OVERALL SUMMARY:

The Center for Research on Environmental Chemicals in Humans (CRECH) has been organized to:

1. Support, fund, and conduct the first-ever university-approved human scientific research study on environmental chemicals primarily those in food and beverages but including select other environmental sources.

2. Develop papers for scientific journals on the study results.

3. Develop a communications campaign to inform average individuals and health professionals how to better avoid environmental chemicals.

4. Conduct follow-up research and communications efforts.

SUMMARY RESPONSES TO FORM 1023, Part IV. "Narrative Description of Your Activities"

Who:

- Lewis Perdue, Principal Scientific Co-Investigator, CRECH Director, President
- Rebecca Yeamans-Irwin, Scientific Collaborator, CRECH Director, Secretary
- Dr. Victor Reus, Scientific Co-Investigator, CRECH Director
- Andrew Starr, CRECH Director, Treasurer

All of the CRECH officers will be involved in all activities either directly or in support or advisory roles.

When:

- <u>Funding</u>: Internet Crowdfunding, starting July 1, 2017-Dec. 31, 2017 (Possibly beyond).
- <u>Organization and coordination of research study resources</u> Ongoing since Nov. 2015
- <u>Conduct of study</u> Aug. 15-Oct, 31, 2018
- <u>Analysis of study</u> Nov. 1, 2018-Feb 28, 2019

- <u>Creation and submission of scientific papers for publication</u> -- Mar. 1, 2019-Aug. 31, 2019
- <u>Information campaign</u> for health professionals and individuals -- Mar. 1, 2019-Aug. 31, 2019
- <u>Follow-up research and continuation of core activities</u> To be determined by results and an organizational assessment of future need and ability to contribute.
- <u>Grant applications and further crowdfunding</u> are likely to be ongoing through the life of the organization

Where is the activity conducted?

San Francisco Bay Area

How does the activity further your exempt purposes?

Creates needed science. Science provides answers for making valid health decisions.

What percentage of your total time is allocated to the activity?

100% of CRECH time is devoted to our goals, but the proportion will gradually shift as resources and research study efforts progress.

DETAILED RESPONSE TO FORM 1023: "Describe completely and in detail your past, present, and planned activities"

CRECH's mission is to enable individuals and health professionals to take medically valid actions against the risks of environmental chemicals (ECs) that the Centers for Disease Control has determined are found in most Americans.

To do this, CRECH's first-ever human research – which has been approved by the University of California, San Francisco Medical School -- is designed to establish a scientific cause-and-effect connection between ECs and their effects on clinically proven health indicators such as standard hospital blood tests.

The UCSF approval letter the study protocol which was approved are attached to this narrative.

CRECH Director Lewis Perdue and UCSF Professor Victor Reus are Co-Principal Investigators on the study. Director Rebecca Yeamans-Irwin is also an investigator collaborating on the study.

Biographical information about Perdue, Reus and Yeamans-Irwin are included with this narrative.

One additional result of this research will be to develop a program of risk-reduction actions that are easily incorporated into everyday lives. Those actions and other information will be distributed through a variety of public outreach including such communications channels as Internet, broadcast and print.

It is hoped that accomplishing the CRECH mission will move environmental chemical risk assessment and regulation past its current ambiguous and contentious stalemate of links, relationships, and associations toward a more solid cause-and-effect basis which can provide a factual basis for individual decisions and actions.

CRECH came about because of an important confusion

In mid-2012, Lewis Perdue began to explore the emerging issue of environmental chemicals, particularly those that disrupt hormones. His research revealed widespread confusion among scientists, medical professionals, chemical manufacturers, and government regulators at both the state and federal levels.

That confusion – which still exists – was an even bigger puzzle for consumers who were frightened by news accounts of those chemicals being linked to cancer, obesity, diabetes, heart disease, Alzheimer's and other health problems.

The confusion, especially among the general public and health professionals, was particularly acute because some chemicals – such as Bisphenol A (BPA) – were resoundingly condemned by most scientific studies, and yet were deemed "safe" by regulators and manufacturers.

The first efforts at addressing the confusion: Nano Active

Perdue decided to tackle the confusion and set about intensive research into the issues, primarily by researching peer-reviewed, published scientific papers.

In mid-2013, after realizing that the massive task he had undertaken was too extensive for one person, Perdue enlisted the help of Rebecca Yeamans-Irwin who was at the University of Virginia managing a national and international multiple sclerosis clinical research trial substudy. Perdue approached her about collaborating because he was

familiar with her venture which translated published scientific papers dealing with wine and health into a form that could be understood by non-scientists.

Shortly afterwards, they launched a joint website to address the issue: <u>Nano Active</u> (<u>http://www.nano-active.com/</u>). That effort produced two scientific papers along with entries explaining published studies.

The second effort at addressing the confusion: The Stealth Syndromes Project

By early 2014, extensive research from examining hundreds of peer-reviewed, published studies showed that the topic was larger and broader than the small expeditionary Nano Active site could handle. That was when Perdue and Yeamans-Irwin launched <u>The Stealth Syndromes Project (http://stealthsyndromes.com/)</u>.

Since its beginning, the Stealth Syndromes Project has grown into an educational site encompassing hundreds of thousands of words in scores of articles. Along the way, the research and effort as produced four scientific papers, and discovered a new "precision toxicology" method for evaluating environmental chemicals.

The second effort's pivotal discovery

By mid 2015 Perdue and Yeamans-Irwin discovered that the core scientific discovery that was necessary to make valid health decisions did not exist.

The reason that government regulators and manufacturers were at loggerheads with the vast majority of university-conducted science is:

1. <u>Lab rats are not people.</u> Many promising pharmaceuticals perform well in lab rats, and fail during human trials because of the genetic differences between humans and rats.

Those who are super curious about this can consult this landmark article from the scientific journal, *Nature*: "Initial sequencing and comparative analysis of the mouse genome" (http://www.nature.com/nature/journal/v420/n6915/full/nature01262.html).

The sequencing information in the paper is accurate, but more recent research on gene regulation and expression has outdated the paper's conclusions about introns (often called "junk DNA").

2. <u>No human data.</u> None of the published, peer-reviewed university and NIH-funded research was done in humans because it is unethical to deliberately expose humans to potentially hazardous substances.

3. <u>Correlation does not equal causation</u>. Despite <u>links and associations</u> found in well conducted research, it remains scientifically incorrect to state that an environmental chemical <u>causes</u> any disease. While correlations, links and associations — as discovered by the science of epidemiology — have often saved many lives, correlation is not definitive.

4. <u>The regulatory process</u>, as it exists now, rejects peer-reviewed university and NIHfunded research. Instead, the EPA, FDA and other agencies rely on data generated by private labs who are paid by manufacturers to conduct tests using methods that were current in the 1990s. Those methods have been abandoned by universities as inaccurate and lacking in necessary sensitivity.

The disagreements about these issues and what sorts of research should be considered by regulators are contentious and can get very technical.

A more detailed explanation can be found here at the CRECH website: <u>Why Have</u> <u>Regulators Failed To Regulate?</u>

In addition, the Stealth Syndromes Project has devoted many articles to the intricacies of raised by that link. We'd be happy to guide interested parties to the relevant articles.

The third effort at addressing the confusion: The Stealth Syndromes Study will create the science that doesn't exist

By continuing to grapple with both these intricacies and the broader issues, Perdue and Yeamans-Irwin were able to design a research study protocol that reconciled the first three of the four issues presented, below:

1. The protocol involves humans, no rodents.

2. The ethics issue was solved because the protocol calls for a controlled <u>reduction</u> in environmental chemical levels which the Centers for Disease Control says are present in almost all Americans (see:

<u>https://www.cdc.gov/biomonitoring/bisphenola_factsheet.html</u> for the CDC Biomonitoring program's fact sheet on Bisphenol A which is the reference chemical in our study).

Our study focuses on BPA as a reference chemical because it is one of the most commonly used plastics in the world. BPA is used to make polycarbonate plastics found in some types of beverage containers, compact disks, plastic dinnerware, impactresistant safety equipment, automobile parts, and toys. BPA epoxy resins are used in the protective linings of food cans, in dental sealants, and in many other products.

BPA is also a good reference chemical because there is a huge body of scientific research about it and its effects in lab animals. It is also frequently found in the company of other allegedly harmful environmental chemicals.

3. We measure cause and effect rather than links and associations.

Instead of simply measuring concentrations of BPA and trying to calculate risks based on epidemiology, our study is designed to measure actual health outcomes in relation to BPA levels.

As described in the protocol at the end of this narrative, our study will measure blood and urine concentrations of BPA and compare those to universally accepted health measurements including standard medical lab blood profiles which are diagnostic "gold standards."

We will also compare BPA concentrations to double-stranded DNA breaks which are indicators of a number of unhealthy conditions.

Human research is a serious matter. Approvals and oversight are critical

It's not acceptable for any researcher – government, university, medical, or independent – to simply begin to experiment with humans. There are health and privacy concerns and the need to verify that experiments are valid in complying with accepted U.S. and international standards.

