Human Health Impacts of Exposure to Pesticides

Contract ref: 011005, WWF Australia

Meriel Watts, PhD

Meriel Watts Research and Consulting
PO Box 296, Ostend, Waiheke Island, Auckland, New Zealand
merielwatts@xtra.co.nz

November 2012

Contents
Executive summary
1. Introduction
2. Objectives and methodology
3. Key chronic health impacts
   Cancer
   Neurodevelopment problems, children's IQ, behavioural disorders
   Other neurological damage
   Birth defects, birth outcomes
   Respiratory problems
   Metabolic disorders – obesity, diabetes, metabolic disease
4. Key systemic impacts
   Endocrine disruption
   Immune effects
5. Children at greatest risk
   Greater exposure
   Greater vulnerability
   Future generations – epigenetic effects
6. Key scientific considerations
   The difference between acute and chronic exposures
   The added toxicity of inert ingredients
   Laboratory versus epidemiological evidence
   Bioaccumulation
7. International concerns and approaches
   Endocrine disrupting chemicals
   Low dose exposures
   Chemical mixtures
   Hazard versus risk assessment in pesticide regulation
   Precaution
   Substitution
   Minimum harm
8. Conclusion
References
Executive Summary

The objectives of this paper are to provide a summary scientific review of peer-reviewed literature on the human health impacts of exposure to pesticides, especially those that may be impacting Australia’s Great Barrier Reef; and to briefly review key international concerns and emerging approaches to pesticide issues.

Evidence is provided of the increased risk of some adverse health effects from exposure to pesticides. There is evidence that a number of the pesticides found in the Great Barrier Reef waters and in waterways discharging into the area may cause cancer (e.g. atrazine, 2,4-D, diuron, simazine), neurological conditions (chlorpyrifos), birth defects (atrazine, 2,4-D, diuron, endosulfan, MCPA), reduced foetal growth (atrazine, chlorpyrifos, 2,4-D, metolachlor), and metabolic problems leading to obesity and diabetes (chlorpyrifos).

Foetal and early childhood exposures to pesticides are a key concern, with considerable evidence of links between such exposures to a wide variety of pesticides and a range of childhood cancers, especially brain cancer and leukaemia. Prenatal exposure, particularly to organophosphate insecticides, is strongly linked with a range of developmental, cognitive and behaviour deficits, that can result in lasting adverse effects on the brain and leading to what has been described as a “silent pandemic” of developmental neurotoxicity. Prenatal exposure is also strongly linked with a range of birth defects.

Key systemic effects underlying many of these conditions involve the endocrine and immune systems. Exposures to endocrine disrupting chemicals (EDCs) during these early life stages can have permanent and irreversible effects, with severe health consequences throughout childhood and into adulthood, and even for subsequent generations, the effects continuing long after the exposure to the endocrine disrupting chemical has ceased.

‘Inert’ ingredients are added to pesticide formulations for a number of reasons including helping the product stick to the surface of leaves and soil, spread over surfaces, or dissolve in water. They can be more toxic than the active pesticidal ingredient to humans, nontarget plants, animals and microorganisms. For example the ‘inert’ ingredients in glyphosate increase its aquatic toxicity. Generally there is no requirement to identify the inert ingredients on pesticide labels or publically available registration information, and pesticide proprietors claim the identity of ‘inerts’ as confidential business information. This makes it impossible for the general public or researchers to know what is in the formulations being used.

Areas of pesticide toxicology and policy of key international concern include endocrine disrupting chemicals, low dose exposures, chemical mixtures, hazard versus risk assessment in pesticide regulation, precaution, substitution, and causing minimum harm to humans and the environment through pest management techniques. Increasingly hazard assessment is coming to replace risk assessment as it is realised that the current regulatory process of assessing the risk of a single pesticide at a time fails to account for the reality of human exposure to ongoing low doses of mixtures of pesticides. Currently no country has an adequate regulatory process for assessing these effects, or those of endocrine disrupting pesticides. Nor do they adequately implement the precautionary principle, or the substitution of hazardous pesticides with less hazardous pesticides and nonchemical methods. None at all work on the basis of the principle of minimum harm, asking the first
question: how do we control pest, weeds and diseases in the manner that is least harmful to people and the environment?

1. Introduction

Pesticides are chemicals used for killing or controlling unwanted insects, diseases on plants, weeds, slugs and snails, birds, and vertebrate mammals regarded as pests such as rodents. They are used for controlling physiological functions in plants such as regulating flowering, thinning fruit, preventing fruit drop, defoliating crops before harvest. Pesticide is the generic term that includes insecticides, miticides, nematicides, fungicides, herbicides, algaeicides, fumigants, vertebrate poisons, etc. The term pesticide commonly refers to synthetic chemicals used for these purposes but can also include biopesticides – pesticides based on microorganisms or natural products.

The main classes of insecticides are organochlorines (e.g. DDT), organophosphates (chlorpyrifos), carbamates (carbaryl), synthetic pyrethroids (permethrin), and neonicotinoids (imidacloprid). The main classes of herbicides are phenoxy herbicides (2,4-D), and triazines (atrazine), although the most commonly used herbicide, glyphosate, is not in one of the main families.

Pesticides are used in a multitude of situations including in crops, orchards, forestry, ornamental plantings, sports turf, homes, gardens, parks, industrial premises, shops, restaurants, schools, hospitals, airports, railway lines, roadsides, transmission lines, drains, waterways, on animals, and even on people for pests such as scabies and head lice. They are sprayed in open spaces and city streets for disease vector control. They can be added to products such as paints, textile, clothing and bed nets.

People are exposed to pesticides through direct contact (skin, inhalation) when using them, direct skin contact after someone else has used them, spray drift from neighbouring applications, household fly sprays and insect coils, in food, water and drinks, and applications on pets. People are exposed to residual insecticides used to treat the insides of some airplanes or sprayed as aerosols in other airplanes. Children are exposed before they are born, as pesticides absorbed by their mothers cross the placenta and are taken up by the foetus. The first faeces of newborn infants have been found to contain a number of pesticides. Infants are then exposed again when they are breast fed, for a wide range of pesticides are commonly found in breast milk.

A World Bank (2008) report estimates that 355,000 people worldwide die each year from unintentional pesticide poisoning. An older, but authoritative study (Jeyaratnam 1990) estimates that there are possibly one million cases of serious unintentional pesticide poisonings each year. The author of this study notes that this figure reflects only a fraction of the real problem and estimates that there could be as many as 25 million agricultural workers in the developing world suffering some form of occupational pesticide poisoning each year, though most incidents are not recorded and most patients do not seek medical attention. One of the conclusions this author reaches is that acute pesticide poisoning may
in some developing countries be as serious a public health concern as are communicable
diseases.

Although those figures relate mainly to developing countries where acute exposures are
more evident than in countries such as Australia, they do not tell the story of chronic
exposures either in the developing world or in developed countries. Chronic effects for
which there is substantial evidence of association with pesticide exposures include cancer,
neurodevelopmental and behaviour effects, other neurological effects including
neurodegenerative diseases, birth defects and other adverse birth outcomes, and
respiratory diseases. More recently evidence has begun to emerge of associations with
obesity, type 2 diabetes and metabolic disease. Some effects last a whole lifetime; some are
passed on to future generations. Concern continues to mount about the reality of human
exposure to ongoing low doses of mixtures of pesticides, especially those that cause
endocrine disruption or damage the developing brain of the unborn foetus. Because of the
difficulty in establishing links between specific exposure incidents and the development of
chronic effects, which may take decades to develop, it is impossible to establish the exact
extent of the chronic effects of pesticide exposure in any country, let alone the costs to the
health system, the economy, or people’s wellbeing and happiness. But there is sufficient
evidence to propose that such costs will be far in excess of those of acute exposure.

The uncertainty about the extent and cost of these chronic effects has been used for decades
to delay action in removing the worst offenders and in shifting agricultural production away
from the current chemical input approach and towards an ecosystem approach in which
priority is given to creating a healthy agroecosystem in which natural enemies and
biological controls flourish, and in which pesticides are used only as a last resort. This shift
in focus of agriculture is now espoused at the highest international level, such as Food and
Agriculture Organisation of the United Nations (FAO), UN Special Rapporteur on the Right
2. Objectives and methodology

The objective of this report is to establish that the scientific basis of WWF’s campaign on pesticides is sound, by providing a summary scientific review of peer-reviewed literature on the chronic human health impacts of exposure to pesticides, as well as key scientific concepts, emerging concerns and international approaches, as described in the terms of reference.

Given the vast scale of the peer reviewed literature available on the adverse human health effects of pesticides, and the constraints of time and resources, recent appropriate meta-analyses of scientific papers were used where possible, together with other relevant papers. It was not possible to review all published papers on any one aspect of this report. Rather an indicative overview is given. Emphasis was placed on current use pesticides rather than legacy pesticides such as DDT. In addition, some data was provided on pesticides that have been found contaminating the Great Barrier Reef area, and the waterways that empty into the Reef area, although this report should not be in any way regarded as providing all the information available on the effects of these pesticides.

Pesticides found in the inshore waters surrounding the reef are the herbicides ametryn, atrazine, diuron, hexazinone, simazine, and tebuthiuron (Queensland Government 2011).

Pesticides detected in the waterways discharging to the Great Barrier Reef area include the herbicides ametryn, atrazine (and degradation products), bromacil, 2,4-D, diuron, hexazinone, MCPA, metolachlor, simazine, tebuthiuron; and the insecticides endosulfan, imidacloprid, and malathion – underlining indicating those that are found frequently and at relatively high concentrations (Lewis et al 2009).

Other pesticides in wide use in the Great Barrier Reef catchment include chlorpyrifos, paraquat, and glyphosate (King et al 2012).

