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TOXICITY DATA TO DETERMINE REFRIGERANT CONCENTRATION LIMITS

September 2000

prepared by

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ABSTRACT: This report reviews toxicity data, identifies sources for them, and presents resulting exposure limits for refrigerants for consideration by qualified parties in developing safety guides, standards, codes, and regulations. It outlines a method to calculate an *acute toxicity exposure limit* (ATEL) and from it a recommended *refrigerant concentration limit* (RCL) for emergency exposures. The report focuses on acute toxicity with particular attention to lethality, cardiac sensitization, anesthetic and central nervous system (CNS) effects, and other escape-impairing effects. It addresses R-11, R-12, R-22, R-23, R-32, R-113, R-114, R-116, R-123, R-124, R-125, R-134, R-134a, R-E134, R-141b, R-142b, R-143a, R-152a, R-218, R-227ea, R-236fa, R-245ca, R-245fa, R-290, R-500, R-502, R-600a, R-717, and R-744. It tabulates additional data for R-14, R-115, R-170 (ethane), R-C318, R-600 (n-butane), and R-1270 (propylene) to enable calculation of limits for blends incorporating them. The report summarizes the data and related safety information, including classifications and flammability data. It also presents a series of tables with proposed ATEL and RCL concentrations — in dimensionless form and the latter also in both metric (SI) and inch-pound (IP) units of measure — for both the cited refrigerants and 66 zeotropic and azeotropic blends. They include common refrigerants, such as R-404A, R-407C, R-410A, and R-507A, as well as others in commercial or developmental status. Appendices provide profiles for the cited single-compound refrigerants and for R-500 and R-502 as well as narrative toxicity summaries for common refrigerants. The report includes an extensive set of references.

TOXICITY DATA TO DETERMINE REFRIGERANT CONCENTRATION LIMITS

INTRODUCTION

This report reviews toxicity data, identifies sources for them, and presents resulting exposure limits for refrigerants. The data primarily address those pertinent to *acute* inhalation exposures from *emergency* releases rather than *chronic* exposures. *Acute* toxicity refers to the adverse health effects of a short-term, single exposure. *Chronic* toxicity refers to those from long-term or repeated exposures. *Emergency* signifies unplanned and unintended releases with a view toward mitigating risks for the general public. In contrast, *occupational* exposure limits assume that potentially affected personnel should be cognizant of the potential for exposures, have special awareness or training, and may employ protective measures or devices.

The specific data addressed are those pertinent to a proposed method to set recommended concentration limits, in turn to improve refrigeration safety. This report does not address how those limits should be applied, for example adjustments for specific building occupancies or circumstances. It also does not address measures to assure that the recommended limits are not exceeded, the combinatorial influences of other chemicals that may be present or released in an emergency, or the decomposition products from refrigerant breakdown in fires or other chemical reactions. Based on differences in individual sensitivities to chemical hazards, some people may experience adverse or even life-threatening affects from exposures below the recommended concentration limits.

The scope of this compilation is data gathering and analysis. This report does not present new test results, verify prior findings, or imply endorsement of the identified data. The compilation is intended to assist qualified safety professionals; it is not meant for use by individuals lacking training and experience in control of chemical hazards and refrigeration safety.

The refrigerants covered include those in common use for the last decade, those used as components in common blends, and selected candidates for future replacements.

The data and recommendations are not the result of a consensus determination. Rather this report documents input for consideration by qualified parties in developing guides, standards, codes, and regulations. The primary intended use of the data is to assist the project committees for ASHRAE Standard 34, *Designation and Safety Classification of Refrigerants*,[1] and in turn ASHRAE Standard 15, *Safety Code for Mechanical Refrigeration* (soon to be *Safety Code for Refrigeration*).[2] Indeed, some of the recommended data differ from working and review drafts, prepared by those committees, based on preliminary data from this effort and other sources.

PERSPECTIVE

Most of the dominant refrigerants for the past fifty years have been or are being replaced, to protect the stratospheric ozone layer and to reduce contributions to global warming. Much to the credit of the air-conditioning and refrigeration industry, both chemical and equipment manufacturers have resisted compromise to either safety or performance in developing replacements. None of the alternative refrigerants commercialized are *highly toxic* or even *toxic* as classified by federal regulations.[3] Scrutiny of the new refrigerants shows them to be as safe or safer than those they replace.[4] Most safety concerns with the new refrigerants stem from lack of familiarity and necessary information rather than increased hazard levels.

