Handheld Advisory Circular Update

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May 19-20, 2009
Koeln, Germany

Dos and Don’ts

- FAA Aircraft Certification Service has advised the FAA Fire Safety Team that the Advisory Circular AC 20-42D is considered in the process of rulemaking.
- We cannot release a draft version or discuss the AC because ex parte communication of pending rulemaking is not permitted.
- We can discuss recent data on handheld agents that was not available when the task group was working on the draft AC.

Outline

- **<u>Updated Data:</u>**
  - ➢ Develop 1st order kinetic model that fits ***all*** halocarbon data.

  - ➢ **Halon 1211:** Remove Max Safe W/V Selector Curves for Ventilated Compartments

  - ➢ **HCFC Blend B:**
    - ❖ Set Target Arterial Concentration of HCFC-123 to meet the same criteria as other halocarbons and scale Colton et al's gas concentration data.
    - ❖ Adjust Maximum Safe W/V Data for Ventilated and Nonventilated Compartments

  - ➢ **Halocarbon Blends:** Provide Max Safe W/V Calculation Method.

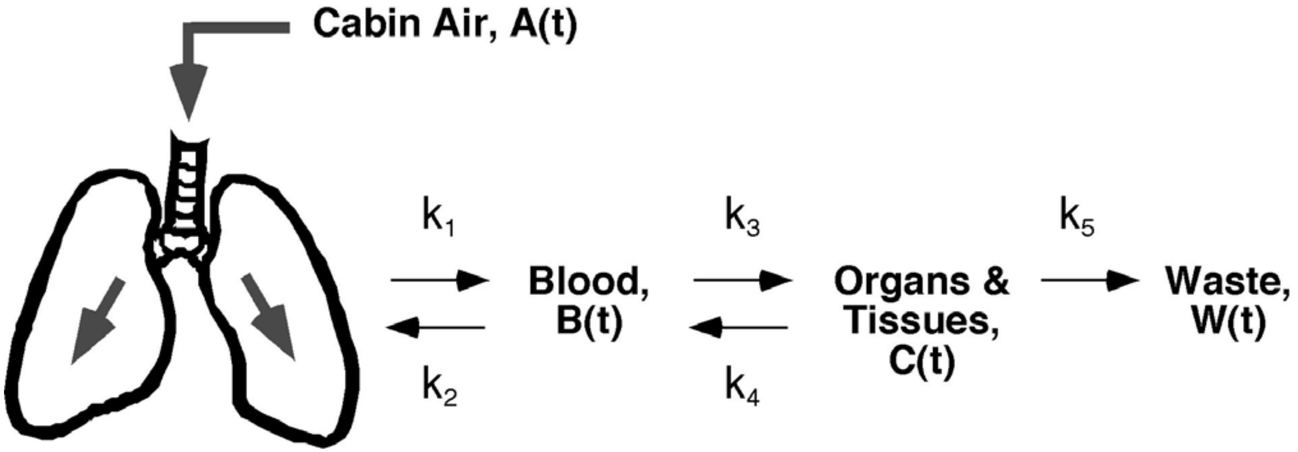
PBPK Modeling Approach

- **LOAEL**
  - Lowest observable adverse effect level for a group of dogs exposed to a chemical **(%V/V)**
- **Standard FAA-accepted PBPK methodology:** is described in
  Allen Vinegar, Gary W. Jepson, Mark Cisneros, Reva Rubenstein, William J. Brock, "Setting Safe Acute Exposure Limits for Halon Replacement Chemicals using Physiologically Based Pharmocokinetic Modeling", *InhalationToxicology. 12, pp. 751-763, 2000.*
- **Human PBPK Model**
  - Describes the uptake, distribution, metabolism, and elimination of inhaled halocarbons in the human body.
  - This PBPK model includes a respiratory-tract region and a pulmonary exchange area
  - **Partition Coefficients:**
    - Liver
    - Fat
    - Lung
    - Gut
    - Slowly perfused tissues
    - Rapidly perfused tissues

PBPK Modeling Approach (cont.)