A note about the terminology used: it is seldom possible to state with absolute certainty that a pesticide causes a particular effect in humans, because the level of proof required to support such an assertion is difficult to obtain in the face of many variables. Instead the terms ‘associated with’, ‘linked with’, or ‘increased risk’ are generally used to describe a scientifically supported level of evidence that such an effect may be caused by the pesticide.
3. **Key chronic health impacts**

The impacts of pesticides on human health are wide-ranging, affecting every part of the body but only the major chronic impacts are considered here. Others include acute poisoning, cardiovascular, skin and eye effects, liver and kidney damage, reduced fertility and fecundity, early onset puberty, endometriosis, and multiple chemical sensitivity.

### 3.1 Cancer

There is a considerable body of epidemiological evidence linking pesticides to cancer, and in particular to child cancer resulting from both parental and direct childhood exposures.

**Child cancer**

The evidence is strongest for leukaemia and brain cancer (Infante-Rivard & Weichenthal 2007; Lyons & Watterson 2010; Van Maele-Fabry et al 2010), but there is evidence also for associations with non-Hodgkin's lymphoma, neuroblastoma (a tumour in nerve tissue), Ewing's sarcoma (a tumour of bone tissue), and Wilms' tumour (kidney). Other child cancers linked to pesticide exposures include soft-tissue sarcoma, colorectal cancer, germ cell cancer, Hodgkin's disease, eye cancer, renal and liver tumours, thyroid cancer, and melanoma (Zahm & Ward 1998, Infante-Rivard & Weichenthal 2007; Carozza et al 2008; Thompson et al 2008; Ferris I Tortajada et al 2008).

Maternal exposures, but also paternal exposures preconception, including both occupational and household exposures, are associated with leukaemia and brain cancer (Infante-Rivard & Weichenthal 2007; Lyons & Watterson 2010; Van Maele-Fabry et al 2010). A large international study across seven countries identified an association between childhood brain tumours and maternal farm exposure to pesticides during the five years preceding the diagnosis (Efird et al 2003). A high rate of brain cancer was found in children playing in orchards in Kashmir, India (Bhat et al 2010).

**Adult onset cancer**

There are also a number of adult cancers associated with exposure to pesticides including breast, lung, multiple myeloma, non-Hodgkin's lymphoma, leukaemia, ovary, pancreas, prostate, kidney bladder, stomach, colon, rectal, lip, connective tissue, brain, and testicular. Of these, at least breast, prostate, and testicular cancer are thought to have origins in early developmental exposures to environmental hormone disruptors (Bassil et al 2007; Waggoner et al 2011; Cooper et al 2011; Alavanja & Bonner 2012). Swedish research has concluded that adult cancer risk is largely established during the first 20 years of life (Czene et al 2002; Hemminki & Li 2002).

One large epidemiological study in the US states of Iowa and North Carolina, the Agricultural Health Study which involved a cohort of 89,656 pesticide applicators and their spouses, found a decrease in overall cancer mortality rate, but an increase in mortality rates for specific cancers: lymphohaematopoietic cancers, melanoma, and digestive system, prostate, kidney, and brain cancers amongst applicators; and among spouses, lymphohaematopoietic cancers and malignancies of the digestive system, brain, breast, and ovary (Waggoner et al 2011).

**Pesticides implicated**
Epidemiological studies have associated an array of cancers with all the main functional classes of pesticides – herbicides, insecticides, fungicides, fumigants – and chemical classes including organochlorine (OC), organophosphate (OP), and carbamate insecticides, and phenoxy acid and triazine herbicides (Alavanja & Bonner 2012). The Agricultural Health Study referred to above produced evidence of increased risk of cancer associated with 12 pesticides: alachlor, aldicarb, carbaryl, chlorpyrifos, diazinon, dicamba, S-ethyl-N,N-dipropylthiocarbamate (EPTC), imazethapyr, metolachlor, pendimethalin, permethrin, and trifluralin (Weichenthal et al 2010). The authors noted that animal toxicity data supports the findings for alachlor, carbaryl, metolachlor, pendimethalin, permethrin, and trifluralin.

Alavanja & Bonner (2012) also reviewed other studies and among the associations they noted were:

- simazine with prostate cancer
- aldicarb with colon cancer
- butylate with prostate cancer
- carbaryl with melanoma
- chlorpyrifos with lung and rectal cancers
- diazinon with lung cancer and leukaemia
- dicamba with colon cancer
- fonophos with prostate cancer
- EPTC with colon and pancreatic cancers
- imazethapyr with colon and bladder cancers
- lindane with non-Hodgkin’s lymphoma
- maneb and mancozeb with melanoma
- parathion with melanoma
- pendimethalin with rectal cancer
- trifluralin with colon cancer

Some other examples of particular pesticide/cancer associations in epidemiological studies include:

- atrazine – bone cancer, leukaemia (Thorpe & Shirmohammadi 2005; Rull et al 2009)
- carbaryl – brain (Zahm & Ward 1998)
- endosulfan – leukaemia (Rau et al 2012)
- metolachlor – bone cancer, leukaemia (Thorpe & Shirmohammadi 2005); lung cancer (Weichenthal et al 2010)
- pyrethroid head lice shampoo – leukaemia (Menegaux et al 2006)
- simazine – prostate cancer (Mills & Yang 2003; Band et al 2011)
- glyphosate – Mink et al (2012) in their review of case control and cohort studies concluded that there was “no consistent pattern of a positive association indicating a casual relationship” with cancer; but the studies reviewed showed a striking tendency of increased risk of non-Hodgkin’s lymphoma. Other cancers showing increased risk ratios included multiple myeloma, breast, rectal, and brain. The authors dismissed the studies for reasons including their being not statistically significant on further analysis, confidence limits too large, or inconsistent results. However this leaves cause for concern about glyphosate and cancer, especially in light of laboratory studies.
- malathion – prostate cancer (Band et al 2011); breast cancer (Mills & Yang 2005).

The WWF list of Australia’s Most Dangerous Pesticides (Immig 2010) contains 17 pesticides registered in Australia that are known, likely or probable carcinogens (indicated by *), and another 42 that are possible or suspected carcinogens, according to regulatory information in the USA, and to assessment by the International Agency for Research on Cancer.
These are:

- acephate
- acrifluorfen
- alpha-cypermethrin
- amitraz
- bifenthrin
- bioallethrin
- bromoxynil
- carbaryl
- carbendazim
- chlorfenapyr
- chlorothal
- chlorothalonil
- cyanazine
- cypermethrin
- dichlorvos
- diclofop
- dicrofo
- linuron
- malathion
- mancozeb
- mecoprop
- mercuric chloride
- metaldehyde
- methidathion
- molinate
- oxadiyl
- pendimethalin
- permethrin
- phosmet
- piperonyl butoxide
- pirimicarb
- prochloraz
- propachlor
- propanil
- propiconazole
- propoxur
- tebuconazole
- tetraconzole
- thiachlorid
- thiodicarb
- triadimefon
- triadimenol
- triclorfon
- zeta cypermethrin
- ziram

Laboratory studies indicating that particular pesticides can cause cancer, or are genotoxic or mutagenic are too numerous to review here. Some of them confirm epidemiological findings, some do not. Diuron is an example of a pesticide for which the laboratory studies clearly indicate carcinogenicity, but for which carcinogenic associations with cancer have not shown up in epidemiological studies so far. The APVMA (2011) review reported that diuron increased incidences of malignant carcinoma in the urinary bladder of males; malignant transitional carcinomas in the urinary bladder epithelium of males and females; and malignant neoplasias in the uterus, and adenocarcinoma in the mammary gland in female rats.

### 3.2 Neurodevelopment problems, children’s IQ, behavioural disorders

Epidemiological studies have shown that prenatal exposure to pesticides, especially organophosphate insecticides such as chlorpyrifos, is associated with pervasive developmental disorders, delayed or reduced cognitive development, learning disabilities, poorer short-term memory and motor skills, longer reaction time, behavioural disorders such as Attention Deficit Hyperactivity Disorder (ADHD), and autism spectrum disorders (Guillette et al 1998; Eskenazi et al 2007, 2008; Roberts et al 2007; Gilbert 2008; Jurewicz & Hanke 2008; Searles Nielsen et al 2010; London et al 2012). Prenatal exposure to pesticides can have lasting adverse effects on the brain leading to what has been described as a “silent pandemic” of developmental neurotoxicity (Harari et al 2010).

- Children from agricultural communities in the US showed poorer response speed and slower learning in neurobehavioural tests than children from non-agricultural communities (Rohman 2005).
- A study of Hispanic children living in an agricultural community in Arizona, USA showed that short-term OP exposure reduced children’s cognitive and behavioural functioning, including speed of attention, sequencing, mental flexibility, visual search, concept formation, and conceptual flexibility (Lizardi et al 2008).
- Garry et al (2002) found an association between children born to pesticide applicators exposed to glyphosate and neurobehavioural deficits; and between...
those exposed to the grain fumigant phosphine and neurological and neurobehavioural deficits, including ADHD and autism. Forty-three percent of children with ADHD had fathers who used glyphosate.