The majority of early refrigerants — those applied before 1930 — were flammable, toxic, or both. The advent of fluorochemicals* ushered in a new era of safety, as illustrated by the dramatic demonstration by Thomas Midgley in April 1930. In announcing the development of fluorochemicals to the American Chemical Society, he inhaled R-12 and blew out a candle with it.[5] Although this dramatic stunt suggested that the new refrigerant was deemed safe for toxicity and flammability, it would clearly violate current safety practices.

As subsequent testing established the low toxicity of the new refrigerants, recognition emerged that the primary safety risks were the pressure hazards inherent to any compressed gas, asphyxiation from possible displacement of air, and frostbite with skin contact at low temperatures. These concerns were, however, common to the volatile compounds used before fluorochemicals. As the level of safety improved, so did expectations. Rules evolved to also address acute exposure hazards under emergency conditions, for example potential decomposition in fires into carbonyl halides as well as hydrochloric and hydrofluoric acids. New safety provisions also address the potential for cardiac sensitization and the effects of chronic exposures for both technicians and building occupants. These standards and regulations restrict the use of refrigerants, set quantity limits in occupied areas, impose isolation requirements for refrigerant-containing components and machinery rooms, and prescribe a range of detection, ventilation, pressure relief, emergency discharge, and other safety provisions.

Recent focus on the effects of refrigerants on the environment spawned three significant safety measures, namely system tightening, modification of service practices to reduce venting, and use of electronic refrigerant detectors. Although motivated by environmental protection, to curtail avoidable emissions, the results also lower both the likelihood and the concentrations of refrigerant exposures. The advent of reliable leak detectors affords a mechanism to warn of leaks before harmful concentrations are reached.

The combination of safer chemicals, system tightening, improved service practices, and use of leak detection has greatly reduced the hazard of refrigerant use. In contrast to safety risks that obstructed wide use of refrigerators 70 years ago, consumers presume such appliances and even much larger systems to pose negligible or at least acceptable safety risks. While very infrequent accidents and deaths from refrigerants still occur, most now result from failure to comply with safety requirements and recommended practices. The most dangerous part of working on refrigeration systems today is getting to and from the job site. The chance of death from a refrigerant exposure, excluding intentional abuse, now is more than twenty times less than of being killed by lightning.† Unlike lightning, refrigeration saves far more — perhaps several magnitudes more — lives each year than are lost in refrigerant-related accidents. The lives saved

* compounds consisting of carbon, fluorine, and possibly hydrogen, other halogens such as chlorine, or other elements

† based on known incidents and published statistics for the United States from 1985-1999

and enhanced result from preservation of foods and pharmaceuticals, conditioning of indoor climates to counter severe heat, and enabling of essential technologies.

While the safety record should improve with new products and compliance with updated safety standards and codes, there still is room for further progress. This report addresses one facet of the problem, to recommend concentration limits as the basis for safety standards and codes to protect the public from unplanned exposures.

A brief review of the fundamental toxicity basis precedes that topic.

CAVEATS

The cited data recommendations are not universal, but are limited in relevance to ATEL determination. Other uses may warrant consideration or use of additional or other data.

The data are not complete. The selections and recommendations are based on specific criteria for ATEL determination (see page 19). Redundant and non-qualifying data generally were excluded except to explain or reinforce the recommendations. Appendix 2 (see page 135) tabulates some additional toxicity data.

The data and recommendations are not the result of a consensus determination. Rather this report documents input for consideration by qualified parties in developing guides, standards, codes, and regulations. The primary intended use of the data is to assist the project committees for ASHRAE Standard 34, *Designation and Safety Classification of Refrigerants*, and in turn ASHRAE Standard 15, *Safety Code for Mechanical Refrigeration* (soon to be *Safety Code for Refrigeration*). Indeed, some of the recommended data differ from working and review drafts, prepared by those committees, based on preliminary data from this effort and other sources.

