

Diflubenzuron in Drinking Water
Use for Vector Control in Drinking Water Sources
and Containers

Background document for development of *WHO Guidelines for
Drinking-Water Quality*

Revision Sept 2006

This document is based on the IPCS EHC No 184 (1996), The JMPR toxicological evaluation (2001) and the WHO/FAO datasheet No 77 (1996).

General Description

Identity

CAS no.: 35367-38-5

Molecular formula: C₁₄H₉ClF₂N₂O₂

The IUPAC name for diflubenzuron is 1-(4-chlorophenyl)-3-(2,6-difluorobenzoyl)urea.

Physicochemical properties

<i>Property</i>	<i>Value</i>
Melting point	230-232C
Density	1.56
Water solubility (20°C)	0.2 mg/litre
Log octanol-water partition coefficient	3.89
Vapour pressure	0.00012mPa. Virtually non-volatile from water

Major uses

Diflubenzuron is a halogenated benzoylphenyl urea, an effective stomach and contact insecticide acting by inhibition of chitin synthesis and so interfering with the formation of the cuticle. It is used in public health applications against mosquito and noxious fly larvae. It is specified for use as a vector control agent in drinking-water sources by WHO. Specific formulations for control of vectors are specified by WHO (2005).

Environmental fate

Diflubenzuron is a direct acting insecticide normally applied directly to plants or water. It is rapidly adsorbed to soil and particles and is immobile in soil. It will also rapidly adsorb to sediments and the sides of vessels and pipes but it may also partition into the surface film because of its low water solubility and high K_{ow}. In soils over 90% is degraded by hydrolysis to 2,6-difluorobenzoic acid and 4-chlorophenylurea. In neutral and alkaline waters it is rapidly hydrolysed. The parent compound and 4-chlorophenylurea may persist on sediment for more than 30 days (IPCS 1996).

EXPOSURE IN DRINKING WATER

It is reported that exposure of the public through either food or drinking-water is negligible (IPCS 1996). However, there is a potential for direct exposure through drinking-water when it is directly applied to drinking-water storage containers.

TOXICOLOGICAL SUMMARY

Diflubenzuron is rapidly absorbed to a moderate extent (approximately 30%) from the gastrointestinal tract. Absorbed diflubenzuron is extensively metabolised and the metabolites with >90% excreted within 48 hours, mostly in the urine, although some biliary excretion and enterohepatic circulation occurs.

Diflubenzuron is considered to be of very low acute toxicity with oral LD₅₀s in mice and rats of >4500 mg/kg body weight.. The primary target for toxicity is the erythrocytes, although the mechanism of haemotoxicity is uncertain. High doses (10,000 mg/kg body weight (bw) 25% formulation) caused a small but significant increase in methaemoglobinaemia in mice and rats. The NOAELs for methaemoglobin and sulfhaemoglobin formation in mice, rats, and dogs were 1.2, 2.0 and 2.0 mg/kg bw per day, respectively after long-term exposure. Haemotoxicity showed both dose and time-related trends with the dose resulting in the detection of methaemoglobin decreasing with the time of exposure. The NOAEL for pathological findings was the same as for methaemoglobin formation in rats and dogs but somewhat higher in mice. These were changes in liver spleen and bone marrow associated with haemotoxicity.

Diflubenzuron has been adequately tested for both genotoxicity and carcinogenicity and there was no evidence that it is either genotoxic or carcinogenic.

It was not fetotoxic or teratogenic and did not show significant signs of reproductive toxicity. There was evidence that young animals were not significantly more sensitive to the effects of diflubenzuron than adults.

In 2001 JMPR re-confirmed the previously established ADI of 0–0.02 mg/kg bw, based on the NOAEL for haematological effects of 2 mg/kg bw per day in the 2-year studies in rats and the 52-week study in dogs. However, the committee also considered that an acute reference dose (RfD) was unnecessary.