- **Human PBPK Model (cont)**
  - **Monte Carlo Method:**
    - ❖Monte Carlo simulations describe the effect of interindividual variability on the output of PBPK models : 2 standard deviations.
    - ❖Accounts for **95%** of the simulated population
  - **Target arterial Concentration:**
    - ❖ Out of a group of dogs exposed to each chemical at the LOAEL gas concentration, the lowest measured 5-min arterial concentration was taken as the target arterial concentration for use in modeling human exposure.
    - ❖Target arterial concentration: same for dogs and humans

Simplified Kinetic Model



- **Allows simulation of human arterial blood concentration histories from inhaled constant or dissipating halocarbon concentrations**

- **The partition coefficients between the blood and air (P_{BA}) and the tissues and air (P_{CA}) are:**

$$P_{BA} = \frac{B(\infty)}{A_0} = \frac{k_1}{k_2} \quad \text{and} \quad P_{CA} \equiv \frac{C(\infty)}{A_0} = \frac{C(\infty)}{B(\infty)} \frac{B(\infty)}{A_0} = \frac{k_3}{k_4} \frac{k_1}{k_2} = \frac{k_3}{k_4} P_{BA}$$

Simplified Kinetic Model:

- **General Solution:** $$B(t) = A_0\alpha\left(e^{-t/\tau} - e^{-k_{23}t}\right) + A_0\beta t e^{-t/\tau}$$

Constants: $\alpha = \dfrac{k_1 - \beta}{k_{23} - 1/\tau}; \quad \beta = \dfrac{k_3 k_4 P_{BA}}{k_{23} - 1/\tau}; \quad k_{23} = k_2 + k_3$

Unventilated Compartment (τ = ∞)

- **HCFCs: Assume: k_5=0**

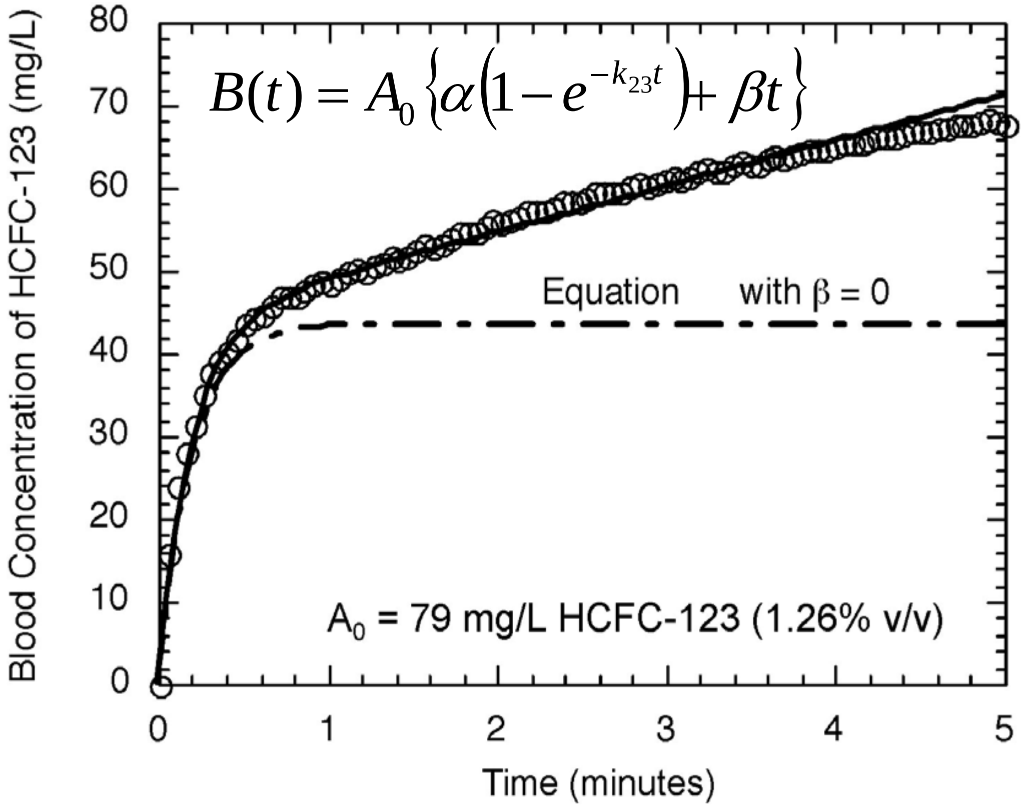
$$B(t) = A_0\left\{\alpha\left(1 - e^{-k_{23}t}\right) + \beta t\right\}$$

Constants reduce to: $\alpha = \dfrac{k_1}{k_{23}}; \quad \beta = \dfrac{k_3 k_4 P_{BA}}{k_{23}}$

Simplified Kinetic Model for HCFC-123:

Unventilated Compartment <u>($\tau = \infty$)</u>

- Plot solution to equation using best-fit parameters :



Best-Fit Parameters

α= 0.55,

β= 0.07 min^{-1},

k_{23} = 5 min^{-1}

Simplified Kinetic Model for Non- HCFCs :

Unventilated Compartment ($\tau = \infty$)