In mid-2015, Dr. Victor Reus, M.D., Distinguished Professor at the University of San Francisco Medical School, reviewed our study plans and felt it was valid and important. (NOTE: "Distinguished Professor is not just an honorific, but actually an official title at UCSF and represents the professorial pinnacle of achievement. Few faculty ever achieve this rank.)

The UCSF Medical School Committee on Human Research approved the study on Nov. 25, 2015 and named Dr. Reus the study's Principal Investigator and Lewis Perdue the Co-Principal Investigator.

Progress of study

So far, we have mapped out the implementation steps and critical paths of the study.

These include locating sources for testing blood and urine samples, creating a program that encourages adherence to protocol by test subjects, locating sources for designing the diet and similar details.

In the process of doing this, it became apparent from cost estimates that this was beyond the financial resources of Lewis Perdue who has funded all costs to date. He, Yeamans-Irwin, and Dr. Reus have volunteered their time.

As an example: According to one lab we contacted, weekly testing for BPA in the blood and urine of one test subject over the nine-week period of the study would cost an estimated \$6,000 per person. That cost is only for the testing lab and does not include the cost of a phlebotomist to draw the blood, special BPA-free vials and materials, or the cost of preparing and shipping the sample to the lab.

In addition, the vital need to standardize and strictly control the ingredients, nutrients and micro-nutrients in each meal requires extensive preparation that far exceeds simple recipes, ingredients and preparation.

Not only will each meal be expensive, but one exemplar of each standard meal must be tested for its BPA concentration so that this exposure can be known. This will cost approximately \$500 per standard meal.

Current state of study efforts

The pace of study progress has been slowed for now by the need to raise funds.

We hope that a crowd-funding effort will get the actual science moving by this fall (2017) while we continue with the creation of the 501(c)(3) non-profit structure of CRECH.

To lend greater discipline and bandwidth to the overall effort, experienced manager and entrepreneur Andrew Starr, MBA agreed in mid-May 1017 to serve as a director.

Future plans

1. Follow-up studies

The completion of the study is a beginning rather than an endpoint because it is a "proof of concept."

Because it is the very first of its type, it must develop procedures, techniques, testing methods, and ways of encouraging compliance by test subjects. What we develop in implementing the approved protocol will save time, effort and financing for other groups of scientific investigators.

We recognize that, as the first, we will encounter problems and difficulties that must be overcome. To make this initial effort affordable and the effort possible with all the unknowns that will occur, the data we develop will be from a very small cohort.

As a result, an expanded study will be necessary – perhaps with hundreds or thousands of people – in order to get data of the highest statistical significance. However, our experience in coping with unseen difficulties and the potential modifications we will have to make will make future studies more accurate as well as time and cost efficient.

Depending upon our experience with this proof-of-concept effort, we may or may not be the right group of investigators to conduct that larger study. CRECH's ability to raise funds to support that follow-on effort will be vital to helping us – or others – take this to the next level.

2. Scientific & medical journal publications

3. Continued scientific & medical community communication by participating in seminars, colloquia, and relevant meetings.

- 4. Outreach to health care providers.
- 5. Consumer public outreach.
- 6. Development of new discoveries.

The scientific research we have done so far has turned up one new avenue of discovery that merits further research.

One of those is a method discovered by Perdue that relies on existing pharmaceutical evaluation results and human trial data as a more accurate paradigm for assessing potential risks of environmental chemical risks.

Perdue's proposed method first looks the ways that a pharmaceutical acts on the cellular processes that make it an effective therapy. The next step determines whether an environmental chemical acts on the same cellular process.

If the environmental chemical which acts on the identical cellular process as a pharmaceutical, but in a manner that decreases the effectiveness of the drug therapy, then there is evidence that the environmental chemical in question should be investigated thoroughly and rigorously as the pharmaceutical in question.

Perdue calls these chemicals "PharmBlockers." A more detailed explanation can be found here: <u>Precision evaluation of environmental chemical risk assessment: Using</u> <u>existing pharmaceutical evaluation results (http://stealthsyndrome.com/?p=2639)</u>.

And an example of BPA acting as a PharmBlocker to make cancer chemotherapy less effective can be found here: <u>Heat Shock Protein Hsp27 points to causal link between</u> <u>BPA and cancer & chemotherapy resistance</u> (<u>http://stealthsyndrome.com/?p=434</u>)

The connections between the cellular activity of pharmaceuticals and environmental chemicals can were made by Perdue's manual searching of existing published scientific research using previously gather information he remembered from reading journals.

If appropriately automated, this could become a fast, inexpensive method to warn of potential risks. Such warnings could save lives.

In the case of Hsp27 and BPA, it's significant that the intravenous chemotherapy bags and the tubing used to dispense the drug both contain BPA which is known to leach into the contents. Making chemotherapy less effective is, obviously, not desirable.

It is well established that cancer, obesity, and Type 2 Diabetes share many of the same pathological cellular processes. It's also well established that environmental chemicals affect many of those same processes. Many benefit could result from correlating those and the effects of pharmaceuticals in a detailed, organized, computer-automated and wide-ranging effort. The same may be possible with Alzheimer's disease, behavioral disorders, fertility and developmental disorders.

Exempt Purpose Benefits to Science and Society

1. It fills a complete gap in knowledge.

Numerous authorities agree with the CDC when it says that: "More research is needed to understand the human health effects of exposure to BPA."

2. As we stated in our mission statement at the beginning of this narrative, it will "enable individuals and health professionals to take medically valid actions against the risks of environmental chemicals."

3. It will offer the first controlled, human-based data that can be used in a health effects risk assessment of environmental chemicals.

4. No scientific data exists to determine what level of BPA exposure is responsible for the persistent levels that CDC programs have found in most Americans. But, because most BPA exposure is thought to come by food and drink, our study procedure of measuring the intake of BPA in every meal, snack and beverage, will offer the first indication ever.

5. Our measurements may be possible to normalize exposure and health effects data between people and lab animals and, possibly, to make better comparisons and risk assessments between the two species.

6. Establishment of a framework to move risk assessment of low-level environmental chemicals beyond traditional toxicological evaluations and toward molecular and epigenetic evaluations.

7. Development of techniques to reduce exposure to environmental chemicals with an emphasis on techniques that can easily and economically be implemented by the average person without significant disruption to daily lives.

8. Overall improvement in public health and a potential path to reducing the incidence of cancer, obesity, Type 2 Diabetes, Alzheimer's disease, behavioral disorders, fertility and developmental disorders.

University of California.				
San Francisco				
	Human Research Protection Program Committee on Human Research			
I	Notification of Expedited Review Approval			
Principal Investigator Dr. Victor I. Reus MD	<u>Co-Principal Investigator</u> Lewis Perdue			
Type of Submission: Study Title:	Submission Correction for Initial Review Submission Packet Clinical blood profile assays as biomarkers to directly assess potential health effects resulting from the controlled elimination of suspected dietary and environmental chemical toxins.			
IRB #: Reference #:	15-17703 147127			
Committee of Record:	San Francisco General Hospital Panel			
Study Risk Assignment	t: Minimal			
Approval Date:	<u>11/25/2015</u> Expiration Date: <u>11/24/2018</u>			
Regulatory Determinati	ions Pertaining to this Approval:			
This research is not subj	ect to HIPAA rules.			
This submission was e	ligible for expedited review as:			
Category 2: Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture (healthy non pregnant adults 110lbs or more, no more than 550mL in 8 weeks and no collection more than 2x a week OR other adults and children not exceeding the lesser of 50 ml or 3 ml per kg in an 8 week period and no collection more than 2x a week)				
Category 3: Prospective collection of biological specimens for research purposes by noninvasive means				
IRB Comments:				
All changes to a study must receive CHR approval before they are implemented. Follow the <u>modification</u> request instructions. The only exception to the requirement for prior CHR review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103.b.4, 21 CFR 56.108.a). In such cases, report the actions taken by following these <u>instructions</u> .				
Expiration Notice: The iRIS system will generate an email notification eight weeks prior to the expiration of this study's approval. However, it is your responsibility to ensure that an application for <u>continuing review</u> approval has been submitted by the required time. In addition, you are required to submit a <u>study closeout report</u> at the completion of the project.				

The Study & Protocol As Approved By UCSF Medical School, Committee on Human Research

By Lewis Perdue on February 17, 2017 in About Stealth Free, The Study As Approved

The Committee on Human Research (CHR) at the University of San Francisco Medical School has approved the Stealth Syndromes experimental protocol.

This study approval allows Stealth Syndromes co-founder <u>Lewis Perdue</u> to become the test subject for a "proof of concept" study to determine if standard clinical blood tests can be used to detect physiological changes that may be caused by the absorption of environmental chemicals, including endocrine disrupting compounds.

The CHR gave its go-ahead for the study on Nov. 11, 2015.

