



Toxicological profile	NTIS order No.	CAS No.
1. DI-N-OCTYLPHTHALATE	PB98-101033	000117-84-0
2. ETHYLENE GLYCOL/	PB98-101108	000107-21-1
PROPYLENE GLYCOL		000057-55-6
3. HEXACHLOROETHANE	PB98-101041	000067-72-1
4. HMX	PB98-101058	002691-41-0
5. HYDRAULIC FLUIDS	PB98-101066	VARIOUS
6. HYDRAZINES	PB98-101025	000302-01-2
1,1-DIMETHYLHYDRAZINE		000057-14-7
1,2-DIMETHYLHYDRAZINE		000540-73-8
DIMETHYLHYDRAZINE		030260-66-3
7. MINERAL-BASED CRANKCASE OIL	PB98-101066	008002-05-9
8. TITANIUM TETRACHLORIDE	PB98-101074	007550-45-0
9. WHITE PHOSPHORUS	PB98-101082	007723-14-0

Dated: December 17, 1997.

Georgi Jones,

Director, Office of Policy and External Affairs,
Agency for Toxic Substances and Disease
Registry.

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BILLING CODE 4163-70-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Centers for Disease Control and Prevention

National Vaccine Advisory Committee (NVAC), Subcommittee on Future Vaccines, Subcommittee on Immunization Coverage, and Subcommittee on Vaccine Safety: Meetings

In accordance with section 10(a)(2) of the Federal Advisory Committee Act (Pub. L. 92-463), the Centers for Disease Control and Prevention (CDC) announces the following Federal advisory committee meetings.

Name: National Vaccine Advisory Committee (NVAC).

Times and Dates: 9 a.m.-2 p.m., January 12, 1998. 8:30 a.m.-1:15 p.m., January 13, 1998.

Place: Hubert H. Humphrey Building, Room 800, 200 Independence Avenue, SW, Washington, DC 20201.

Status: Open to the public, limited only by the space available.

Notice: In the interest of security, the Department has instituted stringent procedures for entrance to the Hubert H. Humphrey Building by non-government employees. Thus, persons without a government identification card should plan to arrive at the building each day either between 8 and 8:30 a.m. or 12:30 and 1 p.m. so they can be escorted to the meeting. Entrance to the meeting at other times during the day cannot be assured.

Purpose: This committee advises and makes recommendations to the Director of the National Vaccine Program on matters related to the Program responsibilities.

Matters To Be Discussed: Agenda items will include updates on the National Vaccine Program Office (NVPO) activities; the

National Vaccine Plan and NVAC's role in defining priorities for action; unmet needs funding—past, present and future; adult immunization: report of the workgroup; use of non-traditional sites for adult immunization; influenza: a growing need for pandemic preparedness; and a discussion on vaccines for international travel.

In addition, there will be updates on welfare reform and effects on immunization; moving towards a Department of Health and Human Services' vaccine safety action plan; work group on philosophical exemptions—final report; the presidential initiative on immunization registries; global use of critically needed vaccines—strategies to consider. There will be reports from the Subcommittee on Immunization Coverage, Subcommittee on Future Vaccines, and Subcommittee on Vaccine Safety.

Name: Subcommittee on Immunization Coverage.

Time and Date: 2 p.m.-5 p.m., January 12, 1998.

Place: Hubert H. Humphrey Building, Room 423A, 200 Independence Avenue, SW, Washington, DC 20201.

Status: Open to the public, limited only by the space available.

Purpose: This subcommittee will identify and propose solutions that provide a multifaceted and holistic approach to reducing barriers that result in low immunization coverage for children.

Matters To Be Discussed: This subcommittee will hold a discussion on the review of recommendations from the document, "Strategies to Sustain Immunization Coverage," and the finalization of those recommendations.

Name: Subcommittee on Future Vaccines.
Time and Date: 2 p.m.-5 p.m., January 12, 1998.

Place: Hubert H. Humphrey Building, Room 405A, 200 Independence Avenue, SW, Washington, DC 20201.

Status: Open to the public, limited only by the space available.