PRACTICAL ASPECTS

Analytical methods and analytical achievability

The concentration of diflubenzuron may be determined by high-performance liquid chromatography (HPLC) with UV detector (the detection limit 0.05mg/L) (Miliadis et al 1999), or with fluorescence detector after on-line post-elution photoirradiation (the detection limit 0.05mg/L) (Martinez-Galera et al 2001). The concentration of diflubenzuron may be also determined by gas chromatograph with electron-capture detection (ECD) (the detection limit 0.05mg/L) (Mensah et al 1997). It may be also determined by liquid chromatography using negative-ion, selected-ion monitoring atmospheric pressure chemical ionization-mass spectrometry (APCI-MS) (the detection limit 0.025mg/L) (Barnes et al 1995), using electrospray-mass spectrometry (ESP) (the detection limit 0.002µg/L) or using thermospray-mass spectrometry (TSP) (the detection limit 0.002µg/L) (Molina et al 1995).

Treatment and control methods and technical achievability

No specific data on treatment for diflurobenzuron have been found. However, the low aqueous solubility (0.08 mg/l) and relatively high log K_{ow} of 3.7 suggest that it may be amenable to adsorption by activated carbon. Diflubenzuron is fairly unstable in water; the half-life was reported to be approximately ½ day for solutions exposed to natural sunlight in the laboratory (Anton et al., 1993).

Use for vector control in drinking water sources

GUIDELINE VALUE

The ADI determined by JMPR in 2001 was 0.02 mg/kg of body weight. Young animals do not appear to be significantly more sensitive than adults so the assessment is based on a 60 kg adult. Where diflubenzuron is used for vector control in potable water this will involve less than life-time exposure. Under these circumstances the maximum dosage in drinking water of 0.25 mg/l would be equivalent to approximately 40% of the ADI allocated to drinking water. Exposure from food is considered to be low. However, in setting local guidelines or standards, health authorities should take into consideration the potential for higher rates of water consumption in the area or region under consideration.

REFERENCES

- Anton FA, Cuadra LM, Gutierrez P, Laborda E (1993) Degradational behavior of the pesticides glyphosate and diflubenzuron in water. *Bulletin Environmental Contamination and Toxicology* 51(6): 881.
- IPCS (1996) Environmental health Criteria No 184. Diflubenzuron. WHO, Geneva.
- JMPR (2001) Pesticides Residues in Food, Toxicological Evaluations, Diflubenzuron. WHO, Geneva
- WHO/FAO (1996) WHO/FAO Datasheets on Pesticides. 77. WHO/PCS/DS/96.77 WHO, Geneva
- Miliadis G. E., Tsiropoulos N. G. and Aplada-Sarlis P. G. (1999) High-performance liquid chromatographic determination of benzoylurea insecticides residues in grapes and wine using liquid and solid-phase extraction. *J. Chromatogr. A*, 835, 113-120.
- Martinez-Galera M., Lopez-Lopez T., Gil-Garcia M. D., Martinez-Vidal J. L. and Vazquez P.P. (2001) Determination of benzoylureas in tomato by high-performance liquid chromatography using continuous on-line post-elution photoirradiation with fluorescence detection. *J. Chromatogr. A*, 918, 79-85.
- Mensah J. K., Lundanes E., Greibrokk T. and Holen B. (1997) Determination of diflubenzuron in apples by gas chromatography. *J. Chromatogr. A*, 765, 85-90.

Barnes K. A., Startin J. R., Thrpe S. A., Reynolds S. L. and Fussell R. J. (1995) Determination of the pesticide diflubenzuron in mushrooms by high-performance liquid chromatography-atmospheric pressure chemical ionization mass spectrometry. *J. Chromatogr. A*, 712, 85-93.

Molina C., Durand G. and Barcelo D. (1995) Trace determination of herbicides in estuarine water by liquid chromatography-high-flow pneumatically assisted electrospray mass spectrometry. *J. Chromatogr. A*, 712, 113-122.