The Stealth Syndromes Project is very fortunate (and grateful) to have had the guidance and institutional mentorship of UCSF Distinguished Professor <u>Victor Reus, M.D.</u>

Dr. Reus is an internationally renowned, and widely published biomedical scientist whose interests include neurobiology and behavior as well as the genetic origins of psychiatric disorders.

iRIS - Let a Thousand Computer Forms Blossom

Study submissions at UCSF are entirely electronic. Everything is submitted through the secure, web-based <u>iRIS system</u> which provides scores of forms in a relatively intuitive framework.

iRIS centralizes all aspects of study, makes sure that all the relevant parts of a study are included, assures compliance with human research protections, and makes all that available to the university compliance process without needing paper versions.

The complexity of the iRIS system lies somewhere between IRS income tax forms and the paperwork associated with buying and mortgaging a new house.

The following is from the <u>iRIS FAQs</u>:

iRIS is a web-based system that enables online application submission, real-time submission tracking, review, post-approval compliance activities, and data management. The system also functions as a document repository, providing investigators with easy access to submission records and study documents.

The committees that will conduct their reviews using the iRIS system include the:

- Committee on Human Research (CHR),
- the CTSI Clinical Research Services (CRS) Advisory Committees, and
- the Human Gamete, Embryo, and Stem Cell Research Committee (GESCR committee).

Investigators can use the system anywhere they have Internet access, helping to connect faculty, researchers, students and partners around the world. The iRIS system also has expedited the CHR review and approval process. In addition, prior to the implmenetation of iRIS, the CHR received about 5 million pieces of paper each year. The electronic system has helped us eliminate this waste and supports UCSF's efforts to incorporate environmentally-friendly practices across campus.

Summarizing the study submission

The text below is taken directly from the UCSF iRIS system.

I have included ALL of the sections relevant to the study and omitted only those sections associated with administrative details and the online human research protection training courses I needed to pass in order to qualify as a study co-principal investigator. Correct section numbers from iRIS are used to designate each portion.

10.0 STUDY DESIGN

This is an interventional dietary study to determine the usefulness of carefully selected tests from standard medical blood profiles to indicate health effects resulting from the reduction of specific foods and substances known 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).

11.1 HYPOTHESIS

The controlled and stepwise elimination of environmental chemicals known as Chemicals of Emergency 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.

11.2 LIST THE SPECIFIC AIMS:

The primary aim of this study is to determine whether a positive correlation exists between CEC intervention, 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.

12.1 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 an 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 widespread²⁰.

More than 84,000 chemicals are approved for use in the United States today¹, 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 incomplete⁵.

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 some⁷, but also increases in concentrations of substitutes which are also of concern³⁹.

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

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 CECs 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 fragrances³⁸.

Still other contamination may result from the harvest and processing of food products¹⁷.

Causes For Concern

Human and animal studies have identified those compounds as contributors to cancer^{24,40-52}, cardiovascular disorders⁵³⁻⁶¹, obesity⁶²⁻⁶⁸, type 2 diabetes⁶⁹⁻⁷², metabolic syndrome⁷³⁻⁷⁷, neurological and behavioral disorders including Alzheimer's Disease⁷⁸⁻⁸⁴, as well as reproductive⁸⁵⁻⁹⁴, and developmental⁹⁵⁻¹⁰² disorders and allergies¹⁰³⁻¹¹⁰.

Specific Exposure Routes

Exposure routes for all products include:

- 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 chemicals¹⁸.

Exposure routes for food and beverages specifically include:

- 1. Incidental contamination via migration/leaching of chemicals from harvesting and processing¹⁷.
- 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.

12.2 PRELIMINARY STUDIES

So far, all studies 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 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 they 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 $(20 40)^{7}$,
- 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.

12.3 REFERENCES

PARTIAL BIBLIOGRAPHY

1. EPA. TSCA Chemical Substance Inventory [website]. Washington, DC:U.S. Environmental Protection Agency (updated 13 March 2014). Available http://www.epa.gov/oppt/existingchemicals/pubs/tscainventory/basic.html [accessed 1 July 2015]

2. European Food Safety Authority (EFSA). Report of ESCO WG on non-plastic food contact materials, 2011 [updated 25 July 201116 June 2013]. http://www.efsa.europa.eu/en/supporting/pub/139e.htm

3. Neltner, T.G., Kulkarni, N.R., Alger, H.M., Maffini, M.V., Bongard, E.D., Fortin, N.D., and Olsen, E.D. 2011. Navigating the U.S. Food Additive Regulatory Program. *Comprehensive Reviews in Food Science and Food Safety* 10:342–68.

4. Muncke, J., Myers, J.P., Scheringer, M., and Porta, M. 2014. Food packaging and migration of food contact materials: will epidemiologists rise to the neotoxic challenge?. *Journal of Epidemiology and Community Health* 68(7): 592-594.

5. Judson, R., Richard, A., Dix, D. J., Houck, K., Martin, M., Kavlock, R., Dellarco, V., Henry, T., Holderman, T., Sayre, P., Tan, S., Carpenter, T., and Smith, E. 2009. The Toxicity Data Landscape for Environmental Chemicals. *Environmental Health Perspectives* 117(5), 685–695.

6. National Report on Human Exposure to Environmental Chemicals, U.S. Centers for Disease Control, Fourth report, Updated 2015 Tables, <u>http://www.cdc.gov/exposurereport/index.html</u>, accessed 11 July 2015.

7. Zota, A. R., Calafat, A. M., and Woodruff, T. J. 2014. Temporal Trends in Phthalate Exposures: Findings from the National Health and Nutrition Examination Survey, 2001–2010. *Environmental Health Perspectives* 122(3), 235–241.

8. Vandenberg, L.N., Hauser, R., Marcus, M., Olea, N., Welshons, W.V. 2007. Human exposure to bisphenol A (BPA). *Reproductive Toxicology* 24: 139-177.

9. Nam, S.H., Seo, Y.M., Kim, M.G. 2010. Bisphenol A migration from polycarbonate baby bottle with repeated use. *Chemosphere* 79: 949-952.

10. Biedermann, S., Tschudin, P., and Grob, K. 2010. Transfer of bisphenol A from thermal printer paper to the skin. *Analytical and Bioanalytical Chemistry* 398: 571-576.

11. Ehrlich, S., Calafat, A.M., Humblet, O., Smith, T., and Hauser, R. 2014. Handling of thermal receipts as a source of exposure of Bisphenol A. *JAMA* 311(8): 859-860.

12. Kloukos, D., Pandis, N., and Eliades, T. 2013. In vivo bisphenol-A release from dental pit and fissure sealants: A systematic review. *Journal of Dentistry* 41: 659-667.

13. Duty, S.M., Mendonca, K., Hauser, R., Calafat, A.M., Ye, X., Meeker, J.D., Ackerman, R., Cullinane, J., Faller, J., and Ringer, S. 2013. Potential sources of bisphenol A in the neonatal intensive care unit. *Pediatrics* 131(3): 483-489.

14. Yang, C.Z., Yaniger, S.I., Jordan, V.C., Klein, D.J., and Bittner, G.D. 2011. Most plastic products release estrogenic chemicals: a potential health problem that can be solved. *Environmental Health Perspectives* 119(7): 989-996.

15. Bhunia, K., Sablani, S. S., Tang, J. and Rasco, B. 2013. Migration of Chemical Compounds from Packaging Polymers during Microwave, Conventional Heat Treatment, and Storage. *Comprehensive Reviews in Food Science and Food Safety* 12: 523–545.

16. Rudel, R.A., Gray, J.M., Engel, C.L., Rawsthorne, T.W., Dodson, R.E., Ackerman, J.M., Rizzo, J., Nudelman, J.L. and Brody, J.G. 2011. Food packaging and bisphenol A and bis (2-ethyhexyl) phthalate exposure: findings from a dietary intervention. *Environmental Health Perspectives* 119(7): 914-920.

17. Sathyanarayana, S., Alcedo, G., Saelens, B,E., Zhou, C., Dills, R.L., Yu, J., and Lanphear, B. 2013. Unexpected results in a randomized dietary trial to reduce phthalate and bisphenol A exposures. *Journal of Exposure Science and Environmental Epidemiology* 23(4): 378-384.

18. Nerin, C., Alfaro, P., Aznar, M., and Domeño, C. 2013. The challenge of identifying non-intentionally added substances from food packaging materials: A review. *Analytica Chimica Acta* 775:14–24.

19. Calafat, Antonia M., Ye, X., Wong, L-Y., Reidy, J.A., and Needham, L.L. 2008. Exposure of the US population to Bisphenol A and 4-tertiary-Octylphenol: 2003-2004. *Environmental Health Perspectives* 116(1): 39-44.

20. Vandenberg, L.N., Chahoud, I., Heindel, J.J., Padmanabhan, V., Paumgartten, F.J., Schoenfelder, G. 2012. Urinary, circulating, and tissue biomonitoring studies indicate widespread exposure to bisphenol A. *Cien Saude Colet* 17:407–434.

