

# **Chemicals and Breast Cancer: a Backgrounder**

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## **Introduction**

One in nine New Zealand women will get breast cancer sometime during their lives.

Breast cancer is the most common form of cancer, if male and female cancer is taken separately. If genders are combined, breast cancer is surpassed by total bowel cancer, but not by much.

Considerable attention has been focused on breast cancer over recent years – but almost all of this has been on either early detection, or on figuring out the genetic factors that underlie only a small percent of cases, less than 10 percent of cases.

Meanwhile the more than 50 percent of breast cancer that is unexplained by known risk factors is ignored.

There has been official silence on the likely environmental causes of this epidemic, despite scientific evidence that implicates hundreds of chemicals in breast cancer. It is on these chemicals that this paper focuses.

## **Cancer statistics**

Female breast cancer accounted for 26 percent of all female cancers during 1994-98, projected to rise to 28 percent by 2012 (Hodgen et al 2002). This is the highest rate for any cancer in either females or males (gender disaggregated).<sup>1</sup>

The age standardised incidence rate for breast cancer in women aged 15 years or over has been rising from an annual average of 59 per 100,000 “person-years” in 1956 to 117 per 100,000 in 1996, an increase of 98 percent. Over the same period the number of *actual* registrations has almost quadrupled, from 488 to 1,936. The incidence rate is expected to increase to 127 per 100,000 by 2011, an increase over 1996 of 9 percent.

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<sup>1</sup> That is, female breast cancer incidence is higher than any other type of cancer in males or females separately. If cancer statistics are combined across gender, then total breast cancer incidence is surpassed by total colorectal cancer, which accounts for 33 percent of all cancers.

Due to the increasing age of the population there is expected to be a dramatic increase in breast cancer burden, with numbers of registrations rising from 1,936 in 1996 to 2,893 in 2011, an increase of almost 50 percent.

The mortality rate for breast cancer is projected to decline slowly, from 18 percent in 1996, to 17 percent in 2012. But this gentle decline is more than offset by the population ageing effect: the actual numbers of deaths have increased from 427 in 1962 to 643 in 1997, an increase of 50 percent, as a result of demographic trends.

Nearly three quarters of breast cancer registrations and over 80 percent of deaths occur in post-menopausal women (50 years and older). Even so, breast cancer is the leading cancer across all age groups of women except for those 75 years or older, where it is overtaken by colorectal cancer:

- up to the age of 44 breast cancer accounts for 35 percent of cancer registrations and deaths, and rising;
- in the 45-64 age group, breast cancer contributes 35 percent of registrations and rising, whilst mortality contributes just over one-quarter but declining.

**Table 1: Female breast cancer incidence, age disaggregated**

Age	Cases per year (1996)	Ranking & % of cancer (1996)	Cases per year (2001)	Ranking (2001)
15-44	297	1 35%	337	1
45-64	873	1 35%	1336	1
65-74	371	1 22%	565	1
75+	395	2 18%	655	2

Source: Hodgen et al 2002

Even without the projected increases in breast cancer, New Zealand already has a very high incidence rate compared with other countries: our age-standardised annual incidence rate of 117 cases per 100,000 “person-years” compares very *unfavourably* with the 22 per 100,000 in Africa and Asia.<sup>2</sup>

These figures are more than just ‘worrying’: they represent a silent epidemic of disease and death that afflicts 1 in 9 women in New Zealand. They reflect untold suffering, and billions of dollars worth of treatment costs, lost productivity, and lost opportunities: in 1997 alone an estimated 6,546 years of women’s lives were lost to breast cancer (MoH & UoA 2003). These figures are the formal face of the spectre that shadows the lives of all women in New Zealand, prompting the unspoken fear “will it be me next?”

<sup>2</sup> A similar situation exists with our overall cancer rate: between 1963 and 1993 our cancer death rate increased at a faster rate, and is now higher than that of comparable countries such as Australia, Canada, the United States and Britain. Cancer is the leading cause of death in New Zealand, accounting for 29 percent of deaths from all causes. About 16,000 people develop cancer per year (MoH 2003).

## **Causes of Breast Cancer**

*Why are breast cancer rates so high?*

Most of the research into the causes of breast cancer has focussed on identifying the genes that make a small percentage of women more susceptible to breast cancer, and on identifying the risk factors of reproductive variables and activities that affect hormone levels (see below). These factors underlie less than 50 percent of cases of breast cancer that actually occur, and they provide poor prediction of individual risk (Brody & Rudel 2003). The remaining more than 50 percent of breast cancer cases are still unexplained (Evans 2002).