- **Halon 1301 and HFCs:** Assume: $k_4 = k_5 = 0$

  Constants reduce to: $\alpha = \frac{k_1}{k_2}; \quad \beta = 0$

  $$B(t) = A_0 \frac{k_1}{k_2}\left(1 - e^{-k_2 t}\right)$$

Simplified Kinetic Model:

Rate Constants for Human Arterial Uptake and Elimination

Halocarbon	k_1 (min^{-1})	$k_{2,3}$ (min^{-1})
HCFC-123a	2.75	5.0
HFC-227ea	0.1610	5.36
HFC-236fa	0.3616	3.924
Halon 1211	[a]	[a]
Halon 1301	0.2578	4.25

a. The PBPK modeling results are not available since the required input canine blood LOAEL arterial blood concentrations and partition coefficients, are not available.

Halon 1211 PBPK-Based Maximum Safe W/V

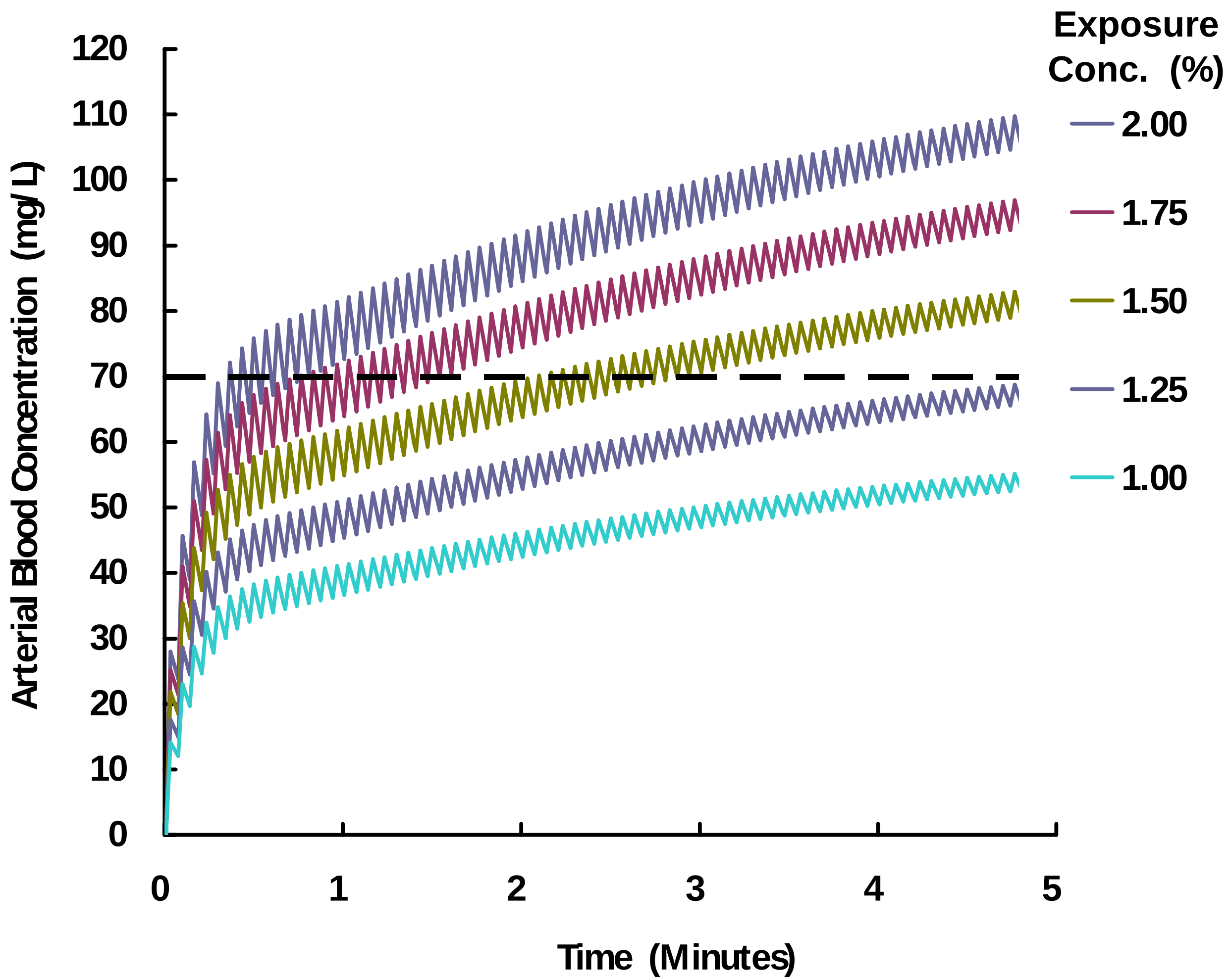
- **Halon 1211 PBPK Modeling Efforts don't meet requirements:**
  - Al Vinegar et al's Halon1211 PBPK modeling articles:
    - Precursor to the more robust modeling efforts that followed.
    - There is no measured dog arterial blood concentration at the LOAEL cardiac sensitization (CS) gas concentration.
    - The human PBPK model was run at the LOAEL 1% gas concentration to simulate arterial blood concentrations to establish the "target" CS blood level of Halon 1211.
  - We can not locate references for the partition coefficients
  - A Monte Carlo sort was not used: Clearly stated