Purpose: The Subcommittee on Future Vaccines will develop policy options and guide national activities which will lead to accelerated development, licensure, and best use of new vaccines in the simplest possible immunization schedules.

Matters To Be Discussed: This subcommittee will hold discussions regarding the continued evaluation of methods to remove barriers to development,

licensure and use of safe and effective new vaccines; combination vaccines, strategic options; and defining future vaccines policy issues for travelers' vaccines.

Name: Subcommittee on Vaccine Safety.
Time and Date: 2 p.m.-5 p.m., January 12, 1998.

Place: Hubert H. Humphrey Building, Room 800, 200 Independence Avenue, SW, Washington, DC 20201.

Status: Open to the public, limited only by the space available.

Purpose: This subcommittee will review issues relevant to vaccine safety and adverse reactions to vaccines.

Matters To Be Discussed: This subcommittee will hold discussions regarding its goals; a report from the Task Force on Safer Childhood Vaccines; a project report on benefit-risk communication curriculum development; and agenda items for the next meeting.

Agenda items are subject to change as priorities dictate.

Contact Person for More Information: Felecia D. Pearson, Committee Management Specialist, NVPO, CDC, 1600 Clifton Road, NE, M/S D50, Atlanta, Georgia 30333, telephone 404/639-4450.

Dated: December 19, 1997.

Carolyn J. Russell,

Director, Management Analysis and Services
Office, Centers for Disease Control and
Prevention (CDC).

[FR Doc. 97-33666 Filed 12-23-97; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 97D-0148]

International Conference on Harmonisation; Guidance on Impurities: Residual Solvents

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is publishing a guidance entitled "Q3C Impurities:

Residual Solvents." The guidance was prepared under the auspices of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). The guidance recommends acceptable amounts of residual solvents in pharmaceuticals for the safety of the patient, and recommends the use of less toxic solvents in the manufacture of drug substances and dosage forms.

DATES: Effective December 24, 1997. Submit written comments at any time.

ADDRESSES: Submit written comments on the guidance to the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1-23, Rockville, MD 20857. Copies of the guidance are available from the Drug Information Branch (HFD-210), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-4573.

FOR FURTHER INFORMATION CONTACT:

Regarding the guidance: John J. Gibbs, Center for Drug Evaluation and Research (HFD-820), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-6430.

Regarding ICH: Janet J. Showalter, Office of Health Affairs (HFY-20), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-0864.

SUPPLEMENTARY INFORMATION: In recent years, many important initiatives have been undertaken by regulatory authorities and industry associations to promote international harmonization of regulatory requirements. FDA has participated in many meetings designed to enhance harmonization and is committed to seeking scientifically based harmonized technical procedures for pharmaceutical development. One of the goals of harmonization is to identify and then reduce differences in technical requirements for drug development among regulatory agencies.

ICH was organized to provide an opportunity for tripartite harmonization initiatives to be developed with input from both regulatory and industry representatives. FDA also seeks input from consumer representatives and others. ICH is concerned with harmonization of technical requirements for the registration of pharmaceutical products among three regions: The European Union, Japan, and the United States. The six ICH sponsors are the European Commission, the European Federation of Pharmaceutical Industries Associations,

the Japanese Ministry of Health and Welfare, the Japanese Pharmaceutical Manufacturers Association, the Centers for Drug Evaluation and Research (CDER) and Biologics Evaluation and Research (CBER), FDA, and the Pharmaceutical Research and Manufacturers of America. The ICH Secretariat, which coordinates the preparation of documentation, is provided by the International Federation of Pharmaceutical Manufacturers Associations (IFPMA).

The ICH Steering Committee includes representatives from each of the ICH sponsors and the IFPMA, as well as observers from the World Health Organization, the Canadian Health Protection Branch, and the European Free Trade Area.

In the **Federal Register** of May 2, 1997 (62 FR 24302), FDA published a draft tripartite guideline entitled "Impurities: Residual Solvents" (Q3C). The notice gave interested persons an opportunity to submit comments by June 16, 1997.

After consideration of the comments received and revisions to the guidance, a final draft of the guidance was submitted to the ICH Steering Committee and endorsed by the three participating regulatory agencies on July 17, 1997.