The ARTI Refrigerant Database[22] identifies additional data and data sources for both the refrigerants addressed herein and others. Both this report and the database are intended to assist in locating information on refrigerants, but they are:

- neither a comprehensive nor authoritative reference source,
- not a substitute for independent data collection by users,
- not a substitute for examination of the data, information on how they were arrived at, underlying assumptions, associated caveats, flaws, and omissions in the cited documents, and
- not an endorsement of suitability or accuracy of referenced data and publications.

Safety considerations and other characteristics affecting suitability or desirability may be influenced by a number of factors. Among them are specific application conditions, additives, impurities, catalytic interactions with other materials used, and changes in compounding between one source or batch and another. Similarly, new findings or corrections may supersede previously published data. Neither the report nor the database should be viewed as the source of data for research, design, analysis, or other purposes.

Table 4: RCL Dimensional Unit Conversions [a]

refrigerant [b] desig-nation	chemical name	ATEL (ppm v/v)	RCL (ppm v/v)	change to ASHRAE 15 [c] *amount* (%)	RCL (g/m^3)	RCL (lb/Mcf)
11	trichlorofluoromethane	1 100	1 100	-73	6.2	0.39
12	dichlorodifluoromethane	18 000	18 000	-55	90	5.6
14 •	*tetrafluoromethane*	*110 000*	*69 000*	*+3*	*250*	*16*
22	chlorodifluoromethane	25 000	25 000	-40	89	5.5
23	trifluoromethane	41 000	41 000	-39 *	120	7.3
32	difluoromethane	40 000	32 000	new	68	4.2
113	1,1,2-trichloro-1,2,2-trifluoroethane	2 600	2 600	-35	20	1.2
114	1,2-dichloro-1,1,2,2-tetrafluoroethane	20 000	20 000	-5	140	8.7
115 •	*chloropentafluoroethane*	*120 000*	*69 000*	*+3*	*440*	*27*
116	hexafluoroethane	97 000	69 000	new	390	24
123	2,2-dichloro-1,1,1-trifluoroethane	9 100	9 100	+810	57	3.5
124	2-chloro-1,1,1,2-tetrafluoroethane	10 000	10 000	new	56	3.5
125	pentafluoroethane	75 000	69 000	new	340	21
134	1,1,2,2-tetrafluoroethane	75 000	69 000	new	290	18
134a	1,1,1,2-tetrafluoroethane	50 000	50 000	-17	210	13
E134	bis(difluoromethyl) ether	0	0	new	0	0
141b	1,1-dichloro-1-fluoroethane	2 600	2 600	new	12	0.78
142b	1-chloro-1,1-difluoroethane	25 000	15 000	new	62	3.9
143a	1,1,1-trifluoroethane	170 000	18 000	new	60	3.8
152a	1,1-difluoroethane	50 000	9300	+33	25	1.6
170 •	*ethane*	*7 000*	*7 000*	*+9*	*8.7*	*0.54*
218	octafluoropropane	90 000	69 000	new	530	33
227ea	1,1,1,2,3,3,3-heptafluoropropane	70 000	69 000	new	480	30
236fa	1,1,1,3,3,3-hexafluoropropane	55 000	55 000	+162 *	340	21
245ca	1,1,2,2,3-pentafluoropropane	0	0	-100 *	0	0
245fa	1,1,1,3,3-pentafluoropropane	34 000	34 000	new	190	12
290	propane	50 000	5 000	+14	9.0	0.56
C318 •	*octafluorocyclobutane*	*80 000*	*69 000*	*+3*	*570*	*35*
500	(calculated as blend in table 6)					
502	(calculated as blend in table 6)					
600 •	*n-butane*	*0*	*0*	*-100*	*0*	*0*
600a	isobutane	25 000	2500	-26	6.0	0.37
717	ammonia	320	320	-36	0.22	0.014
744	carbon dioxide	40 000	40 000	-20	72	4.5
1270 •	*propene (propylene)*	*0*	*0*	*-100*	*0*	*0*

a ATEL and RCL concentrations shown in this table are in air. RCLs shown as g/m^3 and lb/Mcf are at sea level. Italicized data are *provisional* (see page 87).

b from ANSI/ASHRAE Standard 34 [1] and the ARTI Refrigerant Database[22]

c from ASHRAE 15 table 1:[2] Where flagged with an asterisk (*) the reference values from ASHRAE 15 are for the refrigerant that this refrigerant replaces in its primary application, so flagged entries in this table differ from the corresponding entries in table 3.