21. Thayer, K.A., Doerge, D.R., Hunt, D., Schurman, S.H., Twaddle, N.C., Churchwell, M.I., Garantziotis, S., Kissling, G.E., Easterling, M.R., Bucher, J.R., and Birnbaum, L.S.

2015. Pharmacokinetics of bisphenol A in humans following a single oral administration. *Environment International* 83: 107-115.

22. Vandenberg, L.N., Hauser, R., Marcus, M., Olea, N., and Welshons, W. 2007. Human exposure to bisphenol A (BPA). *Reproductive Toxicology* 24(2): 139-177.

23. Diamanti-Kandarakis, E., Bourguignon, J-P., Giudice, L.C., Hauser, R., Prins, G.S., Soto, A.M., Zoeller, R.T., and Gore, A.C. 2009. Endocrine-disrupting chemicals: an Endocrine Society scientific statement. *Endocrine Reviews* 30(4): 293-342.

24. Ferguson, L.R., Chen, H., Collins, A.R., Connell, M., Damia, G., Dasgupta, S., Malhotra, M., Meeker, A.K., Amedei, A., Amin, A., *et al.* 2015. Genomic instability in human cancer: Molecular insights and opportunities for therapeutic attack and prevention through diet and nutrition. *Seminars in Cancer Biology* 35: S5-24.

25. Christensen, K.L.Y., Lorber, M., Koslitz, S., Brüning, T., and Koch, H.M. 2012. The contribution of diet to total bisphenol A body burden in humans: Results of a 48 hour fasting study. *Environment International* 50: 7-14.

26. Vandenberg, L.N., Hunt, P.A., Myers, J.P., and Vom Saal, F.S. 2013. Human exposures to bisphenol A: mismatches between data and assumptions. *Reviews on Environmental Health* 28(1): 37-58.

27. Szic, V., Szarc, K., Declerck, K., Vidakovi, M., and Vanden, B.W. 2015. From inflammaging to healthy aging by dietary lifestyle choices: Is epigenetics the key to personalized nutrition?. *Clinical Epigenetics* 7(1): 33.

28. Ackerman, J.M., Dodson, R.E., Engel, C.L., Gray, J.M., and Rudel, R.A. 2014. Temporal variability of urinary di (2-ethylhexyl) phthalate metabolites during a dietary intervention study. *Journal of Exposure Science and Environmental Epidemiology* 24(6): 595-601.

29. Calafat, A.M., Longnecker, M.P., Koch, H.M., Swan, S.H., Hauser, R., Goldman, L.R., Lanphear, B.P., Rudel, R.A., Engle, S.M., Teitelbaum, S.L., Whyatt, R.M., and Wolff, M.S. 2015. Optimal Exposure Biomarkers for Nonpersistent Chemicals in Environmental Epidemiology. *Environmental Health Perspectives* 123(7): A166-8.

30. Bang, D.Y., Kyung, M., Kim, M.J., Jung, B.Y., Cho, M.C., Choi, S.M., Kim, Y.W., Lim, S.K., Lim, D.S., Won, A.J., Kwack, S.J., Lee, Y., Kim, S.K., and Lee, B.M. 2012. Human Risk Assessment of Endocrine Disrupting Chemicals Derived from Plastic Food Containers. *Comprehensive Reviews in Food Science and Food Safety* 11(5): 453-470.

31. Fasano, E., Bono-Blay, F., Cirillo, T., Montuori, P., and Lacorte, S. 2012. Migration of phthalates, alkylphenols, bisphenol A and di (2-ethylhexyl) adipate from food packaging. *Food Control* 27(1): 132-138.

32. Serrano, S.E., Braun, J., Trasande, L., Dills, R., and Sathyanarayana, S. 2014. Phthalates and diet: a review of the food monitoring and epidemiology data. *Environmental Health* 13(1): 43.

33. Rodgers, K.M., Rudel, R.A., and Just, A.C. 2014. Phthalates in Food Packaging, Consumer Products, and Indoor Environments. *Toxicants in Food Packaging and Household Plastics*: 31-59. **

34. Hayasaka, Y. 2014. Analysis of phthalates in wine using liquid chromatography tandem mass spectrometry combined with a hold-back column: Chromatographic strategy to avoid the influence of pre-existing phthalate contamination in a liquid chromatography system. *Journal of Chromatography A* 1372: 120-127. **

35. Wagner, M., and Oehlmann, J. 2009. Endocrine disruptors in bottled mineral water: Total estrogenic burden and migration from plastic bottles. *Environmental Science and Pollution Research* 16(3): 278-286.

36. Bittner, G.D., Denison, M.S., Yang, C.Z., Stoner, M.A., and He, G. 2014. Chemicals having estrogenic activity can be released from some bisphenol a-free, hard and clear, thermoplastic resins. *Environmental Health* 13(1): 103.

37. Vandermeersch, G., Lourenço, H.M., Alvarez-Muñoz, D., Cunha, S., Diogène, J., Cano-Sancho, G., Kwadijk, C., Barcelo, D., Allegaert, W., Bekaert, K., Fernandes, J.O., Marques, A., and Robbens, J. 2015. Environmental contaminants of emerging concern in seafood–European database on contaminant levels. *Environmental Research* 143(B): 29-45.**

38. Myers, SIL., Yang, C.Z., Bittner, G.D., Witt, K.L., Tice, R.R., and Baird, D.D. 2014. Estrogenic and anti-estrogenic activity of off-the-shelf hair and skin care products. *Journal of Exposure Science and Environmental Epidemiology* 25(3): 271-277.

39. Rochester, J.R., and Bolden, A.L. 2015. Bisphenol S and F: a systematic review and comparison of the hormonal activity of bisphenol A substitutes. *Environmental Health Perspectives* 123(7): 643-650.

CANCER

40. Keri, R.A., Ho, S.M., Hunt, P.A., Knudsen, K.E., Soto, A.M., and Prins, G.S. 2007. An evaluation of the evidence for the carcinogenic activity of bisphenol A. *Reproductive Toxicology* 24: 240-252.

41. Fang, L., Wuptra, K., Chen, D., Li, H., Huang, S.-K., Jin, C., and Yokoyama, K. K. 2014. Environmental-stress-induced Chromatin Regulation and its Heritability. *Journal of Carcinogenesis & Mutagenesis* 5(1), 22058.

42. Fang, L., Wuptra, K., Chen, D., Li, H., Huang, S.-K., Jin, C., and Yokoyama, K. K. 2014. Environmental-stress-induced Chromatin Regulation and its Heritability. *Journal of Carcinogenesis & Mutagenesis* 5(1), 22058.

43. Vega, A., Baptissart, M., Caira, F., Brugnon, F., Lobaccaro, J.-M. A., and Volle, D. H. 2012. Epigenetic: a molecular link between testicular cancer and environmental exposures. *Frontiers in Endocrinology* 3: 150.

44. Tarapore, P., Ying, J., Ouyang, B., Burke, B., Bracken, B., and Ho, S-M. 2014. Exposure to bisphenol A correlates with early-onset prostate cancer and promotes centrosome amplification and anchorage-independent growth in vitro. *PloS ONE* 9(3): e90332.

45. Wong, R.L., Wang, Q., Treviño, L.S., Bosland, M.C., Chen, J., Medvedovic, M., Prins, G.S., Kurunthachalan, K., Ho, S-M., and Walker, C.L. 2015. Identification of secretaglobin Scgb2a1 as a target for developmental reprogramming by BPA in the rat prostate. *Epigenetics* 10(2): 127-134.

46. Ferguson, L.R., Chen, H., Collins, A.R., Connell, M., Damia, G., Dasgupta, S., Malhotra, M., Meeker, A.K., Amedei, A., Amin, A. *et al.* 2015. Genomic instability in human cancer: Molecular insights and opportunities for therapeutic attack and prevention through diet and nutrition. *Seminars in Cancer Biology* 35: S5-24.

47. Zhang, Z., Chen, S., Feng, Z., and Su, L.J. 2015. Pregnancy Exposures Determine Risk of Breast Cancer in Multiple Generations of Offspring. In: *Environmental Epigenetics*. Springer London. pp. 75-103.

48. Gassman, N.R., Coskun, E., Stefanick, D.F., Horton, J.K., Jaruga, P., Dizdaroglu, M., and Wilson, S.H. 2015. Bisphenol A promotes cell survival following oxidative DNA damage in mouse fibroblasts. *PloS ONE* 10(2): e0118819. **

49. Bishop, K.S., and Ferguson, L.R. 2015. The Interaction between Epigenetics, Nutrition and the Development of Cancer. *Nutrients* 7(2): 922-947.

50. Kim, Y-S., Hwang, K-A., Hyun, S-H., Nam, K-H., Lee, C-K., and Choi, K-C. 2015. Bisphenol A and Nonylphenol Have the Potential to Stimulate the Migration of Ovarian Cancer Cells by Inducing Epithelial–Mesenchymal Transition via an Estrogen Receptor Dependent Pathway. *Chemical Research In Toxicology* 28(4): 662-671.