In accordance with FDA's Good Guidance Practices (62 FR 8961, February 27, 1997), this document has been designated a guidance, rather than a guideline.

Residual solvents in pharmaceuticals are organic volatile chemicals that are used or produced in the synthesis of drug substances or excipients, or in the preparation of drug products. They are not completely removed by practical manufacturing techniques. The guidance recommends acceptable amounts of residual solvents in pharmaceuticals for the safety of the patient. The guidance recommends the use of less toxic solvents and describes levels considered to be toxicologically acceptable for some residual solvents. The guidance applies to residual solvents in drug substances, excipients, and drug products, and to all dosage forms and routes of administration. The guidance does not apply to potential new drug substances, excipients, or drug products used during the clinical research stages of development, nor does it apply to existing marketed drug products.

This guidance represents the agency's current thinking on acceptable amounts of residual solvents in pharmaceuticals. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if

such approach satisfies the requirements of the applicable statute, regulations, or both.

As with all of FDA's guidances, the public is encouraged to submit written comments with new data or other new information pertinent to this guidance. The comments in the docket will be periodically reviewed, and, where appropriate, the guidance will be amended. The public will be notified of any such amendments through a notice in the **Federal Register**.

Interested persons may, at any time, submit written comments on the guidance to the Dockets Management Branch (address above). Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. The guidance and received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday. An electronic version of this guidance is available on the Internet (<http://www.fda.gov/cder/guidance.htm>).

The text of the guidance follows:

Q3C Impurities: Residual Solvents¹

1. Introduction

The objective of this guidance is to recommend acceptable amounts for residual solvents in pharmaceuticals for the safety of the patient. The guidance recommends use of less toxic solvents and describes levels considered to be toxicologically acceptable for some residual solvents.

Residual solvents in pharmaceuticals are defined here as organic volatile chemicals that are used or produced in the manufacture of drug substances or excipients, or in the preparation of drug products. The solvents are not completely removed by practical manufacturing techniques. Appropriate selection of the solvent for the synthesis of drug substance may enhance the yield, or determine characteristics such as crystal form, purity, and solubility. Therefore, the solvent may sometimes be a critical parameter in the synthetic process. This guidance does not address solvents deliberately used as excipients nor does it address solvates. However, the content of solvents in such products should be evaluated and justified.

Since there is no therapeutic benefit from residual solvents, all residual solvents should be removed to the extent possible to meet product specifications, good manufacturing practices, or other quality-based requirements. Drug products should contain

¹ This guidance represents the agency's current thinking on acceptable amounts of residual solvents in pharmaceuticals. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

no higher levels of residual solvents than can be supported by safety data. Some solvents that are known to cause unacceptable toxicities (Class 1, Table 1) should be avoided in the production of drug substances, excipients, or drug products unless their use can be strongly justified in a risk-benefit assessment. Some solvents associated with less severe toxicity (Class 2, Table 2) should be limited in order to protect patients from potential adverse effects. Ideally, less toxic solvents (Class 3, Table 3) should be used where practical. The complete list of solvents included in this guidance is given in Appendix 1.

The lists are not exhaustive and other solvents can be used and later added to the lists. Recommended limits of Class 1 and 2 solvents or classification of solvents may change as new safety data becomes available. Supporting safety data in a marketing application for a new drug product containing a new solvent may be based on concepts in this guidance or the concept of qualification of impurities as expressed in the guidance for drug substance (Q3A, Impurities in New Drug Substances) or drug product (Q3B, Impurities in New Drug Products), or all three guidances.

2. Scope of the Guidance

Residual solvents in drug substances, excipients, and drug products are within the scope of this guidance. Therefore, testing should be performed for residual solvents when production or purification processes are known to result in the presence of such solvents. It is only considered necessary to test for solvents that are used or produced in the manufacture or purification of drug substances, excipients, or drug products. Although manufacturers may choose to test the drug product, a cumulative method may be used to calculate the residual solvent levels in the drug product from the levels in the ingredients used to produce the drug product. If the calculation results in a level equal to or below that recommended in this guidance, no testing of the drug product for residual solvents need be considered. If, however, the calculated level is above the recommended level, the drug product should be tested to ascertain whether the formulation process has reduced the relevant solvent level to within the acceptable amount. Drug product should also be tested if a solvent is used during its manufacture.