**Acknowledged risk factors** (Davis et al 1998; Brody & Rudel 2003):

- Hereditary factors - cancer resulting from mutations of susceptible genes:
  - the breast cancer genes BRCA1 and BRCA2, which confer a 60-80 percent lifetime probability of breast cancer, are thought to underlie fewer than 10 percent of breast cancer cases.
- Reproductive characteristics – prolonged exposure to natural oestrogen increases the risk of breast cancer, thus:
  - being younger at menarche (before 12), older at menopause (after 55), non-child bearing, or older at first live- or stillbirth increases risk;
  - whilst higher birthrate, longer lactation and bilateral ovariectomy are thought to be protective against breast cancer.
- Activities and conditions that affect hormone levels:
  - alcohol consumption, lack of physical activity, higher body mass index and weight gain after menopause, low pre-menopausal body mass index.
- Pharmaceutical hormones:
  - both oestrogen only and oestrogen-progesterone hormone replacement therapy increase breast cancer risk;
  - recent, but not long-term, use of oral contraceptives is associated with higher risk.
- Exposure to ionising radiation is a clearly established environmental cause of breast cancer, with exposures early in life imparting greater risk:
  - x-rays, uranium, nuclear waste, other radioactive materials.
- Low income:
  - observed internationally and posited to be linked to chemical exposures through consumer products, waste sites, and pesticides;
  - in New Zealand the Ministry of Health found evidence of a deprivation gradient for incidence rate of breast cancer (Hogden et al 2002).

In addition the Ministry of Health report reveals that Maori suffer significantly higher breast cancer mortality rates than non-Maori.

### **Environmental causes**

There is significant international concern about the role that environmental factors might be playing in the breast cancer epidemic, given the failure to explain away more than 50 percent of breast cancer through known risk factors.

To date the only proven environmental cause of breast cancer is ionising radiation. But there is powerful scientific evidence that some of the estimated 70,000 synthetic chemicals in use today may be involved in breast cancer. Little is known about actual effects of many of these chemicals: fewer than 1,000 have been tested in cancer bioassays, and there has been no systematic analysis for hormonal activity (Brody & Rudel 2003). The effects of mixtures and the idiosyncratic dose-response relationships (e.g. U-shaped instead of positive) that can occur for hormones and hormonally active chemicals adds a layer of complexity that compounds this basic lack of knowledge about individual chemicals.

Despite this, many chemicals have been identified as possible causes of breast cancer, and many of these are ubiquitous pollutants that find their way into our food, drinking water, air, soil and our bodies. They are present in household products, spray paints, paint removers, cosmetics, furnishings, building materials, fuels, pesticides, foods, food containers, and used in or released by many industrial processes. Many of them mimic the effects of natural oestrogen, so that children today are conceived and grow up in an artificially oestrogenic environment.

Yet there appears to be little work being carried out in New Zealand to identify these chemicals and apparently no political will to remove them from the environment. There is an official silence around environmental causes of breast cancer even though they may be responsible for the deaths of more than 320 women per year in New Zealand, more than 1500 cases of breast cancer per year. The government's Cancer Control Strategy acknowledges "it is estimated that about 80 percent of cancers are due to environment or lifestyle, and therefore are potentially preventable" (MoH 2003, p 4), but fails to address environmental causes apart from occupational exposure to carcinogens. It is completely silent on the ubiquitous chemical pollution.

*Is it only coincidence that the increasing risk of breast cancer and other cancers has paralleled the proliferation of synthetic chemicals since World War II?*<sup>3</sup>

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<sup>3</sup> "The age-standardised incidence rate of all adult cancer increased steeply from the mid-1950s to the early 1980s, and has increased more slowly since then" (MoH 2003, p.11).

## ***The Hypothesis***

There are three ways in which chemicals may be instrumental in the breast cancer epidemic:

- as breast carcinogens, i.e. initiating the development of breast cancer cells;
- promoting the growth of breast cancer cells and hormonally sensitive tumours - this is the primary effect of oestrogen in breast cancer; or
- affecting mammary gland development and susceptibility.

Frequently only chemicals that are initiators of cancer cells are acknowledged in cancer causation. However, with breast cancer it appears that there are also many chemicals that act as promoters of cancer cell development, or affect the development or susceptibility of mammary tissue - in particular the hormonally active chemicals, otherwise known as endocrine disruptors.