- **Solution:**
  - Use NOAEL concentration in place of the maximum safe human exposure concentration to calculate the Maximum Safe W/V
  - In the absence of a conforming PBPK solution, selector curves were not developed for the maximum safe Halon 1211 W/V for ventilated aircraft compartments.

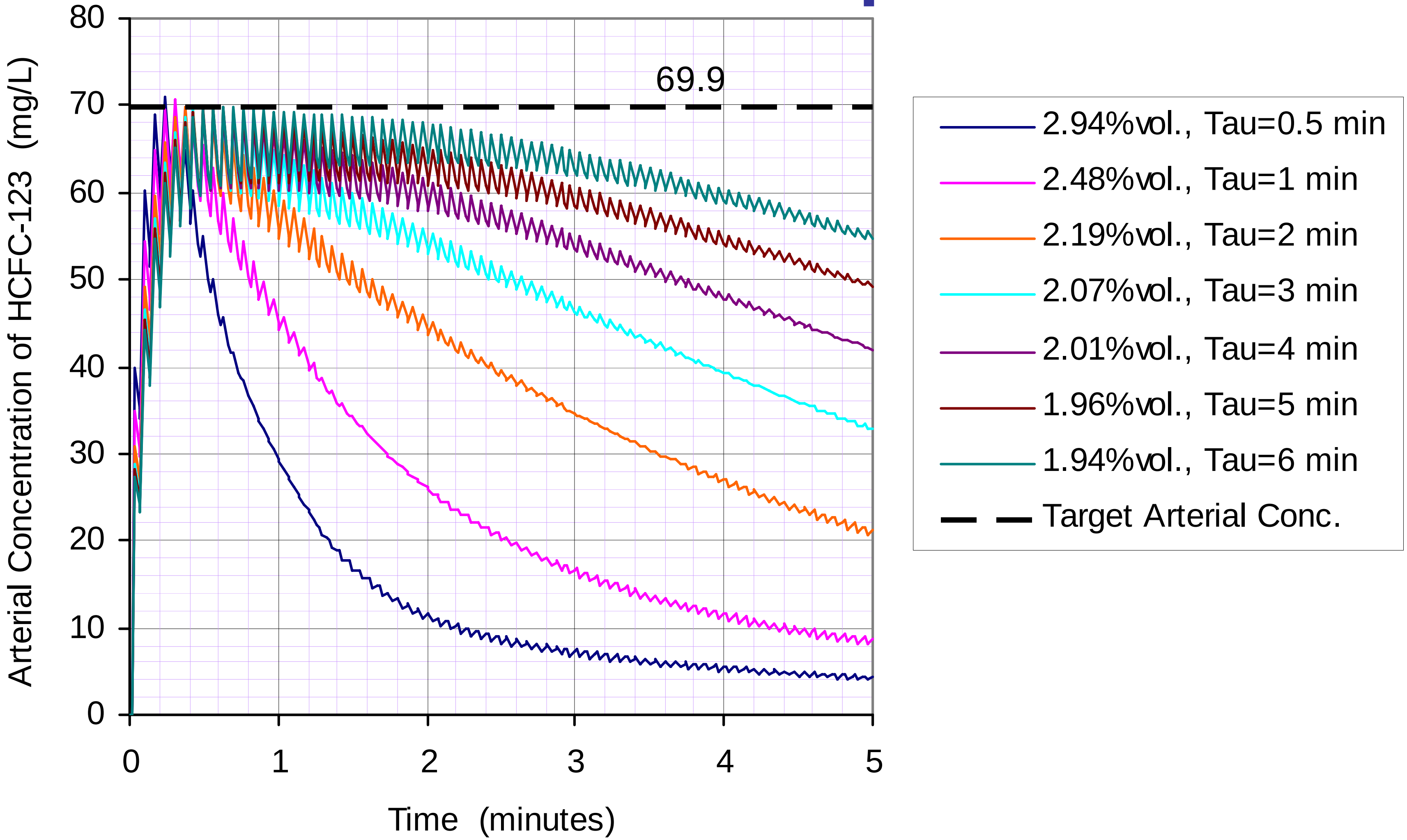
HCFC-123 PBPK-Based Maximum Safe W/V

- **Data presented for HCFC Blend B to obtain the target 5 minute concentration was reviewed.**