This guidance does not apply to potential new drug substances, excipients, or drug products used during the clinical research stages of development, nor does it apply to existing marketed drug products.

The guidance applies to all dosage forms and routes of administration. Higher levels of residual solvents may be acceptable in certain cases such as short-term (30 days or less) or topical application. Justification for these levels should be made on a case-by-case basis.

See Appendix 2 of this document for additional background information related to residual solvents.

3. General Principles

3.1 Classification of Residual Solvents by Risk Assessment

The term "tolerable daily intake" (TDI) is used by the International Program on Chemical Safety (IPCS) to describe exposure limits of toxic chemicals and the term "acceptable daily intake" (ADI) is used by the World Health Organization (WHO) and other national and international health authorities and institutes. The new term "permitted daily exposure" (PDE) is defined in the present guidance as a pharmaceutically acceptable intake of residual solvents to avoid confusion of differing values for ADI's of the same substance.

Residual solvents assessed in this guidance are listed in Appendix 1 by common names and structures. They were evaluated for their possible risk to human health and placed into one of three classes as follows:

Class 1 solvents: Solvents to be avoided—

Known human carcinogens, strongly suspected human carcinogens, and environmental hazards.

Class 2 solvents: Solvents to be limited—

Nongenotoxic animal carcinogens or possible causative agents of other irreversible toxicity such as neurotoxicity or teratogenicity.

Solvents suspected of other significant but reversible toxicities.

Class 3 solvents: Solvents with low toxic potential—

Solvents with low toxic potential to man; no health-based exposure limit is needed. Class 3 solvents have PDE's of 50 milligrams (mg) or more per day.

3.2 Methods for Establishing Exposure Limits

The method used to establish permitted daily exposures for residual solvents is presented in Appendix 3. Summaries of the toxicity data that were used to establish limits are published in *Pharmeuropa*, Vol. 9, No. 1, Supplement, April 1997.

3.3 Options for Describing Limits of Class 2 Solvents

Two options are available when setting limits for Class 2 solvents.

Option 1: The concentration limits in parts per million (ppm) stated in Table 2 can be used. They were calculated using equation (1) below by assuming a product mass of 10 grams (g) administered daily.

$$(1) \text{ Concentration (ppm)} = \frac{1000 \times \text{PDE}}{\text{dose}}$$

Here, PDE is given in terms of mg/day and dose is given in g/day.

These limits are considered acceptable for all substances, excipients, or products. Therefore, this option may be applied if the daily dose is not known or fixed. If all excipients and drug substances in a formulation meet the limits given in Option 1, then these components may be used in any proportion. No further calculation is necessary provided the daily dose does not exceed 10 g. Products that are administered in doses greater than 10 g per day should be considered under Option 2.

Option 2: It is not considered necessary for each component of the drug product to comply with the limits given in Option 1. The PDE in terms of mg/day as stated in Table 2 can be used with the known maximum daily dose and equation (1), as shown in Option 1 in the previous paragraph, to determine the concentration of residual solvent allowed in drug product. Such limits are considered acceptable provided that it has been demonstrated that the residual solvent has been reduced to the practical minimum. The limits should be realistic in relation to analytical precision, manufacturing capability, and reasonable variation in the manufacturing process and the limits should reflect contemporary manufacturing standards.

Option 2 may be applied by adding the amounts of a residual solvent present in each of the components of the drug product. The sum of the amounts of solvent per day should be less than that given by the PDE.

Consider an example of the use of Option 1 and Option 2 applied to acetonitrile in a drug product. The permitted daily exposure to acetonitrile is 4.1 mg per day; thus, the Option 1 limit is 410 ppm. The maximum administered daily mass of a drug product is 5.0 g, and the drug product contains two excipients. The composition of the drug product and the calculated maximum content of residual acetonitrile are given in the following table.