- Each 10-fold increase in urine levels of OP metabolites in children was associated with a 55 to 72 percent increase in the likelihood of ADHD in children aged eight to 15 years, in a US study (Kuehn et al 2010).
- Each 10-fold increase in a pregnant mother’s urinary concentration of OP metabolites led to a 500 percent increased risk that her child would be diagnosed with ADHD by age five (Marks et al 2010).
- Eskenazi et al (2007) found a 230% increased risk of Pervasive Developmental Disorders, which include autism, for each 10 nanomole/litre increase in urinary metabolites of OPs.
- After reviewing published data Dr David Bellinger (2012), of the USA’s Children Hospital Boston, concluded that OPs were responsible for lowering the country’s IQ level by 17 million points, not much less than the 23 million points lost to lead poisoning, a widely recognised cause of cognitive loss in children.
- Three recent studies in the US confirmed that prenatal exposure to OPs results in lower IQs, and reduced memory and perceptual reasoning in children. Engel et al (2011) showed elevated levels of OP metabolites in a woman’s urine during the third trimester of pregnancy resulted in reduced cognitive development in her child at 12 months of age, particularly perceptual reasoning. Bouchard et al (2011) correlated elevated levels of OP metabolites in pregnant women with significantly reduced IQ in their children at the age of 7, by as much as 7 points, as well as reduced working memory, processing speed, verbal comprehension, and perceptual reasoning. Rauh et al (2011) found that as little as 4.6 picograms of chlorpyrifos per gram of cord blood during gestation resulted in a drop of 1.4 percent of a child’s IQ and 2.8 percent of her/his working memory.

This is a small selection of epidemiological studies illustrating neurodevelopmental problems resulting from foetal and early childhood exposure to pesticides. There are many more such studies. Additionally there are numerous laboratory studies on animals demonstrating similar effects and confirming the biological plausibility of, and mechanisms involved in, these outcomes, especially for organophosphate insecticides (Slotkin 2004; Colborn 2006; Slotkin et al 2006; Flaskos 2012).

The potential societal effects of these findings cannot be overstated. Rates of mental illness and suicide are higher in children suffering developmental, learning and behavioural disabilities, with increased likelihood of substance abuse and criminal activity later in life (Szpir 2006). Attention deficit at the age of 10 has been associated with lower employment rates, worse jobs, lower earnings if employed, and lower expected earnings overall, in a study of 38-year-olds in the UK (Knapp et al 2011). In Canada the estimated cost to the country of the loss of 5 IQ points is 29 billion Australian dollars per year (Muir & Zegarac 2001) – and recent studies in the US have found prenatal exposure to OPs reducing children’s IQ by as much as 7 points.

### 3.3 Other neurological damage
Many pesticides can act through neurotoxic mechanisms that are relevant to human health, including organophosphates (OPs), organochlorines (OCs), carbamates and pyrethroids (London et al 2012). The effects can range from mild cognitive dysfunction (Bosma et al 2000) through, impaired peripheral nervous system function (Starks et al 2012), delayed neuropathy (Jokanovic et al 2011), mood disorders (Meyer et al 2010), and psychological distress (Wesseling et al 2010), to suicides and neurodegenerative diseases (London et al 2012; Malek et al 2012).

High levels of exposure, such as with occupational exposures and poisonings, may result in increased risk of neuropsychiatric outcomes including increased anxiety, depression and suicide; and increased agricultural injury as a result of the depression (Stallones & Beseler 2002; London et al 2012). A recent cohort study of grain farmers in Canada has linked exposure to phenoxy herbicides (2,4-D and MCPA) with physician diagnosed mental ill-health, particularly for hospital admissions amongst those who had been exposed for 35 years for more (Cherry et al 2012).

The effects of OP exposures during adolescence can manifest as mental and emotional disturbances (Jurewicz & Hanke 2008). A relatively consistent pattern of neurobehavioural deficits, including increased neuroses, have been observed in studies of pesticide applicators, greenhouse workers, agricultural workers and farm residents exposed repeatedly over months or years to low levels of OPs (Abdel Rasoul et al 2008; London et al 2012).

Pesticide exposures can also influence sleep: one case–control study found an association between previous occupational exposure and idiopathic REM sleep behaviour disorder (a common prediagnostic sign of parkinsonism and dementia) (Posthuma et al 2012).

There is evidence of an association between chronic exposure to pesticides with neurodegenerative disease including dementia, Alzheimer’s disease, Parkinson’s disease, amyotrophic lateral sclerosis (a form of motor neuron disease) and multiple sclerosis (Parrón et al 2011; Malek et al 2012). A systematic meta-analysis of occupational exposure to pesticides by Van Maele-Fabry et al (2012) concluded that there is a statistically significant increased risk of Parkinson’s disease with occupational exposure, especially amongst banana, sugarcane and pineapple plantation workers. A second meta-analysis, of 46 studies, concluded that there is a positive association between Parkinson’s disease and exposure to herbicides and insecticides, but not fungicides (van der Mark et al 2012). A third review associated increased risk of Parkinson’s disease with exposure to chlorpyrifos, paraquat, and maneb (Freire & Koifman 2012).1

### 3.4 Birth defects, birth outcomes

**Birth defects**

Animal studies have identified a number of pesticides that cause birth defects. These include diuron (delayed ossification of vertebrae and sternum and other skeletal alterations in rats – APVMA 2011), atrazine (feminisation of male frogs – Hayes et al 2006a), a metabolite of metolachlor (2-ethyl-6-methyline, teratogenic in frogs – Osanao et al 2002), and 2,4-D (urinary tact malformation, extra ribs – USEPA 2007).

1 Since the publication of the third meta-analysis (Freire & Koifman 2012), the work by researcher Mona Thiruchelvam has been discredited. This study cites some of her work but the conclusions are not dependent on it, as other studies cited have implicated the same pesticides.
Numerous epidemiological studies have been carried out to try to determine whether pesticides do cause birth defects in humans, and if so which pesticides are implicated. Studies vary in quality, and in the questions they address. Some have not found a positive link with pesticides, but many have. A recent review of studies by Sanborn et al. (2012) concluded that “all of the high-quality birth defect studies reported positive associations” with hypospadias, neural tube defects, and congenital diaphragmatic hernia. Other birth defects positively associated with pesticide exposure include cryptorchidism (Kristensen et al. 1997; Carbone et al. 2006; Rocheleau et al. 2009) and micropenis (Gaspari et al. 2011); missing or reduced limbs (Schwartz & LoGerfo 1986, 1988); anencephaly (Lacasana et al. 2006); spina bifida (Brender et al. 2010); and congenital heart disease (Yu et al. 2008).

Association between pesticides and birth defects have been found for a number of different exposure scenarios: families of pesticide applicators (Garry et al. 1996); families living in rural areas (Schreinemachers 2003); and maternal exposure (Blatter et al. 1996; Shaw et al. 1999; Engel et al. 2000; Medina-Carrillo et al. 2002; Rojas et al. 2000; Calvert et al. 2007; Rocheleau et al. 2009; Brender et al. 2010; Dugas et al. 2010; Gabel et al. 2011), especially in floriculture (Restrepo et al. 1990a, 1990b; Idrovo & Sanín 2007), gardening (Weidner et al. 1998), in orchards, greenhouses or grain farming (Kristensen et al. 1997; Andersen et al. 2008), and use in the home (Brender et al. 2010).

Associations have also been made between exposure to pesticides during particular time periods and certain birth defects: for example maternal exposure preconception with spina bifida (White et al. 1988); maternal exposure during the period from the month before conception and the first trimester with multiple anomalies including nervous system defects and oral clefts (Nurminen et al. 1995; Garcia et al. 1998); use of insect repellents during the first trimester with hypospadias (Dugas et al. 2010); and paternal exposure in greenhouses producing vegetables and flowers during the 3 months prior to conception with hypospadias (Brouwers et al. 2007) and cryptorchidism (Pierik et al. 2004).

In a number of studies, specific pesticides have been linked with birth defects:

- atrazine: one study found a relationship between gastroschisis and exposure to atrazine, in particular in women who resided <25 km from a site of high atrazine concentration (Waller 2010). An earlier study had found a correlation between higher incidence of abdominal wall defects (including gastroschisis and omphalocoele) and surface water contamination with atrazine in the US (Mattix et al. 2007);
- herbicides: 2,4-D, MCPA, atrazine, and trifluralin are associated with anomalies of the central nervous system, circulatory, respiratory, urogenital, and musculoskeletal systems, particularly in male children (Garry et al. 1996, 2002; Schreinemachers 2003);
- 2,4-D and 2,4,5-T: paternal exposure to Agent Orange (2,4,5-T and 2,4-D) is associated with spina bifida (Ngo et al. 2010);

---

2 Hypospadias is the abnormally placed urinary opening on the penis.
3 Cryptorchidism is the absence of one or both testes.
4 Anencephaly is the absence of a major part of the brain and skull, caused by failure of the neural tube to close, usually between the 23rd and 26th days of pregnancy. It may also involve facial distortions and heart defects.
5 Gastroschisis is a birth defect in which the baby’s intestines protrude through a hole in the abdominal wall.
• endosulfan: parental exposure to endosulfan is linked to a variety of birth defects and congenital conditions in India (NIOH 2002);
• diclofop-methyl: maternal exposure to diclofop-methyl during pregnancy is associated with increased risk of hypospadias (Meyer et al 2006);
• cyanazine and dicamba: parental exposure to both cyanazine and dicamba is associated with congenital abnormalities (Weselak et al 2008);
• oxydemeton-methyl: maternal exposure to oxydemeton-methyl at 4 weeks of pregnancy is associated with congenital defects of heart, eye, face and brain (Romero et al 1989).

Parental body burden of organochlorine pesticides such as DDT, DDE, HCH, HCB and endosulfan are also associated with a range of congenital defects including neural tube defects, undescended testicles, cryptorchidism, extra nipple in males, and cretinism (Hoste et al 2000; Longnecker et al 2002; Damgaard et al 2006; Ngayama et al 2007; Brucker-Davis et al 2008; Ren et al 2011).

Foetal growth
Measures of foetal growth commonly include birth weight, head circumference, and intrauterine growth restriction. Again studies show mixed results, especially for organochlorine pesticides, and in part this may be because of the notorious difficulty in properly identifying pesticide exposures, a problem common to all epidemiological studies. Nevertheless the studies that do show positive associations should be taken seriously and not dismissed simply because not all studies confirm their findings.

