FACTSHEET CARBENDAZIM

Summary.
Independent literature shows that the pesticide Carbendazim is a very dangerous "toxin", capable of causing malformations in the foetus at very low doses and it's still uncertain if a safe level exists at all. Carbendazim is also capable of disrupting chromosome unfolding, can cause infertility of men and cancer.

People are exposed to Carbendazim in food. Carbendazim is one of the most detected pesticide residues by Food Authority EFSA in 2011, analysed in 5.8% of the laboratory tests. EU health standards are exceeded in cucumbers, mandarins, pears and oranges. Industry tests of Du Pont to get an approval in the EU were very incomplete and the level of genotoxic impurities is unknown. Additionally, Du Pont didn’t supply available mutagenic studies, thereby misleading the regulators. Germany, acting as the Rapporteur country (responsible for making a first draft assessment of industry's dossier), however did very much its best in 2011 to keep the chemical on the market and to condone uncertainties and data gaps. Germany further promoted a theoretic approach favoured by industry lobby club ILSI to allow an impurity in the active substance at a level where mutagenic effects were already observed.

Carbendazim is very dangerous for aquatic organisms and even a buffer zone of 20 meter towards water bodies is not protective enough according to EFSA to safeguard aquatic organisms. Alternatives for Carbendazim are available.

Being mutagenic plus reprotoxic, Carbendazim should be banned under the new rules of Regulation 1107/2009 which entered into force in June, 2011. In 2011, however, it escaped this obligation for a ban and due to blocking majorities in the pesticide Standing Committee, regulators could not agree on a vote for a ban. As a result DG SANCO decided for a three years prolongation of the approval. In 2014 the Standing Committee finally approved the ban.

1. What independent science tells us about Carbendazim.
   • Carbendazim has adverse effects on reproduction.
     Benomyl (and its metabolite carbendazim) is known for a long time to cause adverse effects on the male reproductive systems, including decreased testicular and epididymal weights and reduced epididymal sperm counts and fertility in the rats (Carter and Laskey, 1982; Barnes et al., 1983; Linder et al., 1987; Hess et al., 1988).
     In the following years, several studies confirmed these adverse effects following carbendazim exposure: Gray, 1990 showed many problems, e.g. in sperm morphology, testicular & epididymal weights, spermal mobility and testicular histology.

2 Gray L.E. et al., Carbendazim induced alterations of reproductive development and function in the rat and hamster, Fund. and Appl. Tox., 15, 281-297, 1990
Jeffay, 1996\(^3\) showed infertility of hamsters and a decrease of implantation.
Lazzari, 2008\(^4\) showed toxicity on germ cells lower than 10 \(\mu M\) (Carbendazim is spindle poison similar to DES).
Moffit, 2007\(^5\) showed impair of Sertolli cells by inhibiting microtubule assembly and loss of testicular function.
Yu, 2009\(^6\) showed effects in rats on spermatogenesis and fertility (meiotic transformation).

- **Carbendazim is a potent endocrine disrupting substance.**
  In vitro tests (Morinaga, 2004\(^7\)) show inhibition of aromatase and interferance with microtubules. In vivo tests in zebrafish show inhibition of brain aromatase at 20 \(\mu M\) (Kim 2008\(^8\)) and embryo malformations. Others also published studies on the endocrine disrupting potency (Goldman, 1989\(^9\)).

- **Carbendazim is a genotoxic substance.**
  Amer, 2003\(^10\) shows sperm head abnormalities at 50 mg/kg. McCarroll, 2002\(^11\) reports liver tumors in mice.

- **Carbendazim causes developmental toxicity.**
  Yoon, 2008\(^12\) shows embryotoxicity, malformation starting at 1 \(\mu M\) and for 100% at 3 \(\mu M\) in frogs and inhibition of the differentiation of neural tissue.

2. **Tests of Du Pont for Carbendazim are incomplete and unconvincing; Rapporteur Germany plays a mysterious role:**
   - Two genotoxic impurities exist (DAP, AHP) in the pesticide used but it is unknown at which level because the specifications of the test-material is lacking; Germany pushes other EU countries to allow this uncertainty;
   - Germany argued to allow (DAP) at a level where mutagenic action is happening; they defend this by embracing the TTC approach, promoted much by industry lobby-club ILSI, in which effects below a certain fixed level are considered an acceptable risk. Even so if mutagenic effects are seen at that level.
   - The fact the applicant Du Pont didn’t report available mutagenic studies with these effects –while they were available- and claiming no genotoxic potential, is a clear obstruction of the approval process.