• *provisional, see page 87*

Table 5: RCL Dimensional Unit Conversions for Zeotropic Blends with Designations [a]

refrigerant [b]				change to ASHRAE 15 [c]		
designation	composition	ATEL (ppm v/v)	RCL (ppm v/v)	*amount* (%)	RCL (g/m³)	RCL (lb/Mcf)
400	R-12/114 (50.0/50.0)	28 000	28 000	new	160	10
400	R-12/114 (60.0/40.0)	26 000	26 000	new	150	9.3
401A	R-22/152a/124 (53.0/13.0/34.0)	20 000	20 000	-50 *	77	4.8
401B	R-22/152a/124 (61.0/11.0/28.0)	21 000	21 000	-48 *	79	4.9
401C	R-22/152a/124 (33.0/15.0/52.0)	17 000	17 000	-58 *	71	4.4
402A	R-125/290/22 (60.0/2.0/38.0)	39 000	39 000	-40 *	160	10
402B	R-125/290/22 (38.0/2.0/60.0)	32 000	32 000	-51 *	120	7.8
403A	R-290/22/218 (5.0/75.0/20.0)	29 000	29 000	-55 *	110	6.9
403B	R-290/22/218 (5.0/56.0/39.0)	34 000	34 000	-48 *	140	8.9
404A	R-125/143a/134a (44.0/52.0/4.0)	130 000	69 000	+6 *	280	17
405A •	*R-22/152a/142b/C318• (45/7/5.5/42.5)*	*32 000*	*32 000*	*-20 **	*150*	*9.2*
406A	R-22/600a/142b (55.0/4.0/41.0)	25 000	25 000	-38 *	92	5.7
	R-22/600a/142b (65.0/4.0/31.0)	25 000	25 000	-38 *	91	5.7
407A	R-32/125/134a (20.0/40.0/40.0)	78 000	69 000	+6 *	260	16
407B	R-32/125/134a (10.0/70.0/20.0)	77 000	69 000	+6 *	290	18
407C	R-32/125/134a (23.0/25.0/52.0)	76 000	69 000	+64 *	240	15
407D	R-32/125/134a (15.0/15.0/70.0)	65 000	65 000	+38 *	240	15
407E	R-32/125/134a (25.0/15.0/60.0)	72 000	69 000	+64 *	240	15
	R-32/125/134a (30.0/10.0/60.0)	66 000	66 000	+57 *	220	14
408A	R-125/143a/22 (7.0/46.0/47.0)	47 000	47 000	+0 *	170	10
409A	R-22/124/142b (60.0/25.0/15.0)	20 000	20 000	-50 *	79	4.9
409B	R-22/124/142b (65.0/25.0/10.0)	20 000	20 000	-50 *	78	4.9
410A	R-32/125 (50.0/50.0)	55 000	55 000	+31 *	160	10
410B	R-32/125 (45.0/55.0)	58 000	58 000	+38 *	180	11
	R-32/125 (32.0/68.0)	71 000	69 000	+21 *	240	15
	R-32/125 (48.0/52.0)	56 000	56 000	+33 *	170	11
411A	R-1270/22/152a (1.5/87.5/11.0)	~ 26 000	~ 26 000	-38% *	86	5.4
411B	R-1270/22/152a (3.0/94.0/3.0)	~ 23 000	~ 23 000	-65% *	80	5.0
	R-1270/22/152a (3/95.5/1.5)	~ 23 000	~ 23 000	-43% *	79	4.9
412A	R-22/218/142b (70.0/5.0/25.0)	26 000	26 000	-45 *	97	6.0
413A	R-218/134a/600a (9.0/88.0/3.0)	49 000	49 000	+23 *	210	13
414A	R-22/124/600a/142b (51/28.5/4.0/16.5)	19 000	19 000	-53 *	76	4.8
414B	R-22/124/600a/142b (50.0/39.0/1.5/9.5)	18 000	18 000	-55 *	73	4.5
416A •	*R-134a/124/600• (59.0/39.5/1.5)*	*~ 21 000*	*~ 21 000*	*-48% **	*96*	*6.0*
417A •	*R-125/134a/600• (46.6/50.0/3.4)*	*~ 45 000*	*~ 45 000*	*+7% **	*200*	*12*