- **HCFC-123 target arterial concentration does not conform to the selection method for Halon 1301, HFC-227ea, and HFC-236fa.**
  - Selection method must be consistent with methodology from Vinegar et al 2000 and Huntington canine data.
  - Target arterial HFC-123 concentration drops from 83.3mg/g to 69.9 mg/g.
  - Safe 5 minute concentration drops from 1.5% to 1.26%.
- **Data is presented in following slides:**

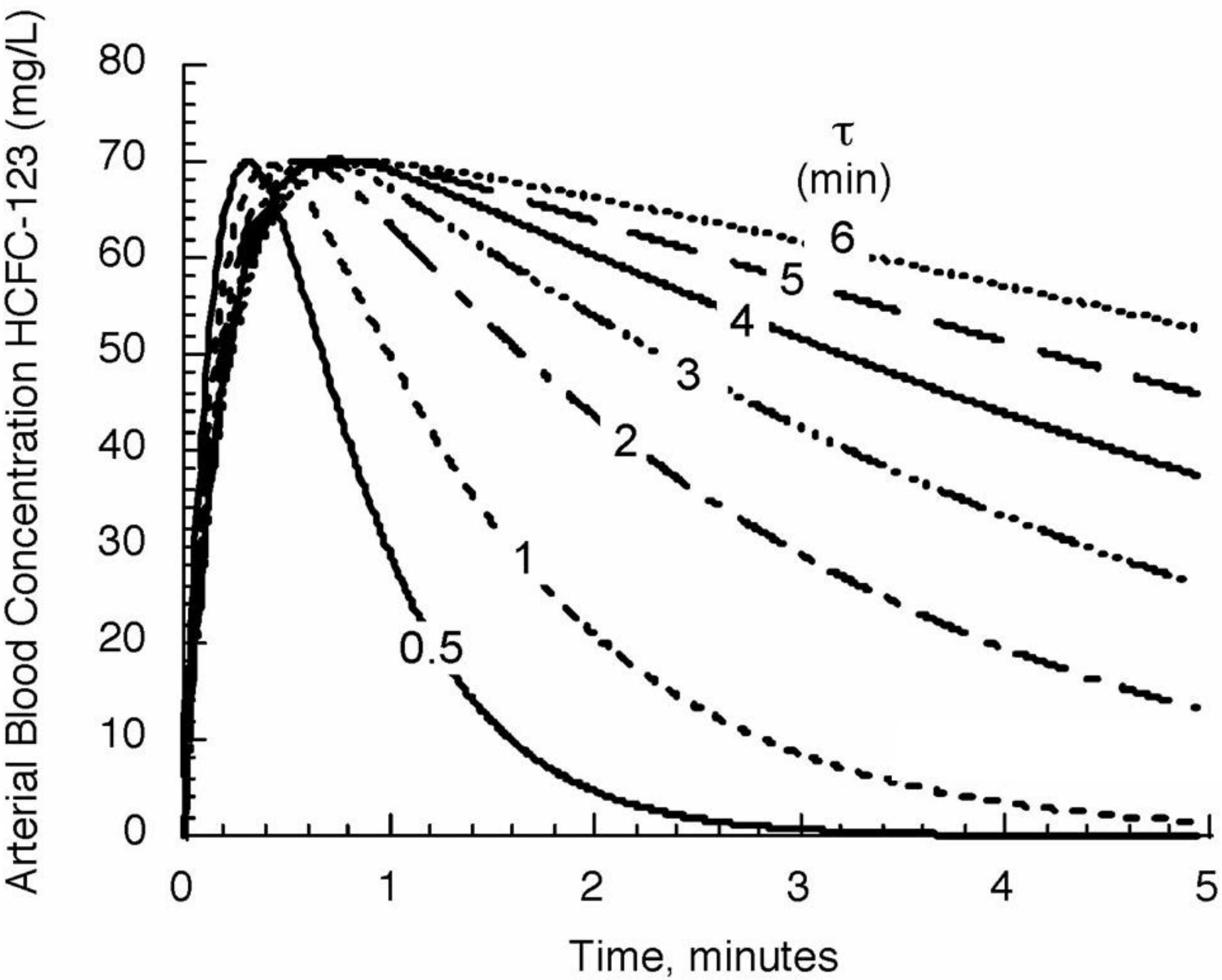
PBPK Modeling + 2SD of Constant Concentrations of HCFC-123