The review by Sanborn et al (2012) found that most studies showed a positive association between non-organochlorine pesticide exposure and foetal growth outcomes, especially low birth weight. They regard this as a public health priority because low birth weight increases the risk of death, disease and disability in infancy and childhood, and of long-term adverse health outcomes in adulthood, such as cardiovascular disease, type 2 diabetes, osteoporosis, depressive disorders, and some cancers (Perera & Herbstman 2011; Sanborn et al 2012). Intrauterine growth influences adult metabolic disorders such as high blood cholesterol, fatty liver and obesity, and non-metabolic disorders like chronic lung disease (Perera & Herbstman 2011).

Decreased head circumference, also found in some studies, is associated with lower cognitive ability in older children and adults (Sanborn et al 2012).

A number of pesticides have been found to affect foetal growth, including:
• atrazine: decreased head circumference (Chevrier et al 2011), intrauterine growth restriction (Colborn & Carroll 2007);
• chlorpyrifos: significant reduction in head circumference (Berkowitz et al 2004), decreased birth weight and length (Perera et al 2003; Whyatt et al 2004);
• 2,4-D: pre-term births (Colborn & Carroll 2007);
• metolachlor: intrauterine growth restriction (Colborn & Carroll 2007), and decreased birth weight (Barr et al 2010b).

Pre-term births have been associated, in epidemiological studies, with use of herbicides especially atrazine, 2,4-D and OPs (Colborn & Carroll 2007), and maternal exposure to DDT, endosulfan or HCH (Wigle et al 2008; Pathak et al 2010).
**Foetal loss:**

Results of studies are mixed but some positive associations between pesticide exposure and foetal loss have been found. Both paternal and maternal exposure to pesticides, including occupational and home use, has been linked to still births (Goulet & Thériault 1991; Rupa et al 1991; Taha & Gray 1993; Nurminen et al 1995; Pastore et al 1997; Medina-Carrilo et al 2002), with one study linking it particularly to exposure during the second trimester (White et al 1988), and one to paternal exposure to DDT (Cocco et al 2005). Foetal death has been found to be higher following maternal occupational exposure to pesticides round the time of conception (Ronda et al 2005). Sanborn et al (2012) reviewed five other studies that all reported an association between foetal loss and working in greenhouses or horticulture as a proxy for pesticide exposure.

Colborn & Carroll (2007) report on studies that have associated exposure to atrazine, 2,4-D, and glyphosate with foetal loss.
3.5 Respiratory problems

The review of pesticides and health issues by the Ontario College of Family Physicians (Sanborn et al 2012) concluded that:

“Overall, there is evidence that exposure to pesticides, and to organophosphate or carbamate insecticides in particular, is associated with the development of respiratory symptoms and a spectrum of obstructive and restrictive lung diseases. Studies of asthma in children reported an association between maternal exposure to organophosphate and organochlorine insecticides, while respiratory tract infections in infants were linked to maternal exposure to organochlorine insecticides in two of three reviewed studies.”

The association with asthma was found for occupational, domestic and environmental exposures especially to parathion and coumaphos. In all 12 studies the authors reviewed, there was a consistent positive association between pesticide exposure and asthma – specifically for maternal organochlorine, organophosphate, biocide and fungicide exposure. In utero and post-natal (to one year) exposures were associated with asthma and wheeze up to six years of age (Sanborn et al 2012).

There is evidence too of an association between exposure to pesticides and chronic bronchitis, although the association is not as robust as for asthma, with an odds ratio of <2. The strongest relationship was for paraquat, with OC, OP, carbamate and pyrethroid insecticides all showing an association (Sanborn et al 2012).

Occupational exposures such as in farming, pesticide manufacturing, and pesticide spraying all showed a “subtle but persistent association between decreased lung function and exposure to a broad range of herbicides and insecticides”. Most striking was a strong association between chlorpyrifos and wheeze, chronic cough and shortness of breath in many studies. Carbamate, organophosphate, and neonicotinoid insecticides in general were associated with restricted lung function. Sarcoidosis and farmer’s lung were both associated with occupational exposure to insecticides (Sanborn et al 2012).

3.6 Metabolic disorders – obesity, diabetes, metabolic disease

In recent years scientific attention has begun to focus on environmental factors implicated in escalating rates of obesity, diabetes and metabolic disorder, a condition in which obesity is associated with hypertension, type 2 diabetes and cardiovascular disease. As a result there are now a number of peer reviewed studies linking pesticide exposure with these conditions (Lee et al 2006, 2007; Rignell-Hydbom et al 2007; Jones et al 2008; Montgomery et al 2008).

Particular attention is being paid to prenatal and early childhood exposures, especially those causing what is known as foetal programming, in which in utero exposures cause epigenetic changes that lead to overweight, obesity, and diabetes, with these effects being passed on to subsequent generations (Newbold et al 2007; Valvi et al 2012).

Pesticides, especially organochlorines, are thought to cause weight gain are through interference with the mechanisms involved in weight control. The pesticides are thought to disrupt weight-controlling hormones such as catecholamines, thyroid hormones, estrogens, testosterone, corticosteroids, insulin, growth hormone, and leptin; alter the levels of and
sensitivity to the neurotransmitters dopamine, noradrenaline, and serotonin; interfere with metabolic processes; and damage nerve and muscle tissues (Baillie-Hamilton 2002).

A number of epidemiological studies have linked exposure to largely obsolete organochlorine insecticides, such as DDT, with increased body mass index (e.g. Verhulst et al 2009; La Merrill & Birnbaum 2011; Mendez et al 2011; Valvi et al 2012).

However, currently used pesticides are also implicated: a Danish study found that children exposed prenatally to currently use pesticides – their mothers worked in greenhouses during early pregnancy – were not only born with lower birth weight but by the ages of 6 to 11 years had significantly higher body mass index and body fat percentage, the later being nearly one third higher (Wohlfahrt-Veje et al 2011). Laboratory studies support such findings, with chlorpyrifos, parathion and diazinon found to have effects on rats that include excessive weight gain, signs of a pre-diabetic state, metabolic patterns that resembles adult risk factors for atherosclerosis and type 2 diabetes, and appetite disorders in adulthood (Aldridge et al 2004; Slotkin et al 2005; Lassiter & Brimijoin 2008; Lassiter et al 2008; Adigun et al 2010).

Sulfonylurea herbicides and imidazole fungicides have also been identified as potentially implicated in obesity and diabetes, because of their effects on weight gain, blood sugar levels, or the pancreas (Thayer et al 2012).

In reporting on a workshop of scientists gathered to discuss the role of environmental chemicals in diabetes and obesity, Thayer et al (2012) commented that "the general findings are that early-life exposures to otherwise sub-toxic levels of OPs results in pre-diabetes, abnormalities of lipid metabolism, and promotion of obesity in response to increased dietary fat".
4. Key systemic impacts

4.1 Endocrine disruption

The Endocrine Society, an organisation of 15,000 scientists in more than 100 countries, has recently defined an endocrine disrupting chemical (EDC) simply as “a chemical that interferes with any aspect of hormonal action” (Zoeller et al 2012).

The endocrine, or hormonal system, is a delicately balanced system of glands and hormones that maintain homeostasis in the body, regulating metabolism, growth, responses to stress, the function of the digestive, cardiovascular, renal and immune systems, sexual development and reproduction, and neurobehavioural processes including intelligence (Birnbaum 2010). The mechanisms involved are complex and include binding to hormone receptors where they exert agonist or antagonist effects, binding to allosteric sites and producing unexpected effects, and interfering with hormone synthesis, metabolism, transport or degradation (Zoeller et al 2012).

Normal hormonal action changes over the lifetime of an individual. The most critical aspect of an endocrine disruptor is when exposure occurs, rather than the level of exposure. Because the endocrine system operates on tiny amounts of hormones, endocrine disruption occurs at levels of exposure far lower than those normally considered toxic. There are times when there is no normal endogenous hormone exposure and even very low dose exposures to EDCs at these times can have potent and irreversible effects. Additionally, hormones and hormonally active chemicals can cause different effects at different levels of exposure, and low dose exposure commonly experienced by humans can have profoundly serious effects even when the high dose exposures normally tested on rats in laboratories may not have an effect. So EDCs cannot be regarded as if they are general toxins but must be seen in the context of endocrine function under both normal and pathological conditions. In fact the dose response curve, normally assumed for general toxins to be positive and linear (monotonic), is never linear with hormones and EDCs but tends to be sigmoidal except when it is non-monotonic. Additionally, there is no threshold for EDC effects. This means that the data normally used to register pesticides utterly fails to reflect the reality of exposure to low levels of endocrine disrupting pesticides, especially when that exposure occurs during the critical stages of development in utero and in early childhood. (Myers et al 2009; Birnbaum 2010; Zoeller et al 2012)

Exposures to EDCs during these early life stages can have permanent and irreversible effects, with severe health consequences throughout childhood and into adulthood, and even for subsequent generations, the effects continuing long after the exposure to the EDC has ceased. Some of the effects do not manifest until adulthood. Most of the health impacts described in the preceding chapter can be precipitated by endocrine disruption in the foetal and early childhood stages – birth defects, cognitive development and behavioural problems; breast, prostate, testicular and cancers; diabetes, obesity, and cardiovascular

---

6 Binding to sites other than the receptor site.
7 S-shaped curve, in which the lowest doses give the greatest responses (Zoeller et al 2012).
8 Not linear; most common non-monotonic dose curve for EDCs is the inverted U-shaped in which intermediate doses give greatest responses (Zoeller et al 2012).
disease; allergies and asthma; and reproductive disorders including those of fertility and fecundity, precocious puberty, and endometriosis (Myers et al 2009; Birnbaum 2010).

