

Endocrine Disrupting Chemicals (EDCs) and Their Potential for Adverse Health Effects

EA: Estrogenic Activity **EA**:** EA and anti-EA **EA**-free:** Free of EA and anti-EA,
AnA: Androgenic Activity **AnA**:** AnA and Anti-AnA **AnA**-free:** Free of AnA and Anti-AnA,
EA/AnA**-free:** Free of EA** and AnA** **PCP:** Personal Care Products.

Growth in human population, development of new technologies, and more consumer-centric cultures are rapidly changing the environment. Well over 1,000,000 chemicals are in commercial use and thousands of new human-created chemicals are registered annually. Many of these chemicals persist in the environment and are virtually invisible, tasteless, and odorless. Many thousands of these chemicals are known or suspected to interfere with the endocrine system in mammals.

The endocrine system produces hormones that are transported via the bloodstream to interact with signal-specific cell-receptors in various tissues to produce proteins, initiate cell division, and/or regulate biological processes. Endocrine disrupting chemicals (EDCs) can produce adverse health effects by blocking or mimicking naturally occurring hormones. EDCs most frequently exhibit EA** or AnA**; an animal, such as humans near the top of a food chain, can concentrate EDCs many-fold. Chemicals having EA** or AnA** have been linked to a variety of adverse health effects in mammals (including humans), including reproductive problems (reduced sperm counts, ovarian and uterine dysfunctions), obesity, increased fetus mortality, various cancers, type II diabetes, learning disabilities, behavioral abnormalities, and increased rates of sexual maturation in females. Fetal, infant, and juvenile mammals are potentially especially sensitive to very low dosages (ppb to < ppt levels) of chemicals having EA** or AnA**.

EDC Contamination of the Chemical Commons

The “tragedy of the commons” is a metaphor used by Garrett Hardin for economic problems where it is hard to coordinate and pay for public goods. It is a problem long-recognized by game theorists and economists (including Adam Smith and David Ricardo) and biologists. It is often modeled as the fate of a common pasture shared among rational, utility-maximizing herdsmen: As the population of sheep increases, the pasture is destroyed because no individual has meaningful property rights that prevent placing many sheep on the commons that destroy the utility of the commons. However, no one herdsman, or his sheep, is responsible for the tragedy. In today’s world, the tragedy of the chemical commons means that many commercially-available products release chemicals having EA**/AnA** in small quantities whose additive effects have significant adverse effects on our “commons environment”, especially on fetuses, newborns, and juveniles. But, like sheep, no one product or manufacturer is responsible. The “chemical commons tragedy” of combined effects of many products releasing chemicals having EA**/AnA** is perhaps the most serious chronic health problem not yet fully recognized by companies, consumers, and governments -- and is a problem we try to solve at several levels.

CertiChem has developed, robotized, and validated with ICCVAM/NICEATM/OECD (or undergoing validation) a battery of *in vitro* assays using MCF-7 cells or BG1-Luc cells to detect EA** and MDA-Kb2-cells to detect AnA** that are the most accurate and sensitive currently available, in part due to our developing Confirmation Assays. Using these assays, CertiChem has demonstrated that the great majority of plastic, silicone and personal care products release a variety of chemicals having EA**/AnA**. Using these assays, we have created a knowledge base of commonly-used chemicals and materials having EA**/AnA** or EA/AnA**-free used to make plastics and personal care products. Using this knowledge base and a knowledge of polymer chemistry, we have identified or developed formulations for products that leach **no** chemicals having detectable EA**/AnA** after extraction with hydrophilic or hydrophobic solvents or after common-use stresses of heating, boiling microwaving, UV radiation. This approach differs from that used at present by various commercial, academic, regulatory or government entities that address problematic ingredients having EA**/AnA** (e.g., BPA) one-at-a time without

considering that many other ingredients also have significant hormonal activity, that more than one solvent is [often](#) needed and [products may](#) be exposed to common use stresses that create new chemicals. Furthermore, replacing chemicals one-by-one is much more costly than reformulating to eliminate all ingredients having EA**/AnA**.

CertiChem believes that when a large variety of EA**/AnA**-free** products become available to the public, this will reduce the potential health problems associated with EDCs of which EA**/AnA** are the most frequent hormonal effects in the “chemical commons”. We believe CertiChem is the leading laboratory in this area of hazard analysis, public awareness and genuine health-related product solutions to a problem now being recognized by government agencies and consumer groups.