51. Nahta, R., Al-Mulla, F., Al-Temaimi, R., Amedei, A., Andrade-Vieira, R., Bay, S., Brown, D.G., Calaf, G.M., Castellino, R.C., Cohen-Solal, K.A. *et al.* 2015. Mechanisms of environmental chemicals that enable the cancer hallmark of evasion of growth suppression. *Carcinogenesis* 36(S1): S2-S18.

52. Hajjari, M., and Salavaty, A. 2015. HOTAIR: An oncogenic long non-coding RNA in different cancers. *Cancer Biology & Medicine* 12(1): 1.

CARDIOVASCULAR

53. Fang, L., Wuptra, K., Chen, D., Li, H., Huang, S.-K., Jin, C., and Yokoyama, K. K. 2014. Environmental-stress-induced Chromatin Regulation and its Heritability. *Journal of Carcinogenesis & Mutagenesis* 5(1), 22058.

54. Gao, X., and Wang, H-S.. 2014. Impact of bisphenol A on the cardiovascular system—epidemiological and experimental evidence and molecular mechanisms. *International Journal of Environmental Research and Public Health* 11(8): 8399-8413.

CARDIAC

55. Rancière, F., Lyons, J.G., Loh, V.H, Botton, J., Galloway, T., Wang, T., Shaw, J.E., and Magliano, D.J. 2015. Bisphenol A and the risk of cardiometabolic disorders: a systematic review with meta-analysis of the epidemiological evidence. *Environmental Health* 14(1): 46.

56. Bae, S., and Hong, Y-C. 2015. Exposure to Bisphenol A From Drinking Canned Beverages Increases Blood Pressure Randomized Crossover Trial. *Hypertension* 65(2): 313-319.

57. Belcher S.M., Chen Y., Yan S., and Wang H.S. 2012. Rapid estrogen receptormediated mechanisms determine the sexually dimorphic sensitivity of ventricular myocytes to 17β -estradiol and the environmental endocrine disruptor bisphenol A. *Endocrinology* 153: 712–720.

58. Gao X., Liang Q., Chen Y., and Wang H.S. 2013. Molecular mechanisms underlying the rapid arrhythmogenic action of bisphenol A in female rat hearts. *Endocrinology* 154: 4607–4617.

59. Liang Q., Gao X., Chen Y., Hong K., and Wang H.S. 2014. Cellular mechanism of the nonmonotonic dose response of bisphenol A in rat cardiac myocytes. *Environmental Health Perspectives* 122 :601–608.

60. Melzer D., Osborne N.J., Henley W.E., Cipelli R., Young A., Money C., McCormack, P., Luben, R., Khaw, K.T., Wareham, N.J., and Galloway, T.S. 2012. Urinary bisphenol A concentration and risk of future coronary artery disease in apparently healthy men and women. *Circulation* 125: 1482–1490.

61. Yan S., Song W., Chen Y., Hong K., Rubinstein J., and Wang H.S. 2013. Low-dose bisphenol A and estrogen increase ventricular arrhythmias following ischemia– reperfusion in female rat hearts. *Food and Chemical Toxicology* 56: 75–80.

OBESITY

62. Regnier, S.M. and Sargis, R.M. 2014. Adipocytes under assault: Environmental disruption of adipose physiology. *Biochimica et Biophysica Acta* 1842(3): 520-533.

63. Ellero-Simatos, S., Claus, S.P., Benelli, C., Forest, C., Letourneur, F., Cagnard, N., Beaune, P.H. and de Waziers, I. 2011. Combined Transcriptomic–1H NMR Metabonomic Study Reveals That Monoethylhexyl Phthalate Stimulates Adipogenesis and Glyceroneogenesis in Human Adipocytes. *Journal of Proteome Research* 10(12): 5493-5502.

64. Marmugi, A., Ducheix, S., Lasserre, F., Polizzi, A., Paris, A., Priymenko, N., Bertrand-Michel, J., Pineau, T., Guillou, H., Martin, P.G., and Mselli-Lakhal, L. 2012. Low doses of bisphenol A induce gene expression related to lipid synthesis and trigger triglyceride accumulation in adult mouse liver. *Hepatology* 55(2): 395-407.

65. Hugo, E.R., Brandebourg, T.D., Woo, J.G., Loftus, J., Alexander, J.W., Ben-Jonathan, N. 2008. Bisphenol A at environmentally relevant doses inhibits adi- ponectin release from human adipose tissue explants and adipocytes. *Environmental Health Perspectives* 116(12): 1642-1647.

66. Menale, C., Piccolo, M.T., Cirillo, G., Calogero, R.A., Papparella, A., Mita, L., Del Giuduce, E.M., Diano, N., Crispi, S., and Mita, D.G. 2015. Bisphenol A effects on gene expression in children adipocytes: association to metabolic disorders. *Journal of Molecular Endocrinology* 54(3): 289-303.

67. Savastano, S., Tarantino, G., D'Esposito, V., Passaretti, F., Cabaro, S., Liotti, A., Liguoro, D., Perruolo, G., Ariemma, F., Finelli, C., Bequinot, F., Formisano, P., and Valentino, R. 2015. Bisphenol-A plasma levels are related to inflammatory markers,

visceral obesity and insulin-resistance: a cross-sectional study on adult male population. *Journal of Translational Medicine* 13(1): 1-7.

68. Seidlová-Wuttke, D., Jarry, H., Christoffel, J., Rimoldi, G., and Wuttke, W. 2005. Effect of bisphenol-A (BPA), dibutylphtalate (DBP), benzophenone-2 (BP2), procymidone (Proc), and linurone (Lin) on fat tissue, a variety of hormones and metabolic parameters: A 3 month comparison with effects of estradiol (E2) in ovariectomized (ovx) rats. *Toxicology* 213: 13-24.

DIABETES

69. Alonso-Magdalena, P., Morimoto, S., Ripoll, C., Fuentes, E., and Nadal, A. 2006. The estrogenic effect of bisphenol A disrupts pancreatic β -cell function in vivo and induces insulin resistance. *Environmental Health Perspectives* 114(1): 106-112.

70. Nadal, A., Alonso-Magdalena, P., Soriano, S., Quesada, I., and Ropero, A.B. 2009. The pancreatic beta-cell as a target of estrogens and xenoestrogens: implica- tions for blood glucose homeostasis and diabetes. *Molecular and Cellular Endocrinology* 304:63-68.

71. Bouchard, L., Thibault, S., Guay, S.P., Santure, M., Monpetit, A., St. Pierre, J., Perron, P., and Brisson, D. 2010. Leptin gene epigenetic adaptation to impaired glucose metabolism during pregnancy. *Diabetes Care* 33(11): 2436 – 2441.

72. Savastano, S., Tarantino, G., D'Esposito, V., Passaretti, F., Cabaro, S., Liotti, A., Liguoro, D., Perruolo, G., Ariemma, F., Finelli, C., Bequinot, F., Formisano, P., and Valentino, R. 2015. Bisphenol-A plasma levels are related to inflammatory markers, visceral obesity and insulin-resistance: a cross-sectional study on adult male population. *Journal of Translational Medicine* 13(1): 1-7.

METABOLIC

73. Ellero-Simatos, S., Claus, S.P., Benelli, C., Forest, C., Letourneur, F., Cagnard, N., Beaune, P.H., and de Waziers, I. 2011. Combined Transcriptomic–1H NMR Metabonomic Study Reveals That Monoethylhexyl Phthalate Stimulates Adipogenesis and Glyceroneogenesis in Human Adipocytes. *Journal of Proteome Research* 10(12): 5493-5502.

74. Hofmann, P.J., Schomburg, L., and Köhrle, J. 2009. Interference of endocrine disrupters with thyroid hormone receptor-dependent transactivation. *Toxicological Sciences* 110(1): 125-137.

75. Marmugi, A., Ducheix, S., Lasserre, F., Polizzi, A., Paris, A., Priymenko, N., Bertrand-Michel, J., Pineau, T., Guillou, H., Martin, P.G., and Mselli-Lakhal, L. 2012. Low doses of bisphenol A induce gene expression related to lipid synthesis and trigger triglyceride accumulation in adult mouse liver. *Hepatology* 55(2): 395-407.

76. Schmutzler, C., Bacinski, A., Gotthardt, I., Huhne, K., Ambrugger, P., Klammer, H., Schlecht, C., Hoang-Vu, C., Gruters, A., Wuttke, W., Jarry, H., and Köhrle, J. 2007. The UV filter benzophenone 2 interferes with the thyroid hormone axis in rats and is a potent in vitro inhibitor of human recombinant thyroid peroxidase. *Endocrinology* 115(Suppl. 1): 77–83.

77. Hugo, E.R., Brandebourg, T.D., Woo, J.G., Loftus, J., Alexander, J.W., and Ben-Jonathan, N. 2008. Bisphenol A at environmentally relevant doses inhibits adiponectin release from human adipose tissue explants and adipocytes. *Environmental Health Perspectives* 116: 1642-1647.

