A Simplified Kinetic Model for Predicting Arterial Blood Concentrations for Humans Exposed to Gaseous Halocarbon Fire Extinguishing Agents

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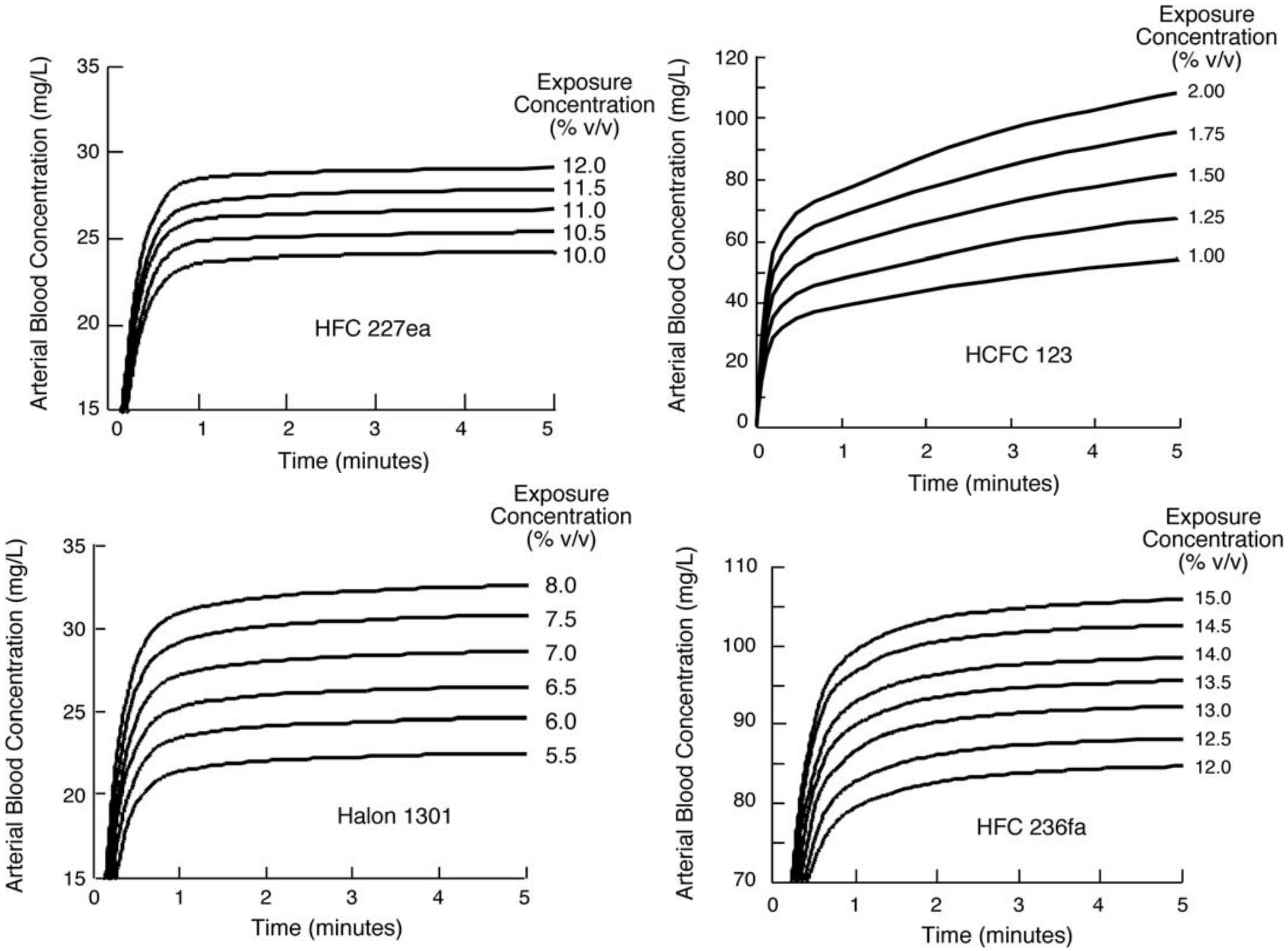
Goal

Provide an economical methodology for calculating safe human exposure limits for time-varying concentrations of gaseous halocarbon fire extinguishing agents when only PBPK-derived human blood concentration histories for constant exposure concentrations are available.