An Example of CertiChem’s Efforts to Reduce the Problem of Human Exposure to EDCs The Problem with Personal Care Products PCPs

On average, American consumers daily use 10 PCPs that contain 126 ingredients³. PCPs include skincare creams, lotions, powders, perfumes, lipsticks, fingernail and toe nail polish, eye and makeup, baby products, towelettes, permanent waves, hair colors, hair sprays, deodorants, hand sanitizer, bath oils, bubble baths, bath salts, butters and other make-up. PCPs are not subject to FDA premarket approval or regulation, with the exception of color additives and a few regulated chemicals. The only additional FDA requirement is accurate labeling of PCP ingredients, except for those ingredients that are considered trade secrets. The FDC does **not** test PCPs to evaluate compliance with labeling regulations and therefore distributors and manufacturers of PCPs are responsible for assuring product safety. The Environmental Working Group has reported that an industry panel had reviewed the safety of just 13 percent of 10,500 listed PCP ingredients.

Many PCPs, including those used by pregnant mothers, infants, and juveniles, currently contain chemicals with demonstrated EA**/ AnA** that can be absorbed through the skin, inhaled, or orally ingested (see Tables 1-5,7, in Research Strategy). Epidemiological studies suggest that EDCs having EA** and/or AnA** may cause significant adverse health effects, especially for chronic use for which very few, if any, risk analyses have been published for PCP use by humans. Hence, there is a health-related need for safer EA**/AnA**-free PCP ingredients and commercial products, at least as assessed by hazard analyses such as proposed herein.

Demand for Safer PCPs

Over 69,000,000 commercially available chemicals exist, of which over 1,000,000 are in active use of which perhaps 6,000 – 10,000 have EA** or AnA**. Since many chemicals are released by PCPs, it is possible health risks associated with use could be widespread. These possible risks have been published by well-respected scientists and have been brought to consumer awareness through efforts of multiple consumer-based groups and proactive product manufacturers.

Many major PCP manufacturers and their suppliers perceive an ability to advertise safer PCPs as a significant market differentiator (e.g., paraben-free, BPA-free). Improved safety, sustainability, and “naturalness” are the most desirable traits in the PCP industry today. The worldwide PCP marketplace is estimated by market researcher Lucintel to reach \$630 billion by 2017. Natural PCPs represent approximately 6% of this market and are growing rapidly. Therefore, a significant opportunity exists to market EA**/AnA**-free products to consumers, and for CertiChem to formulate, test, and certify ingredients and products as EA**/AnA**-free.

Current Solutions Are Incomplete

Current efforts to solve EA**/AnA** issues with PCPs address problematic ingredients having EA**/AnA** one-at-a time⁵³, such as BHT, parabens, or BPA, without addressing or considering many other ingredients that also have significant hormonal activity. Replacement chemicals can easily have as much EA**/AnA** as the original chemical (e.g., propylgallate for BHT) according to CertiChem’s proprietary data. Furthermore, replacing chemicals one-by-one is much more costly than reformulating to eliminate all ingredients having EA**/AnA**. In addition, one-by-one replacement cannot address synergistic effects or secondary reactions that produce PCP chemicals having EA**

and/or AnA**. The PCP market needs a solution that eliminates the most-frequently occurring EDCs (i.e., those having EA**/AnA**), and is commercially viable to implement.

CertiChem's Health-Based Solution Addresses Current and Future Markets

In a Phase 1 NIH SBIR Grant, CertiChem showed that it is possible to identify EA**/AnA**-free ingredients usable for many types of PCPs and in collaboration with 4X Naturals also showed it is possible to make an EA**-free/ AnA**-free PCP, both unscented and with two scents. CertiChem is now amassing a repository of EA**/AnA** data on PCP ingredients such as emulsifiers, fragrances, preservatives, and colorants. CertiChem has developed innovative testing protocols to test PCPs for release of chemicals having EA**/AnA** and has access to EA**/AnA**-free plastic containers commercialized through its strategic partner PlastiPure. To access a market for EA**/AnA**-free PCPs*, CertiChem has offered.. and will offer... the following services:

- 1) Fee for services testing: testing for EA** and AnA** of PCPs and/or their ingredients.. CCI has negotiated a contract with Silent Spring for just such tests.
- 2) New Product/Remediation Consulting: Using extensive EA**/AnA** experience, patented IP, and database to help ingredient and product manufacturers develop safer PCPs. CCI has worked with 4XNaturals to develop three such products that are EA**AnA**-free and is working with 4XNaturals to develop other products.
- 3) EA**/AnA** Certification: Certify PCPs as EA**/AnA**-free for an annual fee to allow consumers to know that those PCPs are as hormonally safe as is currently commercially possible.
- 4) Licensing of IP: After EA**/AnA**-free PCPs garner initial market traction some companies will wish to license this technology versus trying to overcome CertiChem patents and replicate its 14 years of R&D