NEUROLOGICAL

78. Fang, F., Chen, D., Yu, P., Qian, W., Zhou, J., Liu, J., Gao, R., Wang, J., and Xiao, H. 2015. Effects of Bisphenol A on glucose homeostasis and brain insulin signaling pathways in male mice. *General and Comparative Endocrinology* 212: 44-50.

79. El-Missiry, M.A., Othman, A.I., Al-Abdan, M.A., and El-Sayed, A.A. 2014. Melatonin ameliorates oxidative stress, modulates death receptor pathway proteins, and protects the rat cerebrum against bisphenol-A-induced apoptosis. *Journal of the Neurological Sciences* 347(1): 251-256.

80. Kundakovic, M., and Champagne, F.A. 2011. Epigenetic perspective on the developmental effects of bisphenol A. *Brain, Behavior, and Immunity* 25(6): 1084-1093.

81. Hofmann, P.J., Schomburg, L., and Köhrle, J. 2009. Interference of endocrine disrupters with thyroid hormone receptor-dependent transactivation. *Toxicological Sciences* 110(1): 125-137.

82. Testa, C., Nuti, F., Hayek, J., De Felice, C., Chelli, M., Rovero, P., Latini, G., and Papini, A.M. 2012. Di-(2-ethylhexyl) phthalate and autism spectrum disorders. *ASN Neuro* 4(4): 223-229.

83. Clark-Taylor, T., and Clark-Taylor, B.E. 2004. Is autism a disorder of fatty acid metabolism? Possible dysfunction of mitochondrial β -oxidation by long chain acyl-CoA dehydrogenase. *Medical Hypotheses* 62(6): 970-975.

84. Fang, L., Wuptra, K., Chen, D., Li, H., Huang, S.-K., Jin, C., and Yokoyama, K. K. 2014. Environmental-stress-induced Chromatin Regulation and its Heritability. Journal of Carcinogenesis & Mutagenesis, 5(1), 22058.

REPRODUCTIVE

85. Hannon, P.R., Peretz, J., and Flaws, J. 2014. Daily exposure to Di (2-ethylhexyl) phthalate alters estrous cyclicity and accelerates primordial follicle recruitment potentially via dysregulation of the phosphatidylinositol 3-kinase signaling pathway in adult mice. *Biology of Reproduction* 90(6): 136.

86. Hannon, P.R., and Flaws, J.A. 2015. The effects of phthalates on the ovary. *Frontiers in Endocrinology* 6:8.

87. León-Olea, M., Martyniuk, C.J., Orlando, E.F., Ottinger, M.A., Rosenfeld, C.S., Wolstenholme, J.T., and Trudeau, V.L. 2014. Current concepts in neuroendocrine disruption. *General and Comparative Endocrinology* 203: 158-173.

88. Meeker, J.D., and Ferguson K.K. 2014. Urinary phthalate metabolites are associated with decreased serum testosterone in men, women, and children from NHANES 2011–2012. *The Journal of Clinical Endocrinology & Metabolism* 99(11): 4346-4352

89. Hannon, P. R., Peretz, J., and Flaws, J. A. 2014. Daily Exposure to Di(2-ethylhexyl) Phthalate Alters Estrous Cyclicity and Accelerates Primordial Follicle Recruitment Potentially Via Dysregulation of the Phosphatidylinositol 3-Kinase Signaling Pathway in Adult Mice. *Biology of Reproduction* 90(6), 136.

90. Braun, J.M., Just, A.C., Williams, P.L., Smith, K.W., Calafat, A.M., and Hauser, R. 2014. Personal care product use and urinary phthalate metabolite and paraben concentrations during pregnancy among women from a fertility clinic. *Journal of Exposure Science and Environmental Epidemiology* 24(5): 459-466.

91. Soares, A., Guieysse, B., Jefferson, B., Cartmell, E., and Lester, J.N. 2008. Nonylphenol in the environment: a critical review on occurrence, fate, toxicity and treatment in wastewaters. *Environment International* 34(7): 1033-1049.

92. Lyche, J.L., Gutleb, A.C., Bergman, Å., Eriksen, G.S., Murk, A.J., Ropstad, Lyche, J.L., Gutleb, A.C., Bergman, Å., Eriksen, G.S., Murk, A.J., Ropstad, E., Saunders, M., and Skaare, J.U. 2009. Reproductive and developmental toxicity of phthalates – a review. *Journal of Toxicololgy and Environmental Health B Critical Reviews* 12(4): 225-249.

93. Wetherill, Y.B., Akingbemi, B.T., Kanno, J., McLachlan, J.A., Nadal, A., Sonnenschein, C., Watson, C.S., Zoeller, R.T., and Belcher, S.M. 2007. In vitro molecular mechanisms of bisphenol A action. *Reproductive Toxicology* 24(2): 178-198.

94. Vega, A., Baptissart, M., Caira, F., Brugnon, F., Lobaccaro, J.-M. A., and Volle, D. H. 2012. Epigenetic: a molecular link between testicular cancer and environmental exposures. *Frontiers in Endocrinology* 3: 150.

DEVELOPMENTAL

95. Resendiz, M., Mason, S., Lo, C.-L., and Zhou, F. C. 2014. Epigenetic regulation of the neural transcriptome and alcohol interference during development. *Frontiers in Genetics* 5: 285.

96. Mason, S., and Zhou, F. C. 2015. Editorial: Genetics and epigenetics of fetal alcohol spectrum disorders. *Frontiers in Genetics* 6: 146.

97. Kim, J.H., Sartor, M. A., Rozek, L.S., Faulk, C., Anderson, O.S., Jones, T.R., Nahar, M.S., and Dolinoy, D.C. 2014. Perinatal bisphenol A exposure promotes dosedependent alterations of the mouse methylome. *BMC Genomics* 15:30.

98. Walker, C. L. 2011. Epigenomic Reprogramming of the Developing Reproductive Tract and Disease Susceptibility in Adulthood. *Birth Defects Research. Part A, Clinical and Molecular Teratology* 91(8), 666–671.

99. Vega, A., Baptissart, M., Caira, F., Brugnon, F., Lobaccaro, J.-M. A., and Volle, D. H. 2012. Epigenetic: a molecular link between testicular cancer and environmental exposures. Frontiers in Endocrinology 3: 150.

100. Zhang, Z., Chen, S., Feng, Z., and Su, L.J. 2015. Pregnancy Exposures Determine Risk of Breast Cancer in Multiple Generations of Offspring. In: *Environmental Epigenetics*. Springer London. pp. 75-103.

101. Cao, J., Rebuli, M.E., Rogers, J., Todd, K.L., Leyrer, S.M., Ferguson, S.A., and Patisaul, H.B. 2013. Prenatal Bisphenol A Exposure Alters Sex-Specific Estrogen Receptor Expression in the Neonatal Rat Hypothalamus and Amygdala. *Toxicological Sciences* 133(1), 157–173.

102. Crinnion, W.J. 2010. Toxic effects of the easily avoidable phthalates and parabens. *Alternative Medicine Review* 15(3): 190-196.

ALLERGIES

103. Wang, I.-J., Karmaus, W. J., Chen, S.-L., Holloway, J. W., and Ewart, S. 2015. Effects of phthalate exposure on asthma may be mediated through alterations in DNA methylation. *Clinical Epigenetics* 7(1): 27.

104. Dodson, R.E., Nishioka, M., Standley, L.J., Perovich, L.J., Brody, J.G., and Rudel, R.A. 2012. Endocrine disruptors and asthma-associated chemicals in consumer products. *Environmental Health Perspectives* 120(7): 935.

105. Hoppin, J.A., Jaramillo, R., London, S.J., Bertelsen, R.J., Salo, P.M., Sandler, D.P., Zeldin, D.C. 2013. Phthalate exposure and allergy in the U.S. population: results from NHANES 2005–2006. *Environmental Health Perspectives* 121: 1129–1134.

106. Markey, C.M., Wadia, P.R., Rubin, B.S., Sonnenschein, C., and Soto, A.M. 2005. Long-term effects of fetal exposure to low doses of the xenoestrogen Bisphenol-A in the female mouse genital tract. *Biology of Reproduction* 72: 1344-1351.

107. Benachour, N., and Aris, A. 2009. Toxic effects of low doses of Bisphenol-A on human placental cells. *Toxicology and Applied Pharmacology* 241: 322-328.

108. LaPensee, E.W., Tuttle, T.R., Fox, S.R., and Ben-Jonathan, N. 2009. Bisphenol A at low nanomolar doses confers chemoresistance in estrogen receptor-α-positive and – negative breast cancer cells. *Environmental Health Perspectives* 117(2): 175-180.

109. vom Saal, F.S., and Welshons, W.V. 2006. Large effects from small exposures. II. The importance of positive controls in low-dose research on bisphenol A. *Environmental Research* 100: 50-76.

110. Baldi, E., and Muratori, M. 2013. Genetic damage in human spermatozoa. *Advances in Experimental Medicine and Biology* 791. New York. Springer-Verlag. 195p.