Component	Amount in formulation	Acetonitrile content	Daily exposure
Drug substance	0.3 g	800 ppm	0.24 mg
Excipient 1	0.9 g	400 ppm	0.36 mg
Excipient 2	3.8 g	800 ppm	3.04 mg
Drug product	5.0 g	728 ppm	3.64 mg

Excipient 1 meets the Option 1 limit, but the drug substance, excipient 2, and drug

product do not meet the Option 1 limit. Nevertheless, the product meets the Option

2 limit of 4.1 mg per day and thus conforms to the recommendations in this guidance.

Consider another example using acetonitrile as residual solvent. The maximum administered daily mass of a drug

product is 5.0 g, and the drug product contains two excipients. The composition of the drug product and the calculated

maximum content of residual acetonitrile are given in the following table.

Component	Amount in formulation	Acetonitrile content	Daily exposure
Drug substance	0.3 g	800 ppm	0.24 mg
Excipient 1	0.9 g	2,000 ppm	1.80 mg
Excipient 2	3.8 g	800 ppm	3.04 mg
Drug product	5.0 g	1,016 ppm	5.08 mg

In this example, the product meets neither the Option 1 nor the Option 2 limit according to this summation. The manufacturer could test the drug product to determine if the formulation process reduced the level of acetonitrile. If the level of acetonitrile was not reduced during formulation to the allowed limit, then the manufacturer of the drug product should take other steps to reduce the amount of acetonitrile in the drug product. If all of these steps fail to reduce the level of residual solvent, in exceptional cases the manufacturer could provide a summary of efforts made to reduce the solvent level to meet the guidance value, and provide a risk-benefit analysis to support allowing the product to be utilized with residual solvent at a higher level.

3.4 Analytical Procedures

Residual solvents are typically determined using chromatographic techniques such as gas chromatography. Any harmonized procedures for determining levels of residual solvents as described in the pharmacopoeias should be used, if feasible. Otherwise, manufacturers would be free to select the most appropriate validated analytical procedure for a particular application. If only Class 3 solvents are present, a nonspecific method such as loss on drying may be used.

Validation of methods for residual solvents should conform to ICH guidances "Q2A Text on Validation of Analytical Procedures" and "Q2B Validation of Analytical Procedures: Methodology."

3.5 Reporting Levels of Residual Solvents

Manufacturers of pharmaceutical products need certain information about the content of residual solvents in excipients or drug substances in order to meet the criteria of this guidance. The following statements are given as acceptable examples of the information that could be provided from a supplier of excipients or drug substances to a pharmaceutical manufacturer. The supplier might choose one of the following as appropriate:

- Only Class 3 solvents are likely to be present. Loss on drying is less than 0.5 percent.
- Only Class 2 solvents X, Y, * * * are likely to be present. All are below the Option 1 limit. (Here the supplier would name the Class 2 solvents represented by X, Y, * * * .)
- Only Class 2 solvents X, Y, * * * and Class 3 solvents are likely to be present. Residual Class 2 solvents are below the Option 1 limit and residual Class 3 solvents are below 0.5 percent.

If Class 1 solvents are likely to be present, they should be identified and quantified.

"Likely to be present" refers to the solvent used in the final manufacturing step and to solvents that are used in earlier manufacturing steps and not removed consistently by a validated process.

If solvents of Class 2 or Class 3 are present at greater than their Option 1 limits or 0.5 percent, respectively, they should be identified and quantified.

4. Limits of Residual Solvents

4.1 Solvents to Be Avoided

Solvents in Class 1 should not be employed in the manufacture of drug substances, excipients, and drug products because of their unacceptable toxicity or their deleterious environmental effect. However, if their use is unavoidable in order to produce a drug product with a significant therapeutic advance, then their levels should be restricted as shown in Table 1, unless otherwise justified. The solvent 1,1,1-Trichloroethane is included in Table 1 because it is an environmental hazard. The stated limit of 1,500 ppm is based on a review of the safety data.