It is known that the hormonal environment plays a critical role in the development of breast cancer, and there is strong scientific evidence that chemicals which mimic or disrupt these natural hormones, may also play a critical role in the development of breast cancer.

## ***The Evidence***

The following brief analysis of some of the evidence of chemical involvement in breast cancer is based largely on the recent reviews by the US Breast Cancer Fund (Evans 2002) and Brody & Rudel's (2003) review published in *Environmental Health Perspectives*, the Journal of the US National Institute of Environmental Health Sciences.

In summary:

- Epidemiological studies consistently show that women who have prolonged exposure to oestrogen are at higher risk of breast cancer (Brody & Rudel 2003).
- Steroidal oestrogens are listed as known human carcinogens in the US National Toxicology Program 10<sup>th</sup> Report on Carcinogens (NTP 2002).
- Animal studies have shown that exposure to known carcinogens in the absence of endogenous hormones does not result in cancer (Russo & Russo 1996, 1998).
- There is strong evidence from *in vitro* laboratory tests that oestrogen-mimicking chemicals promote the growth of human breast cells in laboratory conditions, just as natural oestrogen does.

- Additionally, at least 42 synthetic chemicals have been shown by the US National Toxicology Program to cause mammary tumours in rodents (Brody & Rudel 2003).
- Numerous studies have documented as many as 200 different synthetic chemicals, in human breast milk (Evans 2002). Some of these pollutants have been linked to mammary tumours in animals. Others, including dioxin, are classified as known carcinogens.
- Compounds identified in laboratory studies that are mammary carcinogens, or promote the growth of breast cells and hormonally sensitive tumours, or affect mammary gland development and susceptibility, are used in common commercial products and are ubiquitous pollutants to which women are widely exposed in everyday life.

### Laboratory studies

The US National Toxicology Programme, using animal carcinogenicity bioassays, has identified 42 chemicals that cause mammary tumours. Other research organisations have identified a further 160 chemicals as mammary carcinogens – including polyaromatic hydrocarbons (PAHs), common industrial solvents, vinyl chloride, vinyl fluoride, styrene, acrylamide, atrazine, dichlorvos (Pinter et al 1990; Wolff et al 1996; IARC1999).

In the early 1990s researchers discovered that *p*-nonylphenol, an additive commonly used in plastics causes breast cancer cells to grow (Soto et al 1991). Since then more than 500 chemicals have been found to be weakly oestrogenic in various assays (Jobling et al 1995; Soto et al 1995; Nishihara et al 2000). Many of these have been shown to stimulate breast cancer cells *in vitro* to proliferate (Korach & McLachlan 1995; Soto et al 1995; Shelby et al 1996).

There has been limited research on the effects of *in utero* exposure to hormonally active chemicals (Brody & Rudel 2003). However studies have shown that 2,3,7,8-TCDD (dioxin), atrazine and bisphenol A all affect mammary gland development; and a mixture of organochlorines (DDT, DDE, PCBs) increased susceptibility to chemically induced mammary tumours (Brown et al 1998; Desaulniers et al 2001; Fenton et al 2002; Birnbaum & Fenton 2003).

Mice exposed *in utero* to bisphenol A showed mammary gland development was altered in ways that are associated with the development of breast cancer in rodents and humans (Markey et al 2001). Bisphenol A is a chemical commonly found in plastic food containers, including baby bottles, and the lining of metal food cans. It can leach into the food (Brotons et al 1995).

Long-term exposure of laboratory animals to airborne vinyl chloride has been found to result in an increased risk of mammary tumours (US CDCP 1997). Vinyl chloride is released into the air during the manufacture of polyvinyl chloride (PVC) which is used in food packaging, medical products, appliances, cars, toys, etc, and released from hazardous waste sites, landfills and tobacco smoke (Evans 2002).

Although the hormonal potency of these chemicals is typically much lower than endogenous oestrogen, there is concern about the endocrine disrupting effects when exposures take place at times when levels of endogenous oestrogen are normally low and tissues exquisitely sensitive to it, such as *in utero*, pre-puberty and post menopause. Additionally animal studies have demonstrated that mixtures of oestrogenic chemicals can act together to exert an effect even when the level of each individual chemical is too low (Silva et al 2002). Exposure to mixtures of chemicals is the reality of everyday life for women in New Zealand, so this is an important component of the breast cancer puzzle.