15.1 PROCEDURES/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 phthalates 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
- Effects on G-Protein Coupled Receptors
- WBC
- Cytokines:II-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
- Vitamins 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 & Phthalates 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 data on the health effects of 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 packaging⁸
- 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.

15.2 INTERVIEWS, QUESTIONNAIRES, AND/OR SURVEYS WILL BE ADMINISTERED OR FOCUS GROUPS WILL BE CONDUCTED:

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.

STEA	LTH SY	NDRO	MES P	ROJEC	т					
Cont	trolled E	ndocrin	ne Disru	ptor R	eduction					
			y Timelir	•						
10701/170/	Week									
ACTIVITY	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										

16.4 BENEFITS TO SOCIETY

- 1. First connection established between dietary intervention and health indicators.
- Establishment of a framework to move risk assessment of low-level Chemicals of Emerging Concern beyond traditional toxicological evaluations 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.

Biographies

(Presented in chronological order of their initial involvement with CRECH)

William Lewis Perdue III

Director, CRECH Director & Chairman, Co-founder Stealth Syndromes Project, Co-Principal Investigator, Stealth Syndromes Study

Education

B.S., Communications & Biology (Ecology, Evolution & Systematics), With Distinction, Cornell *University, 1972*

A.S., Math & Science, (1st in class, 1st ever 4.0 graduation GPA), State University of New York (SUNY)/Corning Community College, 1970

Fellowship, Aerospace Engineering, Mississippi State University, summer 1966

Internship, Westinghouse Electric (Nuclear Reactor and Special Purpose Tube Divisions), summer 1967

Independent Study, Multiple collaborators & mentors including: Dr. Arthur C. Guyton, Dean of the University of Mississippi Medical School, NASA, Oak Ridge National Laboratory, *1960-1967*

Publications

Perdue, L., & Yeamans-Irwin, R.L. "Low-Dose BPA Paper in Toxicological Sciences is Contaminated by Massive Errors & Should Be Retracted." Uploaded February 2014. (<u>Please click this link for a .pdf version.</u>)

Perdue, L., "<u>Heat Shock Protein Hsp27 points to causal link between BPA and cancer & chemotherapy resistance.</u>" Uploaded May 12, 2016

Perdue, L., "Precision evaluation of environmental chemical risk assessment: Using existing pharmaceutical evaluation results as a more accurate paradigm," Uploaded May 12, 2016

Research & Teaching Experience

Cornell University – 1970-72

- Teaching Assistant, Organic Chemistry Lab, specializing in assisting students with the use of gas chromatography and mass spectrometry equipment in lab experiments.
- Received the only A+ awarded in an organic chemistry class of 150. Also only student to accurately answer final exam extra credit question to diagram the quantum resonance bonding orbitals of ozone.
- As a first semester junior, offered a scholarship to change biology major to chemistry after finding 27 errors (many in quantum bonding orbital diagrams) in the new text book for organic chemistry.
- Added communications as an unsanctioned double major. (Cornell did not formally support double majors at the time.)
- Financially self-supporting since age 18: paid for college and living expenses by working as a journalist and photographer. Financial considerations mandated interrupting a lifelong passion for science and technology to follow a temporary vocational path in communications instead.
- Honors program: allowed to take courses at Cornell Law School.
- Teaching Assistant, Mass Communications Law.

State University of New York (SUNY)/Corning Community College – 1968-1970

- Independent research: Conducted abiogenesis experiments including complete replication of Miller-Urey experiment confirming that complex organic compounds including vital amino acids, could have been created from simple inorganic compounds during the by postulated primitive environmental conditions which mat have been present on Earth more than 4 billion years ago.
- Teaching Assistant & Faculty-Appointed Tutor, Calculus, Physics, & Biology

Westinghouse Electric Internship – Summer 1967

- Course work in the theory and practice of nuclear fission, reactor design, and mechanics of neutron cross sections, capture, fission moderation.
- Responsible for calibrating neutron sensors used in civilian and military reactors. Created custom calibration curves unique for each neutron counter.
- Responsible for construction of, and suggesting design changes for, solar flux measurement sensor tubes for NASA's 1969 Mariner 6 Mars flyby.
- Course work in theory of electron guns used in color cathode ray tubes.
- Hands on experience with efforts to reduce corner landing misplacement of electron beams in color picture tubes.
- Course work in the theory of quantum-based spectral output of specific pure elements, primarily metals.
- Hands on work in the utilization and calibration of the Westinghouse Hollow Cathode spectral output tubes.

Independent Study – 1966-67

Research focus: Magnetohydrodynamics, plasma physics, ultra-high-vacuum physics.

- Designed and built a magnetohydrodynamic thrust accelerator for space propulsion. The ionized particle stream was provided by a plasma jet. The thruster used sequential electromagnetic field compression to provide thrust.
- A variation of this is currently used in NASA's deep space probes such as dawn.

Mississippi State University - Summer 1966

- Coursework and lab experience in plasma physics, fluid flow instrumentation, mechanical resonance.
- Collaborated with faculty in further exploring ion thruster linear accelerator.

Independent Study, 1965-66

Mentors: Werner Von Braun, NASA scientists at Redstone Arsenal (George C. Marshall Space Flight Center) and the Oak Ridge National Laboratory.

Research focus: high-energy particle physics, plasma physics, ultra-high-vacuum physics, interplanetary and interstellar particle flux density, ultra-high-vacuum technology

With a suggestion from NASA that they would welcome a way to increase the relatively small thrust of the ion engine as it currently existed, I designed and built a two-stage thruster. And a vacuum chamber capable of 10^{-12} Torr to simulate the vacuum of outer space.

The first stage was an improved version of my previous ion engine design coupled with a linear particle accelerator for the second stage.

This thruster was designed to use the interplanetary particle flux as fuel. This required an electromagnetic collector to attract and compress a simulated solar plasma (He and H ions). The particles from the collector were then separated using mass spectrometer principles to provide a uniform He+ stream to the particle accelerator.

Dubbed "The Cosmic Engine" by the media, the entire system won a number of awards at the International Science and Engineering Fair. I became a Westinghouse Science Talent Search Finalist and received a fellowship from the Aerospace Engineering Department of Mississippi State University where I attended classes and continued to explore the capabilities of my system.

Independent Study – 1964-65

Research focus: plasma physics, fluidics of ionized gases

- Completed design and construction of electromagnetic ion space thruster and vacuum chamber required for operation.
- Exhibited and demonstrated ion space thruster and modulated laser combined under the title, "Space Communications and Propulsion." Won First Class overall ay state science fair along with numerous awards from NASA, AAAS and other entities.

Independent Study – 1963-64

Research focus: optical and electromagnetic radiation and high-energy particle physics.

- Completed construction of a visible spectrum Ne/He ion laser approximately 18 months after the first one was developed by Bell Labs in 1962. Further research into removal of trace contaminants from the Ne/He plasma along with precision optical adjustment of mirrors and interface windows resulted in a functional laser.
- Work began on possible methods for analog amplitude modulation of laser beam. Experiments with materials whose refractive index changes with an imposed electrical field produced erratic results, but indicated that modulation was possible.
- Research and engineering experience also developed in working with fluid flow and vacuum chambers.

Independent Study – 1961-63

Mentor, Dr. Arthur C. Guyton who also allowed access to laboratory and other facilities at University of Mississippi Medical School.

- Explored the effects of gibberellic acid on podophyllotoxin production in leaves, roots and fruit of Podophyllum peltatum. Very slight increase in cellular density of leaves and volume of fruit and root.
- Second experiment extracted podophyllotoxin from roots of Podophyllum peltatum. Self-tested efficacy on plantar warts. Experimental results were equivocal due to adverse reaction on normal skin.

Rebecca Yeamans-Irwin

CRECH Director & Secretary, co-founder of Stealth Syndromes Project, collaborator in Stealth Syndromes Study

Education

M.S., Environmental Sciences (Ecology), *University of Virginia,* Charlottesville, VA 2011

B.S., Biology, cum laude, Saint Michael's College, Colchester, VT, 2004

Publications

Perdue, L., & Yeamans-Irwin, R.L. Low-Dose BPA Paper in Toxicological Sciences is Contaminated by Massive Errors & Should Be Retracted. Uploaded February 2014.

Yeamans, R.L., Roulston, T.H., and Carr, D.E. (2014) Pollen quality for pollinators tracks pollen quality for plants in Mimulus guttatus. *Ecosphere* 5(7): 1-8.

Banschbach, V.S., Yeamans, R., Brunelle, A., Gulka, A., & Holmes, M. (2012) Edge Effects on Community and Social Structure of Northern Temperate Deciduous Forest Ants. *Psyche*. Doi: 10.1155/2012/548260.

Yeamans, R. L. (2011) Ecological and evolutionary shifts in pollen chemistry and their implications for pollinators.