In their 2011 review Mnif et al (2011) stated there are “about” 105 endocrine-disrupting pesticides, 46% of which are insecticides, 21% herbicides, and 31% fungicides, although additional pesticides are identified in other studies. McKinlay et al (2008) put the figure at 127 pesticides; and PAN International’s list of HHPs (PAN Germany 2011), based on EU classification for endocrine disruption (according to EU Regulation 1272/2008/EC) puts the figure at 98.

The table below briefly summarises some of the endocrine effects of the pesticides of interest here.

**Table 1: Some mammalian endocrine disrupting effects caused by the pesticides of interest**

<table>
<thead>
<tr>
<th>Pesticide</th>
<th>Effect</th>
<th>Biomonitoring</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>atrazine</td>
<td>Inhibits androgens, weak oestrogenic effect. Disrupts hypothalamic control of luteinising hormones and prolactin levels. Induces aromatase activity, increases oestrogen production. Damages adrenal glands and reduces steroid hormone metabolism.</td>
<td>urine, semen, human serum</td>
<td>Mnif et al 2011</td>
</tr>
<tr>
<td>chlorpyrifos</td>
<td>Androgen antagonist.</td>
<td>urine, serum, maternal serum, umbilical cord, hair</td>
<td></td>
</tr>
<tr>
<td>2,4-D</td>
<td>Synergistic androgenic effect when combined with testosterone.</td>
<td>urine, semen</td>
<td>Mnif et al 2011</td>
</tr>
<tr>
<td>diuron</td>
<td>Inhibits action of androgens.</td>
<td></td>
<td>Mnif et al 2011</td>
</tr>
<tr>
<td>glyphosate</td>
<td>Disruption of aromatase activity, prevention of production of oestrogens; causes proliferation of oestrogen-dependent human breast cancer cells.</td>
<td>urine</td>
<td>Lin &amp; Gary 2000; Mnif et al 2011</td>
</tr>
<tr>
<td>imidacloprid</td>
<td>Alters levels of luteinizing hormone, follicle-stimulating hormone and progesterone, decreased testosterone and growth stimulating hormone.</td>
<td></td>
<td>Kapoor et al 2011; Bal et al 2012</td>
</tr>
<tr>
<td>malathion</td>
<td>Inhibits catecholamine secretion; binds to thyroid hormone receptors.</td>
<td>urine, meconium, hair, semen</td>
<td>Mnif et al 2011</td>
</tr>
<tr>
<td>MCPA</td>
<td>Activates pregnane X cellular receptor.</td>
<td>urine, serum, semen, maternal serum, umbilical cord</td>
<td>Mnif et al 2011</td>
</tr>
<tr>
<td>paraquat</td>
<td>Decreases testosterone, follicle-stimulating hormone, luteinizing hormone and prolactin in male rats.</td>
<td></td>
<td>Zain 2007</td>
</tr>
<tr>
<td>simazine</td>
<td>Induces aromatase activity, increases oestrogen production.</td>
<td></td>
<td>Mnif et al 2011</td>
</tr>
</tbody>
</table>

Endocrine disruption by exogenous chemicals is now firmly recognised as a significant issue in environmental health. The State of the Art report on endocrine disruptors prepared for the European Commission by Professor Andreas Kortenkamp and colleagues (Kortenkamp et al...
2011), describes them as “substances of concern equivalent to carcinogens, mutagens and reproductive toxins, as well as persistent and bioaccumulative toxic chemicals”.
4.2 Immune system dysfunction

The immunotoxicity of a wide range of pesticides has been established in laboratory and epidemiological studies, but few meta-analyses are available, compared with endocrine disruptors. However impacts on the immune system are important and can have far-reaching results, especially for exposures that occur whilst immune function is still developing – from conception until around age 18 when the thymus gland gains maturity (Corsini et al 2008).

Exposure to pesticides may result in decreased immunocompetence which can result in more severe and prolonged infections, and the development of cancer; or immunostimulation which can lead to immune-mediated diseases, hypersensitivity reactions, inflammatory responses, asthma, allergies and autoimmune diseases (Corsini et al 2008; Hertz-Picciotto et al 2008). Additionally it seems that there is a strong connection between the development of the immune system and that of the central nervous system, such that disruption to critical events in the development of the immune system may result in neuro-behavioural and psychiatric disorders (Hertz-Picciotto et al 2008).

Evidence suggests that the outcome of exposure to pesticides depends on the window of immune development when the exposure occurs, and so the developmental status of the immune system is a key factor in determining the resulting effects on health (WHO 2006). Foetal exposure to immunotoxic chemicals that cross the placenta may permanently damage the development of the immune system leading to deficient immunity and consequent conditions such as asthma, type 1 diabetes, recurrent otitis media, paediatric coeliac disease, decreased resistance to infectious disease, reduced ability to fight viruses, bacteria, parasites, tumour cells, autoimmune disease, hypersensitivity reactions, and chronic diseases later in life (Peden 2000; Miller et al 2002; Dietert 2011; Winans et al 2011).

Table 2: Some immune effects caused by the pesticides of interest

<table>
<thead>
<tr>
<th>Pesticide</th>
<th>Immune effect</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>ametryn</td>
<td>Suppression of humoral immune response.</td>
<td>Wiltrout et al 1978</td>
</tr>
<tr>
<td>atrazine</td>
<td>Decreased NK cell activity (<em>in vitro</em> - human); developmental exposure (rats) caused altered proliferative responses in B and T lymphocytes.</td>
<td>Corsini et al 2008; Winans et al 2011</td>
</tr>
<tr>
<td>chlorpyrifos</td>
<td>Increased atopy and antibiotic sensitivity (occupational exposure); increased CD26 cells, autoantibodies and autoimmune; decreased CD5 cells and proliferative response to mitogens (environmental exposure).</td>
<td>Corsini et al 2008</td>
</tr>
<tr>
<td>glyphosate</td>
<td>Autoimmune blistering of skin and mucous membranes after inhaling fumes of burning glyphosate (human).</td>
<td>Fisher et al 2008</td>
</tr>
<tr>
<td>imidacloprid</td>
<td>Increased leucocytes, and immunoglobulins, especially IgG; decreased phagocytic activity, chemokinesis and chemotaxis (human).</td>
<td>Mohany et al 2011</td>
</tr>
<tr>
<td>malathion</td>
<td>Allergic contact dermatitis (occupational exposure).</td>
<td>Corsini et al 2008</td>
</tr>
</tbody>
</table>


| paraquat | Decrease in macrophage cells; suppression of T lymphocytes; increased release of histamine from mast cells (rats). Inhibited proliferation of T and B-cells (mice). | Caroleo et al 1996; Sato et al 1998; Repetto & Baliga 1996; Hassuneh et al 2012 |
| simazine | Inhibited cytokine production (in vitro - human); decreased T lymphocytes, induced spleen immune cell apoptosis (mice). | Hooghe et al 2000; Kim et al 2003; Ren et al 2012 |

5. **Groups at greatest risk**

People with compromised immune systems, with compromised livers that cannot adequately detoxify chemicals, and those with specific genetic variations that make them more susceptible to for example breast cancer, or which decrease their ability to metabolise organophosphate insecticides, are all at greater risk than the so-called average person.

But the group at greatest risk from exposure to pesticides are children. This is in part because their exposures are relatively greater than those of other non-occupationally exposed people, and in part because of their greater vulnerability to the effects of pesticides.

5.1 **Greater exposure**

Children eat and drink more than adults in relation to their body weight and so take in relatively more residues. Additionally, their diets tend to include greater amounts of the foods most commonly containing residues, i.e. fruits and vegetables (Landrigan et al 1999). Children eating organic diets in Seattle, USA, were found to have six times lower levels of metabolites of organophosphates in their urine compared with children eating a conventional diet (Curl et al 2003). And when the children changed to organic fruit and vegetables, their urinary levels of chlorpyrifos and malathion metabolites fell to undetectable almost immediately (Lu et al 2006, 2008).

Children also inhale relatively more air than adults, making them more vulnerable to the effects of spray drift and household insecticides. A breathing rate approximately double that of adults, in the first 12 years of life (Miller et al 2002), together with relatively greater lung surface area means the amount of airborne residues reaching the lung surface in a 3-month old child is likely to be about 3-4 times that in adults (WHO 2006).

Children live closer to zones of potential contamination such as house dust on the floor and contaminated soil outside. They put into their mouths various objects that may be contaminated, such as toys after household insecticide use, and dirt in the garden. Levels of household pesticides in indoor air are higher in the infant breathing zone than the adult sitting zone (Fenske et al 1990). Not surprisingly, significantly higher levels of the metabolites of pyrethroid insecticides, commonly used in households, were found in the urine of children than in that of adolescents or adults, in a USA study (Barr et al 2010a).

There are two other routes of exposure to pesticides that are unique to children, and which unfortunately coincide with their most vulnerable stages of development: in the womb and at the breast.

Children’s exposure to pesticides begins before they are born. Many pesticides can be readily transferred from the mother across the placenta to the developing foetus (Daston et al 2004), and children are now frequently born carrying a significant load of pesticides,
including OCs and OPs (Whyatt & Barr 2003; Barr et al 2010b). One study in New York found 29 pesticides in the umbilical cord blood of newborn infants, the most common ones being dicrotan and chlorpyrifos (Whyatt et al 2003). Others included atrazine, metolachlor and malathion. Residues are also found in meconium, the first faeces of newborns, which provides a kind of cumulative catalogue of what they have been exposed to in utero. Chlorpyrifos and malathion have both been found in meconium, along with at least another 12 pesticides (Ostrea et al 2006; Barr et al 2007; Ostrea et al 2009).

Infants are then exposed to an additional load of contaminants through breastfeeding. A large number of studies have shown that breast milk commonly carries loads of pesticide residues: at least 33 have been measured including atrazine, chlorpyrifos and malathion (Sanghi et al 2003; Pathak & Dikshit 2011; Srivastava et al 2011).