### Epidemiological studies

Evidence from epidemiological studies linking breast cancer to particular pollutants is less strong, although this is not surprising given the complexity of variables involved, and the difficulty in achieving meaningful results. This is in part because of the multitude of different exposures women experience over time, the difficulty of establishing when exposure occurred, and because the timing of the exposures can be critical.

Very few of the compounds identified as endocrine disruptors or animal mammary carcinogens have been included in epidemiological studies on human breast cancer (Brody & Rudel 2003). Even so there are some positive indications of a link with some chemicals and breast cancer.

### Occupational studies

Few occupational studies have investigated the breast cancer risk for women with obvious chemical exposures, such as nurses who are likely to have been exposed to the mammary carcinogen ethylene oxide and the hormonally active compounds nonylphenol and bisphenol A (Brody & Rudel 2003).

Some studies have shown an increased risk of breast cancer with exposures to benzene, polyaromatic hydrocarbons, some solvents (including methylene chloride, carbon tetrachloride, formaldehyde), styrene, pesticides, some metals and metal oxides (Cantor 1995; Petralia et al 1999; Band et al 2000; Hansen 2000). In a Danish study breast cancer risk was increased 20-66 percent for women employed longer than a year in jobs with extensive use of organic solvents – in metal products, wood fabrication, furniture, printing, chemical, and

textile industries (Hansen 1999; Pollan & Gustavsson 1999). Elevated risk has also been reported for women in pharmaceutical manufacturing, beauticians, pharmacists, hairdressers, nurses, laboratory technicians, dental hygienists, aircraft and automotive workers (Pollan & Gustavsson 1999; DeBruin & Josephy 2002) – all occupations with potential exposures to known mammary carcinogens and/or endocrine disrupting compounds.

Decreased risk has been found with U.S. farm women, who might reasonably be expected to have greater levels of physical activity, which is protectant against breast cancer; but a 2-fold higher risk was observed with women who did not wear protective clothing when applying pesticides (Duell et al 2000).

### *Population-based studies*

There is a very sparse literature on population-based studies, and that has been mostly confined to organochlorines with generally no link established, e.g. the Long Island Breast Cancer Study Project (Brody & Rudel 2003). A number of things may have contributed to these negative findings, including difficulty in establishing historical exposures, and issues of timing with respect to latency and periods of breast vulnerability (Brody & Rudel 2003). Organochlorines have been favoured for this type of study because of the presence of measurable residues in body fat and blood after exposure. Most rely on DDE as an indicator of the presence of DDT, even though current blood levels of DDE are regarded as a poor measure of the original DDT exposure. DDE is much less hormonally active than DDT, and unsurprisingly these studies have more often than not shown no link (Brody & Rudel 2003). However, where the studies have been based on the blood residue levels measured shortly after exposure, e.g. in the 1970s, a positive relationship has been shown between dieldrin and DDT levels and breast cancer (Hoyer et al 1998, 2000).

Studies relating to accidental exposures have shown a 2-fold increase in breast cancer risk among women with a 10-fold increase in serum level of dioxin (Warner et al 2002), and a moderate to small increase in risk from exposure to tetrachlorethylene leached from vinyl-lined water distribution pipes (Aschengrau et al 2002).

In conclusion, there is a strong body of toxicological evidence pointing to a large number of ubiquitous pollutants that are plausibly linked to breast cancer, either because they initiate mammary tumours, or promote the growth of tumours, or alter breast development to increase susceptibility. Many of these are endocrine disrupters, often mimicking oestrogen, giving rise to what is now referred to as an oestrogenic environment. Epidemiological evidence of a link between these chemicals and breast cancer is more limited, in part because the studies have not been carried out, and in part because of inadequate study design. But there

are a small number of occupational exposure studies that provide information consistent with the toxicological findings.

## **Prevention**

Breast cancer strategy has tended to focus primarily on early detection and treatment to reduce mortality, but these do nothing to prevent the onset of cancer in the first place. Whilst it is right and proper that every effort should be made to prevent women dying from breast cancer, an equal effort is required to prevent women developing it in the first place.

The government's new Cancer Control Strategy brings long overdue attention to bear upon prevention of cancer, acknowledging that this must include all aspects of prevention. It has objectives relating to tobacco use and second-hand smoke, physical inactivity and obesity, nutrition, sunlight, infectious disease, alcohol, and occupational exposure to carcinogens. With the exception of the occupational exposures, these objectives address less than 50 percent of the causes of breast cancer.

