significant disruption to daily lives.
5. Overall improvement in public health and a potential path to reducing the rising incidence of obesity, Type 2 Diabetes, Alzheimer's disease and other behavioral disorders, fertility and developmental disorders

17.5 Explain why the risks to subjects are reasonable:

No risks beyond ordinary daily life. Test subject, like all Americans, is exposed to ubiquitous CECs. Intevention will reduce those exposures.

18.0 Confidentiality and Privacy

18.1 Plans for maintaining privacy in the research setting:

Co-Principal Investigator is test subject.

18.2 Possible consequences to subjects resulting from a loss of privacy:

none.

18.3 Study data are:

- ☐ Derived from the Integrated Data Repository (IDR) or The Health Record Data Service (THREDS) at SFGH
- ☐ Derived from a medical record (e.g. APeX, OnCore, etc. Identify source below)
- ☐ Added to the hospital or clinical medical record
- ☐ Created or collected as part of health care
- ☐ Used to make health care decisions
- ☑ Obtained from the subject, including interviews, questionnaires
- ☐ Obtained from a foreign country or countries only
- ☐ Obtained from records open to the public
- ☐ Obtained from existing research records
- ☐ None of the above

If **derived from a medical record**, identify source:

18.4 Identifiers may be included in research records:

◉ Yes ○ No

If **yes**, check all the identifiers that may be included:

- ☑ Names
- ☑ Dates
- ☑ Postal addresses
- ☑ Phone numbers
- ☑ Fax numbers
- ☑ Email addresses
- ☐ Social Security Numbers*

- [ ] Medical record numbers
- [ ] Health plan numbers
- [ ] Account numbers
- [ ] License or certificate numbers
- [ ] Vehicle ID numbers
- [ ] Device identifiers or serial numbers
- [x] Web URLs
- [x] IP address numbers
- [ ] Biometric identifiers
- [ ] Facial photos or other identifiable images
- [ ] Any other unique identifier

* Required for studies conducted at the VAMC

18.5 Identifiable information might be disclosed as part of study activities:

( ) Yes (•) No

If **yes**, indicate to whom identifiable information may be disclosed:

- [ ] The subject's medical record
- [ ] The study sponsor
- [ ] Collaborators
- [ ] The US Food & Drug Administration (FDA)
- [ ] Others (specify below)
- [ ] A Foreign Country or Countries (specify below)

If **Others**, specify:

18.6 Indicate how data are kept secure and protected from improper use and disclosure (check all that apply): NOTE: Whenever possible, do not store subject identifiers on laptops, PDAs, or other portable devices. If you collect subject identifiers on portable devices, you MUST encrypt the devices.

- [ ] Data are stored securely in My Research
- [ ] Data are coded; data key is destroyed at end of study
- [ ] Data are coded; data key is kept separately and securely
- [ ] Data are kept in a locked file cabinet
- [ ] Data are kept in a locked office or suite
- [x] Electronic data are protected with a password
- [x] Data are stored on a secure network
- [ ] Data are collected/stored using REDCap or REDCap Survey
- [ ] Data are securely stored in OnCore

18.7 Additional measures to assure confidentiality and protect identifiers from improper use and disclosure, if any:

18.8 This study may collect information that State or Federal law requires to be reported to other officials or ethically requires action:

( ) Yes (•) No

Explain:

18.9 This study will be issued a Certificate of Confidentiality:

○ Yes ◉ No

19.0 Subjects

19.1 Check all types of subjects that may be enrolled:

- ☐ Inpatients
- ☐ Outpatients
- ☑ Healthy volunteers
- ☐ Staff of UCSF or affiliated institutions

19.2 Additional vulnerable populations:

- ☐ Children
- ☐ Subjects unable to consent for themselves
- ☐ Subjects unable to consent for themselves (emergency setting)
- ☐ Subjects with diminished capacity to consent
- ☐ Subjects unable to read, speak or understand English
- ☐ Pregnant women
- ☐ Fetuses
- ☐ Neonates
- ☐ Prisoners
- ☐ Economically or educationally disadvantaged persons
- ☐ Investigators' staff
- ☐ Students

Explain why it is appropriate to include the types of subjects checked above in this particular study:

Describe the additional safeguards that have been included in the study to protect the rights and welfare of these subjects and minimize coercion or undue influence:

20.0 Recruitment

20.1 * Methods (check all that apply):

- ☑ Study investigators (and/or affiliated nurses or staff) recruit their own patients directly in person or by phone.
- ☐ Study investigators recruit their own patients by letter. Attach the letter for review.
- ☐ Study investigators send a "Dear Doctor" letter to colleagues asking for referrals of eligible patients. If interested, the patient will contact the PI or the PI may directly recruit the patients (with documented permission from the patient). Investigators may give the referring physicians a study information sheet for the patients.
- ☐ Study investigators provide their colleagues with a "Dear Patient" letter describing the study. This letter can be signed by the treating physicians and would inform the patients how to contact the study investigators. The study investigators may not have access to patient names and addresses for mailing
- ☐ Advertisements, notices, and/or media used to recruit subjects. Interested subjects initiate contact with study investigators. Attach ads, notices, or media text for review. In section below, please explain where ads will be posted.
- ☐ Study investigators identify prospective subjects through chart review. (Study investigators request a Waiver of Authorization for recruitment purposes.)