5.2 Greater vulnerability

Children are more vulnerable to the effects of pesticides than adults because of:

5.2.1 Greater tissue permeability
Children’s skin is more permeable to pesticides; and the blood-brain barrier, which provides some protection to the adult brain and nervous system by preventing chemicals being absorbed by the brain, is not fully developed until about 6 months of age (WHO 2006).

5.2.2 Immature metabolic pathways
The liver and kidney are still developing, so a child’s ability to metabolise, detoxify, and excrete chemicals is also still developing. This can lead to greater concentrations and longer half-lives in the bodies of children compared with adults (Suk et al 2003; Daston 2004). Newborn children can be 65 to 164 times more vulnerable than adults to the OP insecticides such as chlorpyrifos (Furlong et al 2006) because the enzyme responsible for detoxifying them, Paraoxonase 1 (PON 1) is present at very low levels in children under the age of two (Furlong et al 2005), three-to-four fold lower than those of their mothers (Holland et al 2006).

5.2.3 Critical windows of developmental vulnerability
Children undergo rapid growth and development throughout the first years of their lives, especially whilst still in the womb, and the complex delicate processes involved are extremely vulnerable to derailment by pesticides and other toxic chemicals. Critical windows for such damage to occur stretch from the point of conception until around adolescence, depending on the organ system. For example, the brain is still developing until the age of 12, but chlorpyrifos has its greatest impact on neural cell replication and neural signalling with exposures before birth, and its greatest effect on the development of glia cells in the neonatal stage (Slotkin et al 2004). The brain, unlike some other organ systems cannot repair cells that have been damaged, and exposure to even very small amounts of neurotoxins during critical windows of early development can change the architecture of the brain forever (Selevan et al 2000).

Other organ systems are also vulnerable to early exposures to pesticides: full immunocompetence is not achieved until about 18 years of age, and exposures before that can result in immunosuppression, altered resistance to infectious and carcinogenic agents, autoimmunity, hypersensitivity, or carcinogenicity (WHO 2006). Foetal exposure in particular can result in deficient immunity and consequent conditions such as asthma, decreased resistance to infectious disease, reduced ability to fight tumours, autoimmune disease,
hypotheses reactions, and chronic diseases later in life (Peden 2000; Miller et al 2002; Winans et al 2011).

However, it is the endocrine system that is the most vulnerable to insults by pesticides in the early stages of a child's life, and with the most profound outcomes. This system governs virtually every organ and every process in the human body (Birnbaum et al 2010), and exposure to endocrine disrupting chemicals in utero can result in effects felt throughout childhood, into adulthood and even for successive generations if epigenetic effects result (WHO 2006). All of the effects described in the previous chapter can be precipitated by endocrine disruption in the foetal and early childhood stages, including birth defects, behavioural problems, cancer, diabetes, obesity, cardiovascular disease, immune effects including allergies and asthma; and reproductive disorders including infertility, precocious puberty, and endometriosis, and even osteoporosis (WHO 2006; Myers et al 2009; Birnbaum 2010).

5.2.4 More time to develop chronic diseases
Logically, children generally have more of their life still ahead of them than do adults, so they have a longer time period over which diseases and conditions precipitated by exposure to pesticides can develop. This is particularly relevant for diseases such as cancer that have a long latency period, i.e. that require years or even decades to evolve from the initiation of the disease to its actual manifestation (Suk et al 2003). There is increasing scientific evidence for what is termed 'the developmental origins of adult disease': many diseases are triggered by foetal and neonatal exposure to environmental chemicals that would not normally cause such disease with exposures later in life (Newbold et al 2007; Gillman et al 2007). Early exposure to neurotoxic pesticides may increase risk of adult-onset chronic neurologic diseases such as dementia, Parkinson's disease, and amyotrophic lateral sclerosis (Landrigan et al 1999; Suk et al 2003); and to obesity and diabetes (Lassiter et al 2008).

5.3. Future generations – epigenetic effects
Exposure to toxic chemicals during embryonic and foetal development can result in permanent re-programming of heritable traits, with the effects lasting over a number of generations. The chemical causes modification of the operation of the genes, or gene expression, but does not damage the DNA itself. Conditions that may be passed on through epigenetic effects of chemicals include cancer, reproductive abnormalities and diabetes (Grandjean et al 2008). One example is that of the fungicide vinclozolin: exposure during critical windows of development for rat embryos resulted in breast tumour development in at least four subsequent generations (Anway et al 2006).
6. Key Scientific considerations

6.1 The difference between acute and chronic exposures

Acute effects are those signs and symptoms experienced, usually, after a moderate to high level of exposure, although for some people acute effects can occur at low levels of exposure. They can range from mild skin sensations to death. The table below lists the more common symptoms of acute exposure to pesticides.

Table 3: Some acute symptoms of pesticide poisoning

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>numb lips, tongue</td>
<td>weakness, fatigue, lethargy</td>
</tr>
<tr>
<td>sore throat</td>
<td>dizziness</td>
</tr>
<tr>
<td>blurred vision</td>
<td>disorientation, confusion</td>
</tr>
<tr>
<td>lacrimation</td>
<td>agitation</td>
</tr>
<tr>
<td>headache</td>
<td>inarticulate speech</td>
</tr>
<tr>
<td>salivation</td>
<td>depression</td>
</tr>
<tr>
<td>nose bleed</td>
<td>memory loss</td>
</tr>
<tr>
<td>swelling</td>
<td>difficulty in walking</td>
</tr>
<tr>
<td>chest pain, tightness, wheezing</td>
<td>anxiety, restlessness</td>
</tr>
<tr>
<td>suffocation, difficult breathing</td>
<td>involuntary twitching</td>
</tr>
<tr>
<td>sweating</td>
<td>hypotension, hypertension</td>
</tr>
<tr>
<td>burning skin</td>
<td>rapid pulse</td>
</tr>
<tr>
<td>itching</td>
<td>muscular pain, stiffness</td>
</tr>
<tr>
<td>blisters</td>
<td>muscle weakness</td>
</tr>
<tr>
<td>discoloured irregular nails</td>
<td>back pain</td>
</tr>
<tr>
<td>nausea, vomiting</td>
<td>seizures</td>
</tr>
<tr>
<td>abdominal cramps</td>
<td>paralysis</td>
</tr>
<tr>
<td>diarrhoea</td>
<td>coma</td>
</tr>
<tr>
<td>uncontrolled urination</td>
<td>death</td>
</tr>
</tbody>
</table>

Source: Watts 2010

Some acute effects, such as vomiting, headaches, respiratory problems, eye and skin irritation, and stomach troubles, are often confused with common illnesses (Watts 2010).

Chronic effects, such as cancer, neurodegenerative diseases, and reproductive effects, can arise from ongoing exposure to a pesticide, or as a long-term sequel of an acute exposure. For example, OP insecticides, well known for being acutely very toxic, can also cause long-term damage to the nervous system and undermine the immune system. Visible acute effects may represent the tip of the iceberg, with chronic effects going unrecognised. Chronic effects are complex and difficult to link back to pesticide exposure and, especially, to prove.

6.2 The added toxicity of ‘inert’ ingredients

Pesticides are applied as formulated products that contain the active ingredient, which has the killing power, and other ingredients usually called inert ingredients, or inerts, which have a variety of functions such as (NPIC 2011):

- preventing caking or foaming;
• extending product shelf-life;
• helping the product stick to the surface of leaves and soil, spread over surfaces, or dissolve in water;
• allowing herbicides to penetrate plants;
• preventing clogging during application; or
• making ingredients compatible.

In this context inert does not mean non-toxic, it only means that it is not the killing agent in the formulation (US EPA 2012). In fact inert ingredients used in pesticides may have biological activity and some can be highly toxic (NPIC 2011). They can increase developmental toxicity, genotoxicity and disruption of hormone function, and enhance toxicity to the cardiovascular system and mitochondria. They can also increase dermal absorption and decrease the protectiveness of clothing. Glyphosate formulations have been found to cause greater genotoxicity, toxicity to placental cells, inhibition of progesterone production, and reduced activity of the enzyme aromatase than the active ingredient alone. Formulations of 2,4-D caused human breast cancer cells to proliferate whereas the active ingredient did not. One formulation of atrazine increased DNA damage in human lymphocytes but the active alone did not. (Cox & Surgan 2006)

Inerts can also increase the ecotoxicity of pesticides to nontarget plants, animals and microorganisms. 2,4-D formulations have been found to be more genotoxic to poultry than the active ingredients alone. One glyphosate formulation is up to 100 times more toxic to fish that the active alone. Some glyphosate formulations are also more toxic to tadpoles and ciliated protozoa. (Cox & Surgan 2006)

Inerts can also affect the distribution of pesticides in the environment, sometimes enhancing runoff, leaching and volatilisation. Run off from turf treated with a granular formulation of imidacloprid was twice as high as that treated with a wettable powder (Cox & Surgan 2006).

The enhanced effects experienced with the presence of some inert ingredients in formulations may be a result of direct toxic effect of the inert, or an interaction with the active (Cox & Surgan 2006).

Generally there is no requirement to identify the inert ingredients on pesticide labels or publically available registration information, and pesticide proprietors claim their identity as confidential business information (Cox & Surgan 2006). This makes it impossible for the general public or researchers to know what is in the formulations being used. Additionally biomonitoring and environmental monitoring seldom includes inerts ingredients.

6.3 Laboratory versus epidemiological evidence

There are two broad categories of scientific research used to study the effects, and potential effects, of pesticides on people: epidemiological studies and laboratory studies.