a ATEL and RCL concentrations shown in this table are in air. RCLs shown as g/m³ and lb/Mcf are at sea level. Italicized data are *provisional* (see page 87). ATEL and RCL data preceded by a tilda (~) are approximations since toxicity data needed to calculate the ATEL are missing for one or more blend components or because adequate data on the blend flammability to calculate the RCL are not available.

b from ANSI/ASHRAE Standard 34 [1] and the ARTI Refrigerant Database[22]

c from ASHRAE 15 table 1:[2] Where flagged with an asterisk (*) the reference values from ASHRAE 15 are for the refrigerant that this refrigerant replaces in its primary application, so flagged entries in this table differ from the corresponding entries in table 3.

• *provisional, see page 87*

Table 6: RCL Dimensional Unit Conversions for Azeotropic Blends with Designations [a]

refrigerant [b] designation	composition	ATEL (ppm v/v)	RCL (ppm v/v)	change to ASHRAE 15 [c] *amount* (%)	RCL (g/m³)	RCL (lb/Mcf)
500	R-12/152a (73.8/26.2)	29 000	29 000	-49	120	7.4
501	R-22/12 (75.0/25.0)	27 000	27 000	new	100	6.4
502	R-22/115 (48.8/51.2)	35 000	35 000	-46	160	10
503 •	*R-23/13• (40.1/59.9)*	*0*	*0*	*0*	*0*	*0*
504 •	*R-32/115• (48.2/51.8)*	*53 000*	*41 000*	*new*	*130*	*8.4*
505 •	*R-12/31• (78.0/22.0)*	*0*	*0*	--	*0*	*0*
506 •	*R-31•/114 (55.1/44.9)*	*0*	*0*	--	*0*	*0*
507A	R-125/143a (50.0/50.0)	130 000	69 000	+6 *	280	17
508A	R-23/116 (39.0/61.0)	55 000	55 000	-18 *	220	14
508B	R-23/116 (46.0/54.0)	52 000	52 000	-22 *	200	13
509A	R-22/218 (44.0/56.0)	38 000	38 000	-42 *	190	12

a ATEL and RCL concentrations shown in this table are in air. RCLs shown as g/m³ and lb/Mcf are at sea level. Italicized data are *provisional* (see page 87). ATEL and RCL data preceded by a tilda (~) are approximations since toxicity data needed to calculate the ATEL are missing for one or more blend components or because adequate data on the blend flammability to calculate the RCL are not available.

b from ANSI/ASHRAE Standard 34 [1] and the ARTI Refrigerant Database[22]

c from ASHRAE 15 table 1:[2] Where flagged with an asterisk (*) the reference values from ASHRAE 15 are for the refrigerant that this refrigerant replaces in its primary application, so flagged entries in this table differ from the corresponding entries in table 3.

• *provisional, see page 87*

CONCLUSIONS

GENERAL

The toxicity data examined herein provide a consistent basis to set emergency exposure limits to promote safety in use of refrigerants. The report recommends a calculation method, specific data, and proposed limits for common refrigerants for consideration by the committees responsible for ASHRAE 15 and 34 and, in turn, by those developing codes and regulations governing refrigerant use. While the data generally show the alternative refrigerants to be comparable or lower in toxicity than those they replace, and especially so for acute effects, safe use depends on adherence to proper application, handling, and service procedures. The report presents the proposed refrigerant concentration limits (RCLs) in dimensionless form (in ppm v/v) as well as in metric (SI) and inch-pound (IP) units of measure for a total of 99 single-compound refrigerants and zeotropic and azeotropic blends of them.