PBPK Modeling of HCFC 123: Ventilated Compartments



1st Order Kinetic Modeling of HCFC 123: Ventilated Compartments



Maximum Safe Initial Discharge Concentrations (%V/V) for Ventilated Compartments

Agent	Air Change Time, τ (Minutes)							
	0.5	**1.0**	**2.0**	**3.0**	**4.0**	**5.0**	**6.0**	**> 6.0[a]**
Halon 1211[b]	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Halon 1301	12.31	9.83	8.38	7.83	7.52	7.32	7.19	6.25
HCFC-123[c]	2.94	2.48	2.19	2.07	2.01	1.96	1.94	1.26
HCFC Blend B	2.94	2.48	2.19	2.07	2.01	1.96	1.94	1.26
HFC-227ea	19.55	15.95	13.87	13.06	12.67	12.40	12.16	10.84
HFC-236fa	25.82	20.45	17.48	16.11	15.42	15.02	14.76	12.75

a. Unventilated value.

b. Halon 1211 was assigned no aircraft ventilation benefit, as suitable PBPK modeling data was not available that meets the guidelines.

c. Obtained by PBPK modeling

Maximum Safe Exposure Concentrations No Ventilation

Agent	NOAEL (%v/v)	Max Safe 5 Minute Human Exposure Concentration (%v/v)	C_{Safe} (%v/v)
HCFC Blend B	1.0	1.26	1.26
HFC-227ea	9.0	10.84	10.84
HFC-236fa	10.0	12.75	12.75
Halon 1211	0.5	N/A	0.5
Halon 1301	5.0	6.25	6.25

Maximum Safe W/V: No Ventillation

Agent	Maximum Safe W/V (lbs/ft^3)					
	Sea Level (For info only)	Pressurized Aircraft (8k ft. CPA)	Non-Pressurized Aircraft			
			12.5k ft.	14k ft.	18k ft.	25k ft.
HCFC Blend B	0.00491	0.00365	0.00306	0.00288	0.00245	0.00182
HFC-227ea	0.0551	0.0409	0.0344	0.0324	0.0275	0.0205
HFC-236fa	0.0595	0.0442	0.0371	0.0349	0.0297	0.0221
Halon 1211	0.00224	0.00166	0.00139	0.00131	0.00112	0.000829
Halon 1301	0.0260	0.0193	0.0162	0.0153	0.0130	0.00968