6.3.1 Laboratory studies
Laboratory studies are used to identify potential and likely effects of exposures on humans. They can be further divided into in vivo, and in vitro studies. In vivo studies involve testing
pesticides on live animals and observing the effects on behaviour, weight changes and other visible parameters, taking blood samples, and eventually sacrificing the animals to study effects on tissues and organs. *In vitro* studies involve using only a component of the animal, or human, isolated from its usual biological surrounding, such as cell cultures or tissue cultures, sub-cellular components such as mitochondria or ribosomes, or cellular or sub-cellular extracts such as proteins, DNA or RNA. Specific cell lines are often developed to test particular reactions – for example the human breast cancer cell line MCF-7 has been developed to test the effects of chemicals that may have oestrogenic properties.

Whilst regulatory procedures still emphasise *in vivo* studies, many scientists prefer to use *in vitro* studies, partly to avoid unnecessary suffering of animals, and partly because modern *in vitro* techniques allow for better elucidation of mechanisms of action and subtle effects of chemicals not evident when intact animals are fed low, medium or high dose levels of a chemical. Some scientists argue that *in vivo* studies better reflect the exposures humans may experience and that reactions observed in *in vitro* studies may not be relevant in intact animals. Others argue that studies on animals do not necessarily predict effects in humans.

Laboratory generated data suffers from a number of flaws; for example with regard to mammary carcinogens the following flaws were identified by Rudel et al (2007):

- A typical cancer bioassay program using small numbers of animals and high doses in order to detect effects is designed to detect genotoxic effects but is unlikely to detect non-genotoxic carcinogens, such as those that affect mammary gland development or act as promoters, or have transgenerational epigenetic effects (i.e. cause breast cancer in the subsequent generation).
- It cannot be assumed that all chemicals that are carcinogenic in rodents are also carcinogenic in humans and vice versa; animal tests may falsely identify chemicals as mammary carcinogens for humans, or conversely fail to identify chemicals that are in fact mammary carcinogens in humans.
- Typically the tests are carried out on pubertal animals and are not carried out on younger developing animals which can be very much more sensitive to the effects of chemicals.
- Typically the duration of the studies – usually two years – is too short to identify mammary carcinogens with a longer latency period.
- The tests fail to identify the effects of chemical interactions because they test only one chemical at a time.

**6.3.2 Epidemiological studies**

Good epidemiological studies are seen as the gold standard in proof of actual effects on people. However they are notoriously difficult to carry out and especially to establish with an acceptable degree of certainty what levels of exposure have occurred.

There are a number of different types of epidemiological studies. Cohort studies select subjects based on exposures, and then follow them through time to assess their health outcomes – for example the Agricultural Health Study in the US, which has followed over 89,000 pesticide applicators and their spouses since 1993 (*AHS* undated). Case-control studies select participants based on their disease status and compare those with a positive disease status with those of a negative disease status, looking at potential exposures; for example the case-control study of non-Hodgkin’s lymphoma and atrazine exposure in the US (*Hoar Zahm* et al 1993). Ecological studies look at populations rather than individuals; for example

---

26
the study by Van Leeuwen et al (1999) looked at the association between incidence of stomach cancer and drinking water contamination with atrazine and nitrates.

The validity of results of epidemiology studies can be severely compromised by confounding factors, such as lifestyle factors, genetic and other environmental influences, and by the difficulty of establishing what exposures to pesticides occurred, especially at critical periods of development such as in utero. Exposure to mixtures of chemicals and synergism between chemicals is regularly overlooked. Brody et al (2005) warn that there is always a strong likelihood of generating "inconclusive negative findings, which are common in case-control studies of hard-to-assess exposures to pollutants in the general population"; and the results of studies that fail to show an association contribute little because "study design limitations mean we cannot conclude from null results that no association exists".

6.4 Bioconcentration and bioaccumulation of pesticides

Bioaccumulation refers to the accumulation of pesticides, or other chemicals within an organism, usually the fatty tissues; and it occurs when the organism is absorbing the chemical at a greater rate than it is expelling or metabolising it. Bioaccumulation occurs with persistent substances, although not all persistent substances are bioaccumulative.

Bioconcentration refers to the increase in concentration of a chemical from the environment to the first organism in the food chain. Bioconcentration usually refers to uptake from water, whereas bioaccumulation refers to uptake from other sources such as sediment and food. The concentrations of the substance continue to increase up the food chain (biomagnification), and can result in toxic accumulations and consequent health effects (Katagi 2010).

International criteria for bioconcentration and bioaccumulation are provided within the Stockholm Convention on Persistent Organic pollutants. Annex D 1(c) of the Stockholm Convention states:

(i) Evidence that the bioconcentration factor or bioaccumulation factor in aquatic species for the chemical is greater than 5,000 or, in the absence of such data, that the log Kow is greater than 5;

(ii) Evidence that a chemical presents other reasons for concern, such as high bioaccumulation in other species, high toxicity or ecotoxicity;

(iii) Monitoring data in biota indicating that the bioaccumulation potential of the chemical is sufficient to justify its consideration within the scope of this Convention.

The European Union regulatory process has more stringent criteria (Rorije et al 2011):

a) for substances that are bioaccumulative in aquatic organisms

(i) BCF > 2000

(ii) log Kow > 4.5

b) for substances that are very bioaccumulative in aquatic organisms

(i) BCF > 5000

(ii) log Kow > 4.5
7. International concerns and approaches

7.1 Endocrine disruptors

Endocrine disruption has been described in detail in section 5.1, and its health effects will not be revisited here. There is a wealth of scientific knowledge of the importance of EDCs on human and environmental health, yet regulatory processes have been very slow to catch up with the science and regulators have been dismissive of potential effects. There has not even been global consensus on the importance of endocrine disruption – until very recently.

In September 2012, the 3rd International Conference of Chemical Management (ICCM3), which implements the voluntary global agreement, Strategic Approach to International Chemical Management (SAICM), agreed unanimously to include endocrine disruptors as an emerging issue within SAICM, recognizing (by consensus) “potential adverse effects of endocrine disruptors on human health and the environment” and “the need to protect humans, and ecosystems and their constituent parts that are especially vulnerable” (ICCM3 2012). ICCM3 also agreed the need for international cooperation to build awareness and disseminate information on endocrine disrupting chemicals, as well as building capacity to reduce risks from them, signalling that action needs to be taken at the regulatory level.

Meanwhile, no country, including Australia and New Zealand, has an adequate regulatory process for EDCs. Kortenkamp et al (2011) provided a State of the Art report on EDCs for the European Commission in December 2011, including recommendations for EU regulations for EDCs. EU chemical regulations do lay down testing requirements for EDCs but they “do not capture the whole range of endocrine disrupting effects that can be measured with internationally agreed and validated test results”. The EU has recognised at least 98 pesticides as endocrine disruptors placing them in 2 categories depending on the strength of evidence (EU Regulation 1272/2008/EC). In 2010, the US EPA released its draft guidance for its first stage of screening EDCs, Tier 1. Only 67 chemicals have been selected, despite the evidence showing there are many more pesticides alone, than this (Schmidt 2012). The guidelines are criticised by the Endocrine Society for testing only a limited set of end points that do not reflect understanding of endocrinology principle’s, and of testing at doses so high they will miss low dose non-monotonic effects (Zoeller et al 2012).

7.2 Low dose exposures

For some decades now environmental health scientists have been concerned about low dose exposures – in particularly the theory that low doses of chemicals can have effects that are not predicted from high dose exposures (Birnbaum 2012).

Laboratory studies on animals, the key toxicological studies that are used for registering pesticides, are typically carried out at three dose ranges: ‘low’, medium and high, with the expectation of a positive dose response: the higher doses cause greater effect than the lower doses. These studies are used to determine No Observed Adverse Effects Levels (NOAELS) and Lowest Observed Adverse Effects Levels (LOAELS); from these are derived ‘reference’ doses, which are assumed to be safe for humans (Birnbaum 2012).

However, as explained in the section on endocrine disruptors, such assumptions cannot be made, especially in the case of endocrine disruptors where a lower dose may cause worse
effects than a higher dose. Endocrine disruption occurs at levels of exposure far lower than those normally considered toxic (Birnbaum 2010). Low dose exposures, commonly experienced by humans, can have profoundly serious effects even when the high dose exposures normally tested on rats in laboratories may not have an effect (Myers et al 2009; Birnbaum 2010). Effects have been observed on animals at very low doses in laboratories (Melnick et al 2002; Bulayeva & Watson 2004; Wozniak et al 2005), and on fish at or below the detection limits (EC 2004).

Humans experience environmental exposure to thousands of synthetic chemicals at levels thought to be safe from a risk assessment perspective, but which can no longer be assumed to be safe. Low internal doses of endocrine disruptors found in human populations are now linked with obesity, infertility, neurobehavioural disorders, and immune dysfunction (Birnbaum 2012).

7.3 Chemical mixtures

In pesticide regulatory processes, risks are estimated for a single pesticide at a time; but the reality of human experience is that people are constantly exposed to complex chemical mixtures, with some of the chemicals having additive effects and others synergistic interactions to magnify the damaging effects or even cause new kinds of harm (Schettler et al 2000).

In 2009 Kortenkamp et al, in their State of the Art Report on Mixture Toxicity for the European Commission, concluded that there is good evidence chemicals with common specific modes of action, and chemicals with different modes of action, work together to produce combination effects that are larger than the effects of each mixture component by itself. Additivity is most common with chemicals of common mode of action. Hence any concentration of a pesticide needs to be considered, regardless of whether or not it is present at levels above or below its effect threshold, because it adds to the mixture concentration. This phenomenon, termed ‘something from nothing’ has been repeatedly demonstrated for a broad range of chemical mixtures in toxicological and ecotoxicological studies.