Additional Health Considerations

In addition to providing a much more comprehensive solution to address chemicals leaching from PCP with hormonal effects, CertiChem will use selected ingredients to minimize other adverse conditions: (1) gluten-free, (2) free of metals with putative or known toxicity including aluminum nickel, mercury, cadmium, arsenic and lead , (3) free of substances associated with allergic contact dermatitis or irritant contact dermatitis, such as formaldehyde releasing agents (imidazolidinyl urea, diazolidinyl urea, Bronopol, quaternium 15, DMDM hydantoin), (4) photosensitizing agents in topical preparations such as 6-methyl coumarin, musk ambrette, PABA esters, benzophenones, and galloyltrioleate, (5) parabens such as methylparaben, ethylparaben and propylparaben, (6) allergenic fragrances such as cinnamic aldehyde, hydroxycitronellal and geraniol, and their known allergens and irritants such as balsam of Peru, neomycin/bacitracin and cobalt chloride.

Societal Value of Safer PCPs – Healthier Population, Especially Infants and Children

Development of EA**/ AnA**-free PCP ingredients and commercial products could significantly improve human health, especially for populations that are potentially most adversely effected by EDCs having EA** and/or AnA** in small amounts: pregnant women, infants, and children⁵. Other studies strongly suggest that certain population segments (e.g., African-American) who use a higher proportion of PCPs on their children, might greatly benefit from EA**/ AnA**-free PCPs.

Societal Value of Project – Minimize Environmental Impact of PCPs.

Tragedy of the Chemical Commons

Usage levels of PCPs are on a par with agrochemicals, and concerns about the environmental impacts of PCPs were raised over a decade ago. PCPs enter the environment by “down-the-drain” disposal, leaching from landfills, and direct dispersal (e.g., sunscreen wash-off from swimmers). Components of PCPs are among the most commonly detected compounds in surface water. For

example, the amount of ultraviolet light-filtering chemicals released directly into a small lake in Switzerland could be as high 966 kg per year. Some PCP components present in surface water bioaccumulate, and may produce endocrine effects on wildlife, but data are currently insufficient for risk assessment. Industry changeover to EA**/AnA**-free PCPs could greatly reduce their environmental impact.

More generally, and at least as important, is that a reduction in release of chemicals having EA** and/or AnA** in PCPs is part of explicit efforts in both Public Awareness and Product Development by CertiChem to attempt to reduce the tragedy of the Chemical Commons. The problem is relevant because many commercially-available PCPs and other products release chemicals having EA** and/or AnA** in small quantities. The additive effects of these multiple “chemical sheep” have significant adverse effects on the “commons” (i.e. mammals in the environment), especially on fetuses, newborns, and juveniles. But, like sheep, no one product or manufacturer is responsible. **However, the “tragedy of the chemical commons” resulting from the combined effects of many products releasing chemicals having EA** and/or AnA** is perhaps the most serious chronic health problem not yet fully recognized by companies, consumers, and governments.** When a large variety of EA**/AnA**-free** PCP and other products become available to the public, this will reduce the potential health problems associated with endocrine disruption of which EA** and/or AnA** are the most common hormonal effects. CertiChem is at the forefront of hazard analyses, public awareness and health-related product solutions to this problem.

Societal Value of Safer PCPs – Populace Better Educated on Health Drivers and Health-Based Solutions

Although many governmental agencies and scientific committees have recognized the possible serious nature of the problem, no regulations have yet been adopted and the PCPs currently on the US or international market have not been systematically tested for EA**/AnA**. Nevertheless, public awareness of the risks or benefits associated with chemicals having EA** and/or AnA** (e.g., parabens, BPA, phthalates) is increasing. CertiChem knows of no other entity offering EA**/AnA**-free or –specified PCP formulations. CertiChem believes that many proactive consumers would purchase PCP formulations having EA*/AnA**-free ingredients to avoid the possibility of adverse health effects (especially on babies and pregnant women) CertiChem frequently communicates with the Campaign for Safe Cosmetics, Planned Parenthood, and the Breast Cancer Fund who all strongly support the goals of NIEHS/NIH, CertiChem and companies like 4X Naturals to develop EA**/AnA**-free PCP products. CertiChem works with Carl Ginsburg, Silent Spring, Center for Environmental Health and others (**see letters**) to increase public awareness of the problems of EA**/AnA** in PCPs and in the Chemical Commons.

Scientific Value of Project – Breakthrough Technology Based on Innovative Bioassays

CertiChem’s ability to innovate and improve technologies for commercialization has been proven for consumer products, additives, feed, and plastic packaging. With the funding of this grant, CertiChem proposes to develop a comprehensive library of EA**/ AnA**-free ingredients and formulations necessary to rapidly disrupt the PCP industry.