TABLE 1.—CLASS 1 SOLVENTS IN PHARMACEUTICAL PRODUCTS
(SOLVENTS THAT SHOULD BE AVOIDED)

Solvent	Concentration limit (ppm)	Concern
Benzene	2	Carcinogen
Carbon tetrachloride	4	Toxic and environmental hazard
1,2-Dichloroethane	5	Toxic
1,1-Dichloroethene	8	Toxic
1,1,1-Trichloroethane	1,500	Environmental hazard

4.2 Solvents to Be Limited

Solvents in Table 2 should be limited in pharmaceutical products because of their inherent toxicity. PDE's are given

to the nearest 0.1 mg/day, and concentrations are given to the nearest 10 ppm. The stated values do not reflect the necessary analytical precision of

determination. Precision should be determined as part of the validation of the method.

TABLE 2.—CLASS 2 SOLVENTS IN PHARMACEUTICAL PRODUCTS

Solvent	PDE (mg/day)	Concentration limit (ppm)
Acetonitrile	4.1	410
Chlorobenzene	3.6	360
Chloroform	0.6	60
Cyclohexane	38.8	3,880
1,2-Dichloroethene	18.7	1,870

TABLE 2.—CLASS 2 SOLVENTS IN PHARMACEUTICAL PRODUCTS—Continued

Solvent	PDE (mg/day)	Concentration limit (ppm)
Dichloromethane	6.0	600
1,2-Dimethoxyethane	1.0	100
N,N-Dimethylacetamide	10.9	1,090
N,N-Dimethylformamide	8.8	880
1,4-Dioxane	3.8	380
2-Ethoxyethanol	1.6	160
Ethyleneglycol	6.2	620
Formamide	2.2	220
Hexane	2.9	290
Methanol	30.0	3,000
2-Methoxyethanol	0.5	50
Methylbutyl ketone	0.5	50
Methylcyclohexane	11.8	1,180
N-Methylpyrrolidone	48.4	4,840
Nitromethane	0.5	50
Pyridine	2.0	200
Sulfolane	1.6	160
Tetralin	1.0	100
Toluene	8.9	890
1,1,2-Trichloroethene	0.8	80
Xylene ¹	21.7	2,170

¹ Usually 60% m-xylene, 14% p-xylene, 9% o-xylene with 17% ethyl benzene.

4.3 Solvents with Low Toxic Potential

Solvents in Class 3 (shown in Table 3) may be regarded as less toxic and of lower risk to human health. Class 3 includes no solvent known as a human health hazard at levels normally accepted in pharmaceuticals. However,

there are no long-term toxicity or carcinogenicity studies for many of the solvents in Class 3. Available data indicate that they are less toxic in acute or short-term studies and negative in genotoxicity studies. It is considered that amounts of these residual solvents

of 50 mg per day or less (corresponding to 5,000 ppm or 0.5 percent under Option i) would be acceptable without justification. Higher amounts may also be acceptable provided they are realistic in relation to manufacturing capability and good manufacturing practice (GMP).

TABLE 3.—CLASS 3 SOLVENTS WHICH SHOULD BE LIMITED BY GMP OR OTHER QUALITY-BASED REQUIREMENTS

Acetic acid	Heptane
Acetone	Isobutyl acetate
Anisole	Isopropyl acetate
1-Butanol	Methyl acetate
2-Butanol	3-Methyl-1-butanol
Butyl acetate	Methylethyl ketone
tert-Butylmethyl ether	Methylisobutyl ketone
Cumene	2-Methyl-1-propanol
Dimethyl sulfoxide	Pentane
Ethanol	1-Pentanol
Ethyl acetate	1-Propanol
Ethyl ether	2-Propanol
Ethyl formate	Propyl acetate
Formic acid	Tetrahydrofuran

4.4 Solvents for Which No Adequate Toxicological Data Were Found

The following solvents (Table 4) may also be of interest to manufacturers of excipients,

drug substances, or drug products. However, no adequate toxicological data on which to base a PDE were found. Manufacturers

should supply justification for residual levels of these solvents in pharmaceutical products.

TABLE 4.—SOLVENTS FOR WHICH NO ADEQUATE TOXICOLOGICAL DATA WERE FOUND

1,1-Diethoxypropane	Methylisopropyl ketone
1,1-Dimethoxymethane	Methyltetrahydrofuran
2,2-Dimethoxypropane	Petroleum ether
Isooctane	Trichloroacetic acid
Isopropyl ether	Trifluoroacetic acid

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