What is missing from the strategy is the non-occupational exposure to the multitude of chemicals that cause mammary tumours or are endocrine disrupting, and which are found in household products, cosmetics, furnishings, building materials, fuels, pesticides, foods, and used in or released by many industrial processes. Why is there not a systematic programme to find replacements for these chemicals and where the replacements already exist, insist that they be used by removing the offenders from the market place? Is it because there is not proof beyond a shadow of a doubt? Must we wait and watch as more women die, whilst the chemical industry says 'prove it'. Or should we perhaps invoke the precautionary approach on the basis of the significant body of scientific evidence that already exists, to really do something to reduce the incidence of breast cancer. Taking a precautionary approach means that *evidence* of harm rather than *proof* of harm should be the trigger for action. Absolute proof may never be possible, but there is already plenty of evidence of a link between breast cancer and many common chemicals.

As breast cancer rates continue to climb and the science is pointing to a causative factor, there is very little government recognition, the cause officially remains unknown, and nothing is being done to limit these exposures.

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**Appendix 1: Some chemicals associated with increased incidence of mammary tumours in rats and/or mice**

<b><u>Chemical</u></b>	<b><u>Use</u></b>
<b><i>Pesticides</i></b>	
atrazine	herbicide
clonitralid	molluscicide
1,2-dibromo-3-chloropropane <sup>a</sup>	soil fumigant
1,2-dibromoethane <sup>a</sup>	soil fumigant; lead scavenger in petrol
1,2-dichloropropane (propylene dichloride)	fumigant; chemical intermediate; solvent in drying cleaning fluids
dichlorvos	insecticide
malathion	insecticide
parathion	insecticide
sulfallate <sup>a</sup>	herbicide
<b><i>Pharmaceuticals</i></b>	
acronycine	pharmaceutical
cytembena	pharmaceutical
flurosemide	pharmaceutical
isophosphamide	pharmaceutical
nithiazide	antiprotozol compound
nitrofurazone	antibiotic (animal use)
phenesterin	pharmaceutical
procarbazine hydrochloride <sup>a</sup>	pharmaceutical
reserpine <sup>a</sup>	pharmaceutical
<b><i>Food</i></b>	
acrylamide	certain cooked foods
methyleugenol	flavouring additive, also naturally occurring
ochratoxin A <sup>a</sup>	food: mycotoxin
<b><i>Fuels</i></b>	
benzene <sup>c</sup>	petrol solvent
1,3-butadiene <sup>b</sup>	petrol, auto exhaust, rubber manufacture, fungicides
hydrazobenzene <sup>a</sup>	motor oil; dye intermediate
nitromethane	rocket and engine fuel, solvent, mining explosive
<b><i>Flame Retardants</i></b>	
2,2-bis(bromomethyl)-1,3-propanediol (Group 2B – possible human carcinogen)	flame retardant - in polyester resins and polyurethane foams used in computer equipment and building industry
2,3-dibromo-1-propanol	flame retardant – children’s clothing, computer equipment and building industry; intermediate in production of insecticides, pharmaceuticals.
2-chloroacetophenone	(flame retardent), tear gas and chemical mace, intermediate in production of pharmaceuticals, denaturing alcohol
<b><i>Dyes</i></b>	
C.I. acid red 114 <sup>b</sup>	dye - silk, jute, wool, leather
C.I. basic red 9 monohydrochloride <sup>a</sup>	dye - textiles, leather, paper, biological stain
2,4-diaminotoluene <sup>a</sup> (2,4-toluene diamine)	dye – intermediate in synthesis
1,2-dimethoxybenzidine dihydrochloride <sup>a</sup>	dye - intermediate
3,3’-dimethylbenzidine dihydrochloride	dye - intermediate