- [ ] Large-scale epidemiological studies and/or population-based studies: Prospective subjects are identified through a registry or medical records and contacted by someone other than their personal physician. (Study investigators request a Waiver of Authorization for recruitment purposes.)
- [ ] Direct contact of potential subjects who have previously given consent to be contacted for participation in research. Clinic or program develops a CHR-approved recruitment protocol that asks patients if they agree to be contacted for research (a recruitment database) or consent for future contact was documented using the consent form for another CHR-approved study.
- [ ] Study investigators list the study on the School of Medicine list of UCSF Clinical Trials website or a similarly managed site. Interested subjects initiate contact with investigators.
- [ ] Study investigators recruit potential subjects who are unknown to them through methods such as snowball sampling, direct approach, use of social networks, and random digit dialing.
- [ ] Other

If **Other**, explain:

20.2 * How, when, and by whom eligibility will be determined:

Co-Principal Investigator is test subject.

20.3 * How, when, where and by whom potential subjects will be approached:

Co-Principal Investigator is test subject.

20.4 * Protected health information (PHI) will be accessed prior to obtaining consent:

○ Yes ◉ No

21.0 Waiver of Consent/Authorization for Recruitment Purposes

This section is required when study investigators (and/or affiliated nurses or staff) recruit their own patients directly.

21.1 * Study personnel need to access protected health information (PHI) during the recruitment process and it is not practicable to obtain informed consent until potential subjects have been identified:

◉ Yes

If **no**, a waiver of consent/authorization is NOT needed.

21.2 * A waiver for screening of health records to identify potential subjects poses no more than minimal risk to privacy for participants:

◉ Yes

If **no**, a waiver of authorization can NOT be granted.

21.3 * Screening health records prior to obtaining consent will not adversely affect subjects' rights and welfare:

◉ Yes

If **no**, a waiver of authorization can NOT be granted.

21.4 * Check all the identifiers that will be collected prior to obtaining informed consent:

- [ ] Names
- [ ] Dates
- [ ] Postal addresses
- [ ] Phone numbers
- [ ] Fax numbers
- [ ] Email addresses
- [ ] Social Security Numbers*
- [ ] Medical record numbers
- [ ] Health plan numbers
- [ ] Account numbers
- [ ] License or certificate numbers
- [ ] Vehicle ID numbers
- [ ] Device identifiers or serial numbers
- [ ] Web URLs
- [ ] IP address numbers
- [ ] Biometric identifiers
- [ ] Facial photos or other identifiable images
- [ ] Any other unique identifier
- [x] None

Note: HIPAA rules require that you collect the minimum necessary.

21.5 * Describe any health information that will be collected prior to obtaining informed consent:

Co-Principal Investigator is test subject.

Note: HIPAA requires that you collect the minimum necessary.

21.6 * Describe your plan to destroy the identifiers at the earliest opportunity consistent with the research or provide a health or research justification for retaining the identifiers, or indicate and explain that retention is required by law:

Co-Principal Investigator is test subject.

22.0 Informed Consent

22.1 * Methods (check all that apply):

- [x] Signed consent will be obtained from subjects and/or parents (if subjects are minors)
- [ ] Verbal consent will be obtained from subjects using an information sheet or script
- [ ] Electronic consent will be obtained from subjects via the web or email
- [ ] Implied consent will be obtained via mail, the web or email
- [ ] Signed consent will be obtained from surrogates
- [ ] Emergency waiver of consent is being requested for subjects unable to provide consent
- [ ] Informed consent will not be obtained

22.2 * Process for obtaining informed consent:

Co-Principal Investigator is test subject.

22.3 * How investigators will make sure subjects understand the information provided to them:

Co-Principal Investigator is test subject.

23.0 Financial Considerations

23.1 Subjects payment or compensation method (check all that apply):

Payments will be (check all that apply):

- [x] Subjects will not be paid
- [ ] Cash
- [ ] Check
- [ ] Debit card
- [ ] Gift card
- [ ] Reimbursement for parking and other expenses
- [ ] Other:

Specify **Other**:

23.2 Describe the schedule and amounts of payments, including the total subjects can receive for completing the study. If deviating from recommendations in Subject Payment Guidelines, include specific justification below.

23.3 Costs to Subjects: Will subjects or their insurance be charged for any study procedures?

- ( ) Yes
- (•) No

If **yes,** describe those costs below, and compare subjects' costs to the costs associated with alternative care off-study. Finally, explain why it is appropriate to charge those costs to the subjects.

Co-Principal Investigator is test subject.

24.0 CTSI Screening Questions

24.1 * This study will be carried out at one of the UCSF Clinical Research Services (CRS) centers or will utilize CRS services. CRS centers are at the following sites:

- **SFGH Clinical Research Center**
- **Moffitt Adult Clinical Research Center**
- **Moffitt Hospital Pediatrics & NCRC**
- **Mount Zion Hospital Clinical Research Center**
- **Tenderloin Center**
- **CHORI Children's Hospital Pediatrics & Adult Clinical Research Center**
- **Kaiser Oakland Research Unit**
- **SF VA Medical Center Clinical Research Unit**

Please note: Effective 3/1/14, the CRS form will no longer be completed and submitted in iRIS. The CRS budget request form can be found at: https://accelerate.ucsf.edu/files/crs/BudgetRequest2015.docx. Follow the instructions on the form to submit. Even if you click 'Yes' to this question, the form will no longer proceed to the Clinical Research Services (CRS) Application Form section.

- ( ) Yes
- (•) No

24.2 This project involves community-based research:

○ Yes ◉ No

24.3 This project involves practice-based research:

○ Yes ◉ No

25.0 End of Study Application

25.1

End of Study Application Form

To continue working on the Study Application: Click on the section you need to edit in the left-hand menu. Remember to save through the entire Study Application after making changes. If you are done working on the Study Application: Click Save and Continue. If this is a new study, you will automatically enter the Initial Review Submission Packet form, where you can attach consent forms or other study documents. Review the Initial Review Submission Checklist for a list of required attachments. Answer all questions and attach all required documents to speed up your approval.