Kortenkamp et al reiterated this view, with respect to endocrine disruptors, in 2011: “There is good evidence that several EDCs can work together to produce combined effects. Especially when exposure is to multiple chemicals simultaneously that are capable of affecting the same endpoint, combination effects can occur at doses where each chemical individually is without detectable effects” (Kortenkamp et al 2011). Additivity is the usual mode for combination effects of EDCs (Kortenkamp et al 2009).

Synergistic effects have been noted with carcinogens that act together on the same target organ or tissue, and there is “overwhelming evidence” that carcinogens work together to exert tumour-promoting effects after sequential or simultaneous exposures. There is also evidence that genotoxic and mutagenic chemicals can work together at very low concentrations to produce mixture effects (Kortenkamp et al 2009).

Hayes et al (2006b) examined the effects of four herbicides (alachlor, atrazine, metolachlor, nicosulfuron), three insecticides (cyfluthrin, cyhalothrin, tebupirimphos), and two fungicides (metalaxyl and propiconazole) alone or in combinations, on metamorphosis, time
to metamorphosis, and gonadal differentiation in northern leopard frogs. They found that the mixtures had much greater effects than individual pesticides in inhibiting larval growth and development.

Dimethoate, glyphosate and zineb, exhibited mixture toxicity when tested on rats, with the combination causing greater oxidative stress in the plasma, liver and testes, and decrease in hormone levels, than when administered alone (Astiz et al 2009).

In 2012 Hernández et al, in a review of toxicological interactions at molecular levels, drew attention to the ability of organophosphate insecticides to potentiate (i.e. enhance) the toxicity of pyrethroids, carbaryl, and triazine herbicides. Additionally, mixtures of 5 organophosphates (chlorpyrifos, diazinon, dimethoate, acephate and malathion) have produced greater than additive effects (i.e. synergistic effects) on laboratory animals.

Kortenkamp et al (2009) concluded that it is possible to predict the toxicity of chemical mixtures, especially where dose addition occurs, with reasonable accuracy and precision, but this approach is not so far being implemented in any regulatory regime for pesticides.

They also stated: “There is scientific consensus in the field of mixture toxicology that the customary chemical-by-chemical approach to risk assessment might be too simplistic. It is in danger of underestimating the risk of chemicals to human health and to the environment.”

7.4 Precaution

Since 1982 there has been widespread adoption of the precautionary principle in a number of international treaties and conventions, a number of them addressing pesticide issues, including the Stockholm Convention on Persistent Organic Pollutants (POPs) and the Strategic Approach to International Chemicals Management (SAICM). It is variously expressed in these documents but one of the most widely accepted versions is known as the 1998 Wingspread Statement on the Precautionary Principle (SEHN 1998):

*When an activity raises threats of harm to human health or the environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically.*

The precautionary principle was designed to deal with situations exactly such as those involving ongoing low dose exposures to multiple pesticides. It provides a framework, procedures, and policy tools for situations of scientific complexity, uncertainty and ignorance, where there is a need to act before there is strong proof of harm in order to avoid, or reduce, potentially serious or irreversible threats to health or the environment. It acknowledges that pesticides are inherently hazardous and should be presumed harmful until proven otherwise, and accepts the reality that the long-term impacts of toxic chemicals are difficult to predict and often impossible to prove.

7.5 Hazard versus risk assessment in pesticide regulation

Most current pesticide regulatory processes are the exact antithesis of the precautionary principle: they are based on a risk assessment model with its underlying assumption that
there is a ‘safe’ level below which a toxic pesticide is not toxic (Antoniou et al 2011). However there are numerous ways in which this approach fails to take into account the effects of pesticides experienced in everyday life, as already described in this document:

- Risks are estimated for a single chemical at a time when in reality people are exposed to complex chemical mixtures, with some of the chemicals having additive effects and others having synergistic interactions.
- Existing body burdens of chemicals and cumulative effects are ignored in determining safe exposures (Antoniou et al 2011).
- The positive-dose response requirement fails to take into account endocrine disruption that can be stronger at very low doses than at high doses.
- There is a concomitant assumption of a threshold below which there is no significant toxicity, but any exposure level can be significant if mixture toxicity occurs.
- The high dose protocols fail to consider exposures that are environmentally relevant especially to the unborn and newborn, at critical stages of development from foetal life through to adulthood.
- Early life exposures, i.e. during critical windows of foetal development, are not generally included in the tests required for regulatory purposes (Makris 2011).

These are just some of the reasons that best scientific thinking, and international practice, is now moving away from risk assessment as the preferred methodology for regulating chemicals, and replacing it with a hazard-based approach. The European Commission is the first to enshrine such an approach in modern law, complete with cut-off criteria for certain hazardous qualities, such as carcinogenicity, mutagenicity, developmental neurotoxicity, developmental immunotoxicity, and endocrine disruption. Unlike the old risk assessment model this approach does not assume that when a hazard exists the risk can be managed. Instead it is based on the view that if a particular hazard exists, a less hazardous alternative should be used. Governments such as the U.S., Australia, and New Zealand, and the pesticide industry, are all still strongly opposed to this approach and are fighting hard to retain a risk assessment approach. However, at the global level there is progress: a conference room paper at ICCM3 calling for “the progressive ban of Highly Hazardous Pesticides and their substitution with safer alternatives”, although blocked by several developed nations, was supported by 65 countries. The Council of the Food and Agriculture Organisation (FAO) of the United Nations in 2006 decided on a new policy approach that would include “the progressive ban of highly hazardous pesticides” (FAO 2006).

Europe has instituted such a system, to a limited extent, although the hazard cut-off criteria are still insufficient to protect children. Industry is fighting tooth and nail to prevent hazard assessment gaining ground against risk assessment (Antoniou et al 2011), but it is vital that the old industry-protective regime be replaced with a new one supportive of public health and particularly children’s health.

7.6 Substitution

The substitution principle broadly requires the replacement of hazardous pesticides by less hazardous alternatives while attempting to (i) reduce the hazard as much as possible, (ii) retain or increase functionality of the original substance as much as possible, and (iii) keep
costs as low as possible (Hansson et al 2011). The priority accorded each of these points will be determined differently in different settings depending on the values of those involved.

The substitution principle has been in use since the 1985, when it was first incorporated into Swedish pesticide policy:

"According to the Swedish Act on Chemical properties (SFS 1985, p 426) section 5 'anyone handling or importing a chemical product must take such steps and otherwise observe such precautions as are needed to prevent or minimize harm to human beings or to the environment. This includes avoiding chemical products for which less hazardous substitutes are available.'" 

Bergkvist et al 1996

The substitution principle can be applied at two levels: the first involving only consideration of less hazardous pesticides, the second involving consideration of non-chemical methods of pest, weed, and disease management (the latter approach is sometimes called informed substitution – Hansson et al 2011). The first approach, that is simple chemical substitution, is more commonly used, for example in the REACH legislation of the EU. However Sweden's National Board of Agriculture did take the second approach:

"If equally effective, non-chemical methods are available for a certain control a pesticide will be banned for that control."

Liden 1989

The Stockholm Convention on Persistent Organic Pollutants also embodies both chemical and nonchemical substitutes as replacements for chemicals listed under the Convention for global phase out.

According to Hansson et al (2011) substitution should be seen not as a single decision but as a continuous development towards safer processes.

Hansson et al (2011) also provide the following list of methods to promote substitution:

- i) increasing the availability of toxicity data
- ii) increasing the availability of data on the chemical composition of materials (e.g. of inerts in pesticides)
- iii) increasing the availability of information about technical functionality
- iv) developing green chemistry
- v) help desk functions
- vi) list of unwanted substances
- vii) positive lists
- viii) ban of dangerous substances
- ix) required substitution plans
- x) economic incentives

### 7.7 Minimum Harm

There is one further principle that needs to be considered here briefly, and that is the principle of minimum harm. This principle essentially extends the substitution principle and turns the question ‘what is a safer alternative’, on its head, to ask ‘what is the least harmful way of controlling the relevant pest, weed or disease’ (Watts 2000). If implemented it would mean that a pesticide would only be registered if there is no less harmful effective
way of managing the particular pest, weed or disease, including by non-chemical methods. The principle has been given expression for many years, e.g. in *Respect of Nature* (Taylor 1986), and even acknowledged by the World Bank which stated that "to be ethical the project with the least environmental impacts should be selected" (Montague 1996), but is not yet enshrined in pesticide legislation.
8. Conclusion

People are exposed to pesticides through many routes, including spray drift, skin contact even for non-users, and in food and drinking water. Children are born pre-polluted with pesticides, and receive additional doses when breast-fed.

There is sufficient evidence that many pesticides, including some of those found in the waters around Great Barrier Reef, may be causing a range of adverse human health effects, such as cancer, neurodevelopmental problems, and birth defects, for all people involved in the management of pests and pesticides to take a precautionary approach, and substitute them with less hazardous alternatives including nonchemical methods. In fact, all people involved, from government policy makers and regulators to users should be asking the primary question first: how to manage pests effectively by the methods least harmful to humans and the environment.

Children are especially vulnerable to the effects of pesticides, particularly those causing endocrine disruption and immune effects. Endocrine disruption, still not regulated sufficiently by any country, has been recognised at the highest international level, the UN’s International Conference on Chemical Management, as an emerging issue of concern, signalling that action needs to be taken at the regulatory level. Action also needs to be taken at a regulatory level to recognise the problems of ongoing low dose exposure to mixtures of pesticides, the effects of which are not adequately addressed by the standard risk assessment of individual pesticides. For this reason there is a move internationally away from risk assessment and towards regulating on the basis of hazard.

References


Engel LS, O’Meara ES, Schwartz SM. 2000. Maternal occupation in agriculture and risk of limb defects


Kapoor U, Srivastava MK, Srivastava LP. 2011. Toxicological impact of technical imidacloprid on


Yu ZB, Han SP, Guo XR. 2008. [A meta-analysis on the risk factors of perinatal congenital heart