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\(^4\) Lazzari G. et al., **Development of an in vitro test battery for assessing chemical effects on bovine germ cells under the ReProTect umbrella**, Toxicology and Applied Pharmacology 233 (2008) 360-370
\(^5\) Moffit J.S. et al., **Dose-Dependent Effects of Sertoli Cell Toxicants 2,5-Hexanedione, Carbendazim, and Mono-(2-ethylhexyl)phthalate in Adult Rat Testis**, Toxicologic Pathology, 35:719–727, 2007
\(^6\) Yu G. et al., **Effects of subchronic exposure to carbendazim on spermatogenesis and fertility in male rats**, Toxicology and Industrial Health 2009; 25: 41–47
\(^7\) Morinaga H. et al., **A Benzimidazole Fungicide, Benomyl, and Its Metabolite, Carbendazim, Induce Aromatase Activity in a Human Ovarian Granulose-Like Tumor Cell Line (KGN)**, Endocrinology 145(4):1860–1869, 2004

\(^9\) Goldman J.M. et al., **Effects of the Benomyl metabolite Carbendazim, on the hypothalamic pituitary reproductive axis in male rats**, Toxicology 57, 173-182, 1989
\(^11\) McCarroll M.E. et al., **A survey of EPA/OPP and open literature on selected pesticide chemicals III. Mutagenicity and carcinogenicity of benomyl and carbendazim**, Mutation Research 512 (2002) 1–35
\(^12\) Yoon C.S. et al., **Toxic Effects of Carbendazim and n-Butyl Isocyanate, Metabolites of the Fungicide Benomyl, on Early Development in the African Clawed Frog, Xenopus laevis, Inc.** Environ Toxicol 23: 131–144, 2008.

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Liver tumors were observed in exposed mice (but considered not relevant for humans by EFSA)
Carbendazim causes chromosome aberrations (disturbing meiotic spindle proteins) and aneuploidy, a characteristic of cancer; in risk assessment a threshold of no effect was “assumed” rather than demonstrated
A safe level of exposure to man is determined based on a study of “limited evidence”, performed in 1972;
The formulation is more toxic than the active substance alone
Data gaps exist for transformation of Carbendazim in soil and three transformation products are unidentified
Risks for water is very high and even 20 meter wide buffer zones are not enough to prevent harm according to EFSA in their peer review
Sensitive arthropods are killed in field

3. Carbendazim residues in food.
Use of Carbendazim is only allowed in cereals, sugarbeets, rape seed and maize at the moment. Still many food items (like cucumbers, mandarins, oranges, pears, spinach) are contaminated with Carbendazim, including imported products (peppers, rice). Food items often exceeding many times current health standards (pears) create an acute risk in several cases (EFSA residue monitoring report, 2014). In 5,8% of all tests Carbendazim can be found. Thiophanate-methyl is another pesticide giving rise to Carbendazim residues in food, but is used in slightly different crops. Imported food (rice, pepper, passion fruit) also adds to the risk of Carbendazim food contamination.

4. Alternatives.
Carbendazim is a fungicide used in arable fields, and was used in horticulture and orchards in the past. The best approach to prevent the use of Carbendazim is to use resistant varieties of crops. This is a preventive way of pest management which should be used always. For problems as fungal growth during the storage phase of products like apples physical methods (temperature treatment) are available to prevent rotting. For orchards lime is the best substance for prevention of fungi in trees. If problems arise with fungi for a curative approach non-chemicals methods should the method of choice like the use of the biological agent Contans WG in horticulture. Only as a last resort synthetic pesticides like Captan, Thiram and Trifloxystrobine should be used.

5. And what about Benomyl, Thiophanate-methyl, substances metabolising to Carbendazim?
Benomyl is banned in Europe fortunately, but this is not the case with Thiophanate-methyl. This last chemical also needs to be banned without delay.

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