Banschbach, V.S., Brunelle, A., Bartlett, K.M., Grivetti, J.Y., & Yeamans, R.L. (2006) Tool use by the forest ant Aphaenogaster rudis: Ecology and task allocation. *Insectes Sociaux*, 53, (463-471).

Abstracts, Posters, and Presentations

Goldman, M.D., Yeamans, R.L., and Koenig, S. Steroid Exposure & Hyperglycemia in Multiple Sclerosis (MS) and Headache (HA) Patients: A Retrospective Chart Review. American Academy of Neurology 65th Annual Meeting, 2013. San Diego, CA.

Engelhard, M., Patek, S.D., Chen, S., Lach, J., Yeamans, R. and Goldman, M.D. Detecting changes in gait characteristics during a six-minute walk using wireless technology in MS subjects. September 2013.

Yeamans, R.L., The effects of plant inbreeding on pollen nutritional content and solitary bee development. Blandy Experimental Farm 24th Annual Research Forum., 2010.

Yeamans, R.L. and Banschbach, V.S. A study of species diversity among ants in edge versus interior forest habitats in a northwestern Vermont forest. Council on Undergraduate Research Posters on the Hill, Washington, D.C., 2004.

Laboratory, Research, and Teaching Experience

Program Specialist – University of Virginia Department of Neurology, Charlottesville, VA, February 2012-August 2014

- Managed a National and International Multiple Sclerosis clinical research trial substudy.
- Assisted with the development of training materials, manual of operations, as well as patient tracking and interaction with study subjects.
- Administered clinical research trial visits for 100 local study subjects.
- Communicated and distributed study materials to multiple study sites.
- Performed statistical analysis of study data and ensured compliance with study procedures.
- Proficient in software including EPIC, Microsoft Access, and Music (an online research database).
- Performed duties as a Medical Scribe for a prominent Neurologist during weekly clinic visits.

Teaching Assistant – *University of Virginia*, Charlottesville, VA, *August 2008-May* 2011

 Responsible for teaching discussion and laboratory sections of two graduate and undergraduate levels courses, three semesters for each course:

1) Politics, Science, and Values: Introduction to Environmental Policy; and

2) Applied Statistics for Environmental Scientists.

 Graded papers, exams, and laboratory assignments, and provided guidance to undergraduates and graduates as needed both in person and through the university's centrally-supported online collaboration and learning environment (COLLAB).

Senior Research Technician – *Immune Disease Institute* and *DecImmune Therapeutics*, Boston, MA, *May 2004-May 2008*

- Established human to mouse skin transplant surgical model and executed the small animal surgery experiments studying burn injury/inflammation.
- Managed a large mouse colony (n > 1500 mice) for an Immunology research lab at Harvard Medical School.
- Routine genotyping by genomic DNA isolation and PCR analysis and cell preparation for FACS analysis.
- Maintained a Microsoft Access database for censusing animals.
- Responsible for ordering/transferring animals, phlebotomy, drug administration (including tail vein I.V. procedures), mouse cardiac perfusion and surgically isolating lymphoid and non lymphoid tissues.

- Performed statistical analysis of data and prepared presentations for laboratory meetings and retreats.
- Worked efficiently with and assisted postdoctoral fellows.
- Trained and managed an assistant animal technician.
- Prepared various solutions for use in the wet laboratory.
- Ordered various supplies as needed in the laboratory for global use.

Summer Research Technician - *Blandy Experimental Farm at University of Virginia*, Boyce, VA, *May 2008-August 2008*

- Provided technical assistance on various ecological research projects.
- Assisted the Associate Director with essential duties on grounds.
- Worked closely with Associate Director, graduate students, and undergraduate students in the Research for Undergraduates Program.

Senior Laboratory Technician & Teaching Assistant - Saint Michael's College,

Colchester, VT, Aug 2003-May 2004

- Teaching Assistant for General Biology, Ecology, and Animal Behavior labs.
- Provided academic and technical support for students.
- Acted as the Insect Curator by sorting, identifying, and pinning insect species, and creating artificial ant nests.

Other Scientific Writing Experience

Owner, Creator, Writer, Editor – *The Academic Wino,* <u>www.academicwino.com</u> *June 2011-current*

- Manages, writes, and edits content dedicated to dissecting current results in enology and viticulture and presenting it in a way that it is palatable to the educated non-scientist population.
- Edits content for sponsored and guest posts to ensure consistency and adherence of policies.
- Provides fascinating insights and thoughts on the current state of research related to wine.
- Reviews at least two peer-reviewed articles per week, on articles spanning nearly every aspect of academia.
- Manages Twitter, Facebook, Pinterest, and Google+ accounts and searches the internet for wine industry and wine business news to share with followers.

Highlighted Laboratory and Computer Skills

- WordPress
- Basic HTML
- COLLAB Online
 collaboration and
- Microsoft Office
 (Access, Excel, Word, PowerPoint)

learning	
environment	

					environment	
•	Ecological field work	•	Mesquite software	•	Phylomatic software •	SAS statistical software
•	Curating insects	•	Small animal surgery	•	Mouse phlebotomy • and I.V. drug administration	Dissection/Necropsy
•	PCR analysis, ELISA, and micropipetting	•	Bradford Protein Assay	•	Spectrophotometry •	Cryopreservation
•	Mouse colony management	•	Paraffin section analysis	•	Antibody staining • and sectioning	Cell preparation for FACS analysis

Awards and Honors

2010	Ann Warrick Lacy Scholarship, Monticello Garden Club
2010	UVA Department of Environmental Sciences Exploratory Grant
2004	Sigma Xi Research Society Inductee
2003	Clare Booth Luce Research Grant Recipient
2003	Lake Champlain Research Consortium Grant Recipient

Dr. Victor Reus, M.D.

CRECH Director, Principal Investigator, Stealth Syndromes Study

NOTE: This very brief biography is excerpted from <u>Dr. Reus's official online biography</u> <u>at the University of California, San Francisco. Please refer to that web site for more</u> <u>details of his long and illustrious career, M.D</u> (http://profiles.ucsf.edu/victor.reus).

Victor I. Reus, M.D. is a Distinguished Professor 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 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 was Chair of the Board of Directors of the Accreditation Council for Continuing Medical Education (ACCME)in 2016 and is the current 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 300 peer reviewed articles and chapters, with a particular emphasis on the biology and genetics of mood disorders, resulting in over 9400 citations and an h index of 56 (Scopus; 54 WOS). Twenty six papers have received over 100 citations each, with 2 papers designated by Web of Science as in the top 1% of all cited papers for the field and publication year.

Andrew Starr

CRECH Director, Treasurer

Accomplished senior executive and innovation leader with over twenty five years of entrepreneurial and large company experience in identifying new business and new product opportunities, then creating and managing organizations that successfully and profitably develop them.

SIGNIFICANT ACCOMPLISHMENTS AND AREAS OF EXPERTISE

- <u>General Management:</u> President and Founder of Neocork Technologies, the pioneering technology- based, service-intensive, synthetic wine cork pioneer. Starting from a business plan, successfully built, managed and led all functional areas from pre-revenue stage to \$8 million in annual sales.
- <u>Capital Raising</u>: Experience in attracting investors at each stage of an emerging enterprise.
- <u>Change Agent:</u> Overturned the 300 year-old tradition of wood cork via carefully articulated messaging, better technology, and persistence. Winemaker of Israel's first world-class wines. Introduced first 'designer' wine yeasts. Led several successful new product or new business opportunities in a wide range of indstries.
- <u>Marketing and Strategic Planning</u>: Identified and led each stage of the business life cycle in several competitive markets, from early market analysis, research and development, through commercialization, mass production, market development and market maturation.

- <u>Team Building</u>: Created a positive, high-performance work environment that allowed a smaller business to continuously change, thrive and grow when competing against substantially better financed competitors.
- <u>Technology Commercialization</u>: Have taken both manufactured and biological technologies from early stage prototypes through the commercialization process. Strong understanding of legal and intellectual property issues.

PROFESSIONAL EXPERIENCE

Owner, StarrGreen LLC., Yountville, CA 2004-present

StarrGreen provides strategic, marketing and new product development services for emerging technologies in the wine, greentech, and product safety industries.

VP-Business Development, PlastiPure, Inc., Austin TX 2011-2014

PlastiPure is an early stage company that assists manufacturers of infant feeding durables and plastic packaging to make their products free of estrogenic chemicals such as BPA.

Responsible for all marketing efforts to build consumer awareness of widespread issue of reprotoxic estrogenic chemicals in food contact plastics.

Director of Marketing and Business Development, Phyterra Yeast, Inc. Napa, CA 2006-2009

General management role responsible for commercializing early-stage yeast technology to the wine industry for Canadian parent company.

Head Winemaker 1984-1986 Golan Heights Winery. Israel

EDUCATION

UCLA Anderson School of Management, Los Angeles CA – M.B.A. 1988

McKinsey Award Finalist for creating a strategic plan for a homeless services non-profit. Beta Gamma Sigma Honor Society.

University of California, Davis. Davis, CA – B.S. Fermentation Science (Enology). 1981.