Minimum Safe Compartment Volumes No Ventilation

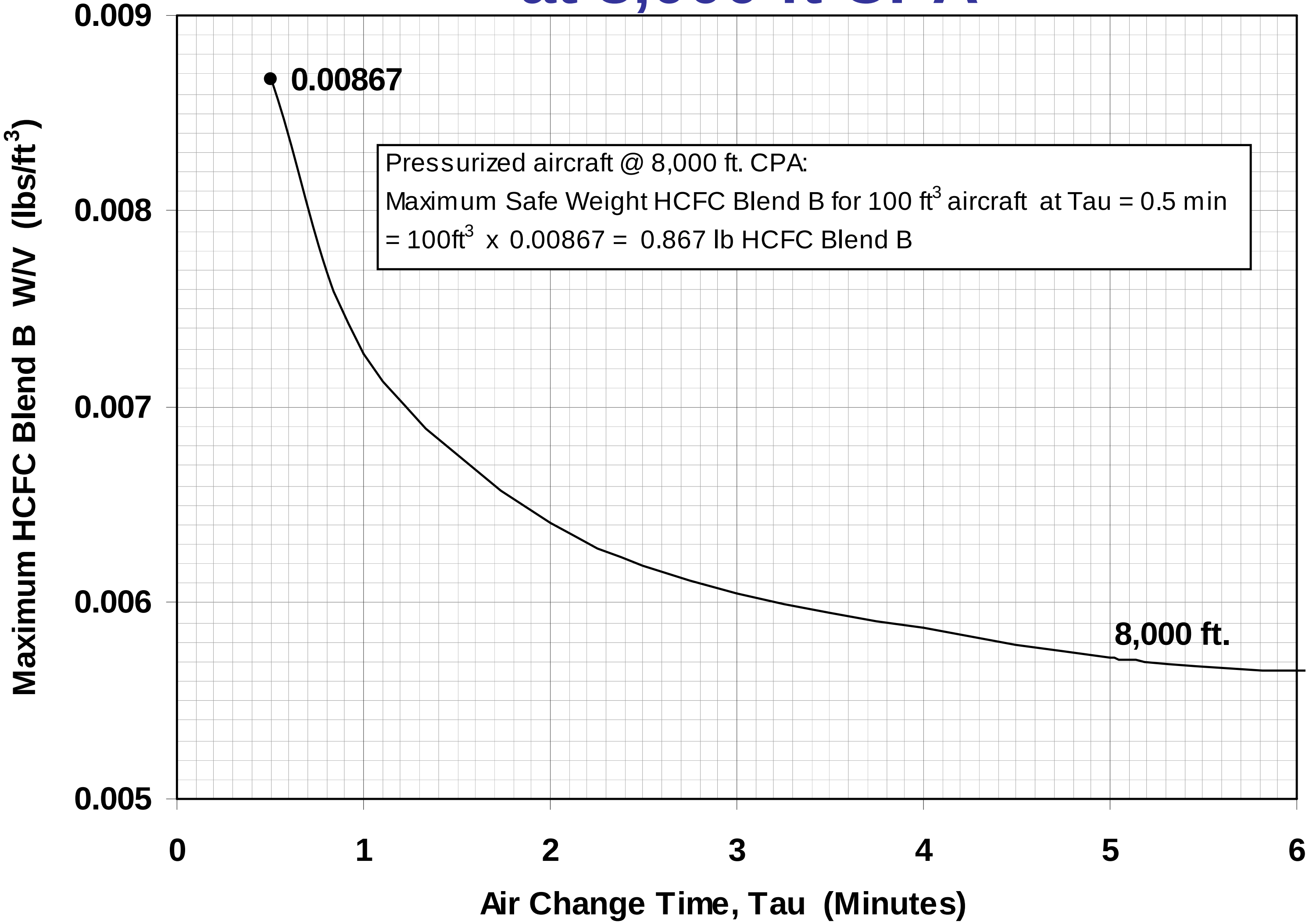
Agent	Agent Weight (lbs)	Minimum Safe Volume For One 5 B:C Extinguisher (ft^3)					
		Sea Level (for info only)	Pressurized Aircraft	Non-Pressurized Aircraft			
			8,000 ft CPA	12,500 ft	14,000 ft	18,000 ft	25,000 ft
HCFC Blend B	5.5	1120	1507	1797	1910	2245	3022
HFC-227ea	5.5	99.8	135	160	170	200	269
HFC-236fa	4.75	79.8	107	128	136	159	214
Halon 1211	2.5	1116	1502	1790	1908	2232	3016
Halon 1301	5.0	192	258	308	327	385	517

