Established limits for residual solvents in technical grade active ingredients

In Health Canada's *Guidance for developing datasets for conventional pest control product applications* (updated February 2021), registrants and applicants are informed of the need to minimize the presence of impurities of toxicological concern (IOCs) in the manufacture of pest control products (DACO 2.13.4) in order to protect the health of Canadians and the environment.

Solvents are commonly used in the manufacturing of products for various industries including pesticides. Although most are removed through purification during the manufacturing process, residual levels of solvents may remain in products and some are considered by the Pest Management Regulatory Agency (PMRA) to be of concern. To provide clarity to registrants and applicants on the data requirements, the PMRA has established generally acceptable limits for certain residual solvents of concern in technical grade active ingredient (TGAI) products. The list of solvents and their limits was established based on a weight-of-evidence approach relying on several sources of information including other jurisdictions and international guidelines, but is specific to the Canadian pesticide context. If a solvent is present in a TGAI below the specified limit, it will be considered acceptable without further data. If a particular limit is exceeded, consultation with the PMRA will be needed to determine whether

further data are required. For example, higher solvent levels for a new source of TGAI could be supported with toxicological data or a well-developed scientific rationale that considers all relevant routes of exposure.

As described in the *Guidance for developing datasets for conventional pest control product applications*, the use of several of these solvents is to be avoided completely where possible, while others are to be limited.

PMRA established limits for residual solvents in TGAIs

Residual solvent	CAS Registry Number	Maximum PMRA general limit (ppm)	Required limit of quantitation (LOQ) (ppm)
carbon tetrachloride	56-23-5	--- (to be avoided)	1
1,2-dichloroethane	107-06-2	--- (to be avoided)	1
benzene	71-43-2	--- (to be avoided)	1
1,4-dioxane	123-91-1	4	1
chloroform	67-66-3	10	1
tetrahydrofuran	109-99-9	100	10
pyridine	110-86-1	200	100
hexane [1]	110-54-3	290	100
dichloromethane	75-09-2	300	100
acetonitrile	75-05-8	410	100
N,N-dimethylformamide	68-12-2	500	100

Residual solvent	CAS Registry Number	Maximum PMRA general limit (ppm)	Required limit of quantitation (LOQ) (ppm)
N-methyl-2-pyrrolidone	872-50-4	530	100
chlorobenzene	108-90-7	600	100
cyclohexane	110-82-7	710	100
methylcyclohexane	108-87-2	1000	500
N,N-dimethylacetamide	127-19-5	1090	500
xylenes [2]	1330-20-7	2170	1000
methanol	67-56-1	3000	1000
toluene	108-88-3	15000	1000

CAS = Chemical Abstracts Service
ppm = parts per million

1 Hexane can include either *n*-hexane (with the specified CAS number) or a mixture of hexane isomers.

2 Xylenes can include *m*-, *o*-, *p*-xylene and ethylbenzene.

These limits are to be applied in the analytical determination of these solvents whenever they are expected to be present in a TGAI source under review in an open submission or during re-evaluation. If a solvent not listed here is used in the manufacturing of a TGAI and may pose a concern, it is recommended that the PMRA be consulted to establish any corresponding data requirements. Health Canada anticipates updating this list as needed.

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