2,4-dinitrotoluene	dye – intermediate, explosives, propellants
o-toluidine hydrochloride <sup>a</sup>	dye - intermediate
<b><i>Solvents (see also fuels)</i></b>	
1,2-dibromomethane	solvent
1,1-dichloroethane	solvent; petrol; used in insecticide formulation
1,2-dichloroethane	solvent; petrol; used in insecticide formulation
methylene chloride	solvent, furniture stripper
<b><i>Other chemicals</i></b>	
ethylene oxide <sup>c</sup>	sterilising gas for medical equipment
chloroprene <sup>a</sup>	used in neoprene manufacture
glycidol <sup>a</sup>	stabiliser in vinyl polymers; intermediate in pesticides and fragrances
indium phosphide	microelectronics, semiconductors, injection lasers, diodes
isoprene	byproduct of ethylene production
5-nitroacenaphthene	research chemical
polyaromatic hydrocarbons	
styrene	
2,4- and 2,6-toluene diisocyanate <sup>a</sup>	in manufacture of flexible polyurethane foams
1,2,3-trichloropropane <sup>a</sup>	chemical intermediate; former solvent and paint remover
vinyl chloride	manufacture of PVC, hazardous waste, landfills, cigarette smoke
vinyl fluoride	

<sup>a</sup> = listed in 9<sup>th</sup> Report on Carcinogens as “reasonably anticipated to be a human carcinogen

<sup>b</sup> = listed in 9<sup>th</sup> Report on Carcinogens as “known human carcinogen”

<sup>c</sup> = listed in 9<sup>th</sup> Report on Carcinogens as “known human carcinogen” with some epidemiological evidence of breast cancer

Sources: Cabello et al 2001; DeBruin & Josephy 2002; Brody & Rudel 2003.

## Appendix 2: Selected endocrine disruptors

<b>Chemical</b>	<b>Use</b>
<b><i>Pesticides</i></b>	
atrazine	herbicide
chlordane	insecticide
chlorpyrifos	insecticide
cypermethrin	insecticide
2,4-D	herbicide
DDT (and associated compounds)	insecticide
dieldrin, aldrin, endrin	insecticides
lindane	insecticide; hair treatment for lice
malathion	insecticide
methoxychlor	insecticide; veterinary pharmaceutical
pentachlorophenol	wood preservative
permethrin	insecticide
sumithrin	insecticide
toxaphene	insecticide
tributyl tin (chloride)	biocide, rodent repellent??
vinclozolin	fungicide
<b><i>Persistent non-pesticide compounds</i></b>	
PAHs (polyaromatic hydrocarbons)	in industrial air pollution, smoke from coal or coke-burning, tobacco tar, some foods
PBBEs (polybrominated biphenyl ethers)	formerly as a flame retardant
PBDEs (polybrominated diphenyl ethers)	flame retardant
PCBs (aroclor 1254)(polychlorinated biphenyls)	obsolete; were used in electrical capacitors and transformers, other electrical equipment, carbonless copy paper
dioxins and furans	produced during incineration, paper manufacturing, production of chlorine aromatics; impurity in some chlorinated herbicides
<b><i>Phenols and alkylphenols</i></b>	
bisphenol A	polycarbonate and polyester-styrene resins: food containers
butylated hydroxyanisole	
4- <i>tert</i> -butylphenol	intermediate in manufacture of varnish and lacquer resins; soap antioxidant
nonylphenol polyethoxylate; 4-nonylphenol, 4-octylphenol	surfactant, detergent, defoaming agent, 'inert' in some pesticide formulations, degradation product of alkylphenol ethoxylated antioxidant in some plastics
<i>o</i> -phenylphenol	disinfectant fungicide, in the rubber industry
<b><i>Phthalates</i></b>	
Bis(2-ethylhexyl)phthalate, butyl benzyl phthalate,	plasticiser for PVC polymers
di- <i>n</i> -butyl phthalate, diethyl phthalate	personal care products such as nail polish, perfume, hair spray, plasticisers, inks, adhesives, and other uses
<b><i>Parabens</i></b>	
Butyl, ethyl, methyl, and propyl paraben	Pharmaceutical aid (antifungal), preservative in foods; preservative in creams, lotions, ointments, other cosmetics; constituent of Foray 48B

<b><i>Other chemicals</i></b>	
Amsonic acid	used in manufacture of dyes, bleaching agents, optical brighteners
stryene	used in manufacturer of plastics, synthetic rubber, resins; insulator
vinyl acetate	Used in production of polymers including polyvinyl acetate, polyvinyl alcohol; widely used in production of adhesives, paints, food packaging
<b><i>Metals</i></b>	
cadmium, lead	Batteries, plastic stabilisers, pigments
mercury	Thermometers, dentistry, pharmaceuticals, agricultural chemicals, anti-fouling paints, and many other uses
<b><i>Phytoestrogens</i></b>	
Genistein, coumestrol, zearalone	Soy, grains, grain moulds

Source: DeBruin & Josephy 2002; Brody & Rudel 2003.