Number of 5 B:C Extinguishers That Can be Safely Installed at 8,000 ft CPA

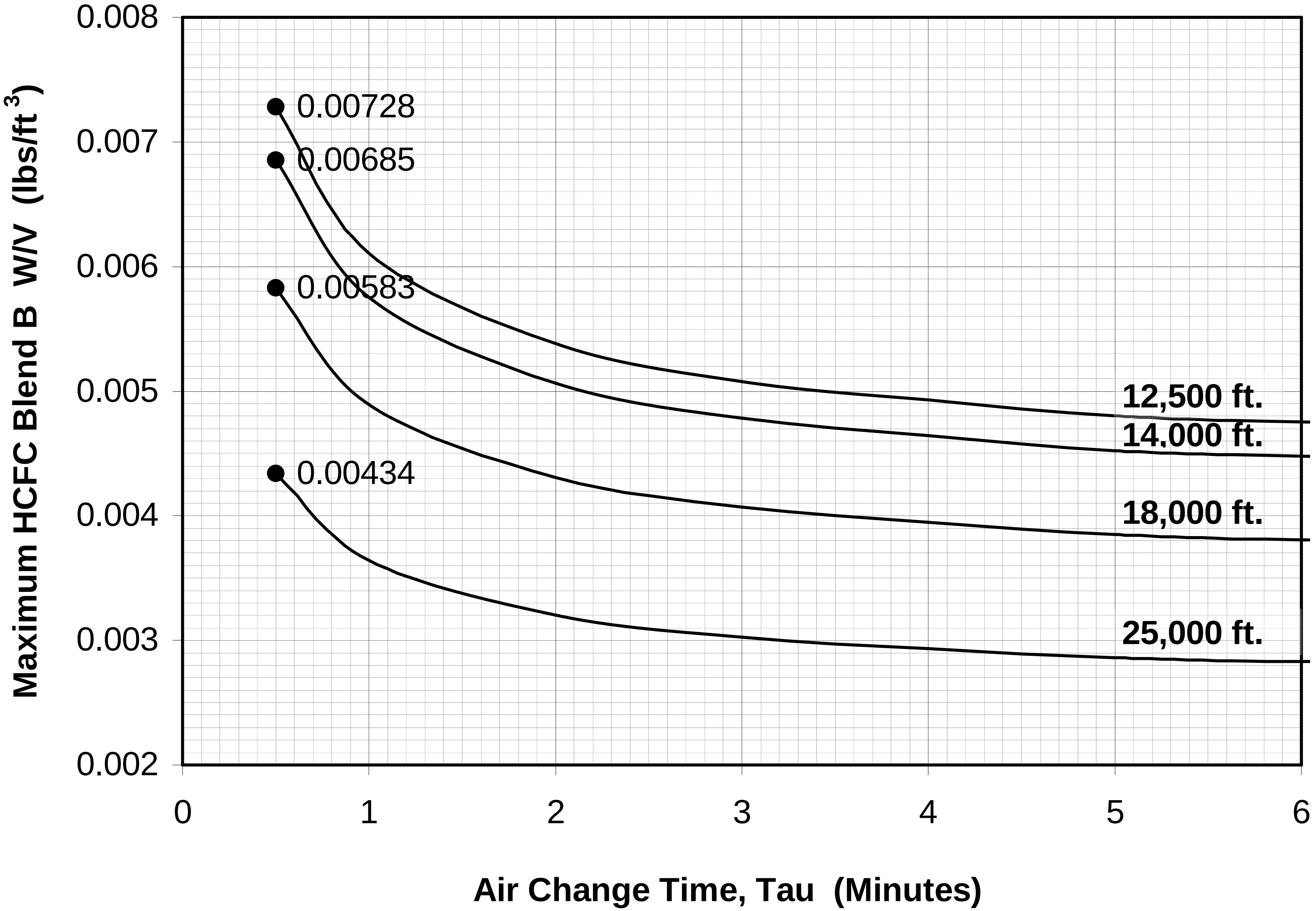
Unventilated

Aircraft	Volume (ft^3)	Max No. Seats	Halon 1211 AC 20-42C and U.S. UL1093	Halon 1211	Halon 1301	HCFC Blend B	HFC-236fa	HFC-227ea
C 152	77	2	0.3	**0.05**	0.3	**0.05**	0.7	0.5
C 210C	140	6	0.5	**0.09**	0.5	**0.09**	1.3	1.0
S76	204	14	0.7	**0.1**	0.8	**0.1**	1.9	1.4
C 421B	217	10	0.7	**0.1**	0.8	**0.1**	2.0	1.5
ERJ135	968	37	3.1	**0.6**	3.8	**0.6**	9.0	6.9
CRJ200	2015	50	6.5	**1.3**	7.8	**1.3**	19	14
B727-100	5,333	131	17	**3.5**	21	**3.5**	50	38
B767-200	11,265	255	36	**7.5**	43	**7.5**	105	80
B747	27,899	500	90	**18**	108	**19**	260	198

Maximum Safe HCFC Blend B W/V at 8,000 ft CPA



Maximum HCFC Blend B W/V



Halocarbon Blends

The maximum safe W/V for a blend can be calculated from the maximum safe W/V of halocarbon A and the maximum safe W/V of halocarbon B as follows:

$$\left(\frac{W_{A+B}}{V}\right)_{Safe} = \chi_A \times \left(\frac{W_A}{V}\right)_{Safe} + \chi_B \times \left(\frac{W_B}{V}\right)_{Safe}$$

where $\chi_A + \chi_B = 1$

and $\chi_A = \frac{n_A}{n_A + n_B}$ $\chi_B = \frac{n_B}{n_A + n_B}$

and $n_A = \frac{m_A}{MW_A}$ $n_B = \frac{m_B}{MW_B}$

ENVIRONMENTAL PROPERTIES

Agent	Formula	ODP	GWP (100 yr)[a]	Atmospheric Lifetime (Years)
Halon 1301	CF_3Br	12	2,700	65
HFC-227ea	CF_3CHFCF_3	0	3800	36.5
Halon 1211	CF_2ClBr	5.1	1300	11
HFC-236fa	$CF_3CH_2CF_3$	0	9400	226
HCFC Blend B	Blend	[b]	[b]	[b]
HCFC-123	CHCl2CF3	0.016	120	2
PFC-14	CF_4	0	5700[b]	50,000
2-BTP	CF_3CBrCH_2	0	1	0.008

[a] From: *Scientific Assessment of Ozone Depletion: 1998, World Meteorological Organization, Global Ozone Research Monitoring Project- Report No. 44*, 1998.

[b] This blend contains a PFC in small proportions