PROVISIONAL AND APPROXIMATED RCLS

The recommended limits for six of the compounds, included as components in eight of the blends, are provisional. While the scope for this project did not include them, data searches for the targeted refrigerants also found sufficient data to calculate provisional limits for the extra refrigerants. Likewise, these searches also found some or all of the data needed to calculate RCLs for more than 200 other refrigerants and candidate refrigerants. Recognizing that the limits calculated with provisional data could increase or decrease with additional data from focused searches, the provisional limits should be used with caution and warrant reduction by a safety factor of approximately 20% for interim use.

The report also flags seven of the blends as approximations based on estimations in light of insufficient toxicity data, for one or more components for one or more effects included in the ATEL. Only four of these blends have designations and ASHRAE 34 safety classifications. The report also flags 18 blends as approximations based on estimates of their flammability; the flammability data needed may be included in future classification applications. These estimated limits should be used with caution and warrant reduction by a safety factor of approximately 50% for interim use.

The suggested factors of 20 and 50% for the provisional and approximated data are intentionally conservative to protect the public and to provide an incentive for parties interested in those refrigerants to supply the missing information. They are indicative of uncertainty rather than known or suspected increases in hazard. No radical changes to the provisional and approximated RCLs, or at least the majority of them, are likely with the added data.

TOXICITY CLASSIFICATION

Neither ASHRAE 15 nor current model building, fire, and mechanical codes use the toxicity component of the ASHRAE 34 safety classification except to prohibit refrigerants in the B toxicity class from use in “high probability” air-conditioning systems for human comfort. “High” and “low probability” distinguish systems for which leaked refrigerant from a failure is likely or unlikely, respectively, to enter an occupied space, generally that served by the refrigeration system involved. Determination of the cited prohibition by an index of chronic — rather than acute — toxicity is illogical since the underlying concern for this purpose is emergency exposures from failures and catastrophic causes. Indeed, ASHRAE15 §7.4.1 and most codes provide exclusions to this restriction for specified systems with small charges (not exceeding 3 kg, 6.6 lb) in listed equipment.[2]

Both the restriction and exclusions are arbitrary. There is no compelling reason to prohibit use of “high probability” systems using refrigerants in the B toxicity class if loss of the full charge would not exceed the RCL. Likewise, the exclusion amount provides no assurance that a highly toxic refrigerant, if used, would not exceed the RCL in some cases.

Accordingly, the author recommends deletion of the toxicity classification from ASHRAE 34, deletion of the restriction based on chronic toxicity for comfort-conditioning systems from ASHRAE 15, and focus instead — in both standards — on the proposed RCLs to minimize risks of acute toxicity, oxygen deprivation, and flammability.

This conclusion is reinforced by noting that the flammability class included in the ASHRAE 34 safety group is inherently “acute” in nature, that is from a single event rather than a continuing or repeated event. ASHRAE 34 determined the toxicity classification from acute toxicity data until the 1989 revision. It determined classifications by lethality or “serious injury” to guinea pigs from a 2-hr exposure at 25,000 ppm v/v,[314] presumably patterned after the early UL toxicity tests and classifications.[20]

UNCERTAINTIES IN FLAMMABILITY DATA

Although also beyond the scope of the project, the report presents sensitivity analyses to examine the impact of uncertainty in some of the flammability data used to calculate the RCLs. The findings show no or small effect for the majority of flammable refrigerants, but they also reveal two with significant consequence. The recommended limits use the most restrictive lowest LFLs identified to be conservative, but these limits may warrant some relaxation with more investigation of the flammability data used.

The author is aware of an ongoing study to measure the flammability of selected refrigerants by a proposed new method (“34p”). The further testing will add to the information base, but not refute the validity of the current data. The new data may increase the data dispersion for some refrigerants, but cannot reduce it. Accordingly, the author recommends critical review of the current data to examine the reasons for the wide variation, to dismiss data from noncomplying methods, and to document consistent data for use in calculating the flammability component of RCLs.

OXYGEN DEPRIVATION LIMIT

Review of the acute inhalation toxicity studies suggests that the currently used ODL warrants examination. Many studies found for this project report tests in atmospheres exceeding 69,000 ppm v/v refrigerant, for four hours or longer, with no clinical signs. The author recommends careful determination of a justified ODL.