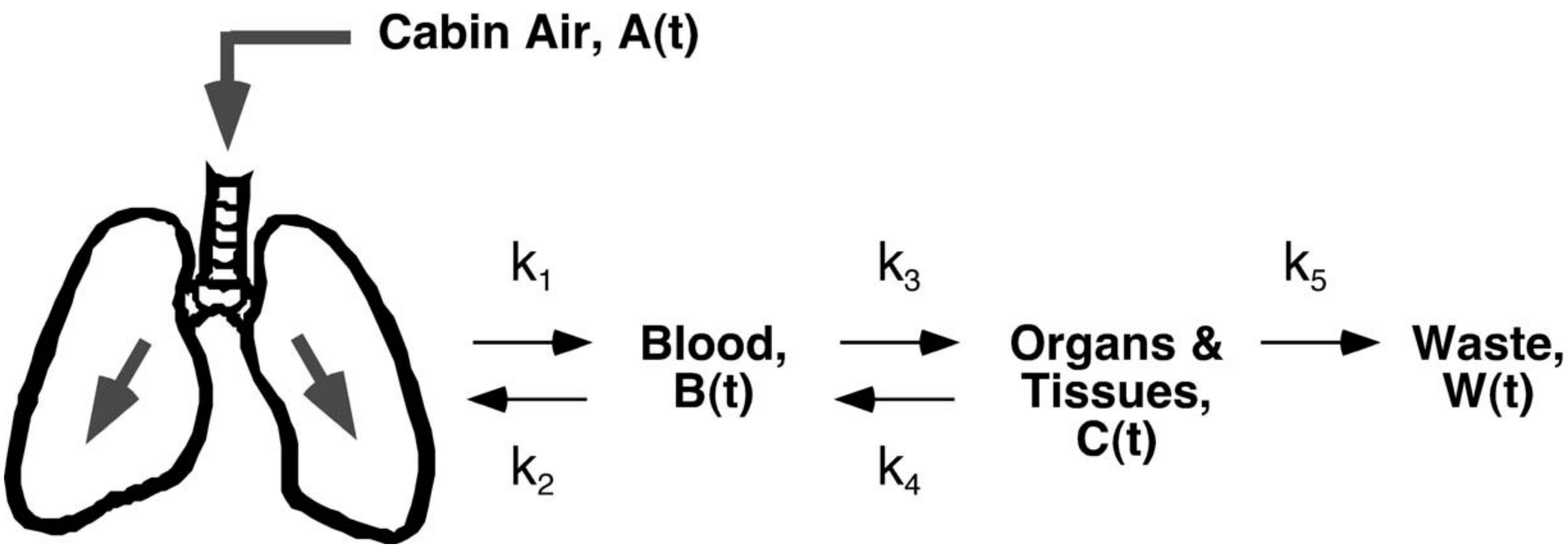
Outline

- Develop a simplified kinetic model to predict the blood concentration history for human inhalation of time varying concentrations of halocarbon fire extinguishing agents.
- Calibrate the simplified kinetic model using published PBPK-derived arterial concentration histories for constant concentration exposure to several fire extinguishing agents.
- Use calibrated kinetic model to predict human arterial blood concentration histories for time varying exposures.

Arterial Blood Concentrations Obtained from PBPK Modeling of Simulated Human Exposure to Constant Halocarbon Concentrations



Kinetic Model of Halocarbon Transport in Humans



$$\frac{dB}{dt} = k_1 A - k_2 B - k_3 B + k_4 C$$

$$\frac{dC}{dt} = k_3 B - k_4 C - k_5 C$$

Kinetic Model of Halocarbon Transport in Humans

- The instantaneous concentrations of halocarbon in the cabin air, bloodstream, organs and tissues, and waste, are *A*, *B*, *C,* and *W*, respectively.

- If the equilibrium concentrations of halocarbon in the blood and organs and tissues are $B(\infty)$ and $C(\infty)$, respectively, for a constant concentration of halocarbon in the air $A(t) = A_0$, the partition coefficients for the halocarbon between blood and air (P_{BA}) and between the tissues and air (P_{CA}) are:

$$P_{\mathrm{BA}} = \frac{B(\infty)}{A_0} = \frac{k_1}{k_2}$$

$$P_{\mathrm{CA}} \equiv \frac{C(\infty)}{A_0} \approx \frac{C(\infty)}{B(\infty)} \frac{B(\infty)}{A_0} = \frac{k_3}{k_4} P_{BA}$$

Kinetic Model Solution for Ventilated Compartment

Gas Concentration History:

$$A(t) = A_0 e^{-t/\tau}$$

Arterial Blood Concentration History:

$$B(t) = A_0 \left\{ \alpha \left(e^{-t/\tau} - e^{-k_{23}t} \right) + \beta \left(e^{-t/\tau} - e^{-k_4 t} \right) \left(1 - e^{-k_{23}t} \right) \right\}$$

The constants are: $\alpha = \dfrac{k_1}{k_{23} - 1/\tau}$; $\beta = \dfrac{k_3 k_4 P_{BA}}{(k_4 - 1/\tau) k_{23}}$

Kinetic Model Solution for Unventilated Compartment

Arterial Blood Concentration History:

$$B(t) = A_0\left(1 - e^{-k_{23}t}\right)\left(\alpha + \beta\left(1 - e^{-k_4 t}\right)\right)$$

$$\alpha = \frac{k_1}{k_{23} - 1/\tau} = \frac{k_1}{k_{23}}; \qquad \beta = \frac{k_3 k_4 P_{BA}}{(k_4 - 1/\tau)k_{23}} = \frac{k_3 P_{BA}}{k_{23}}$$

If halocarbon transport between the tissues and bloodstream is negligible compared to the air-blood process,

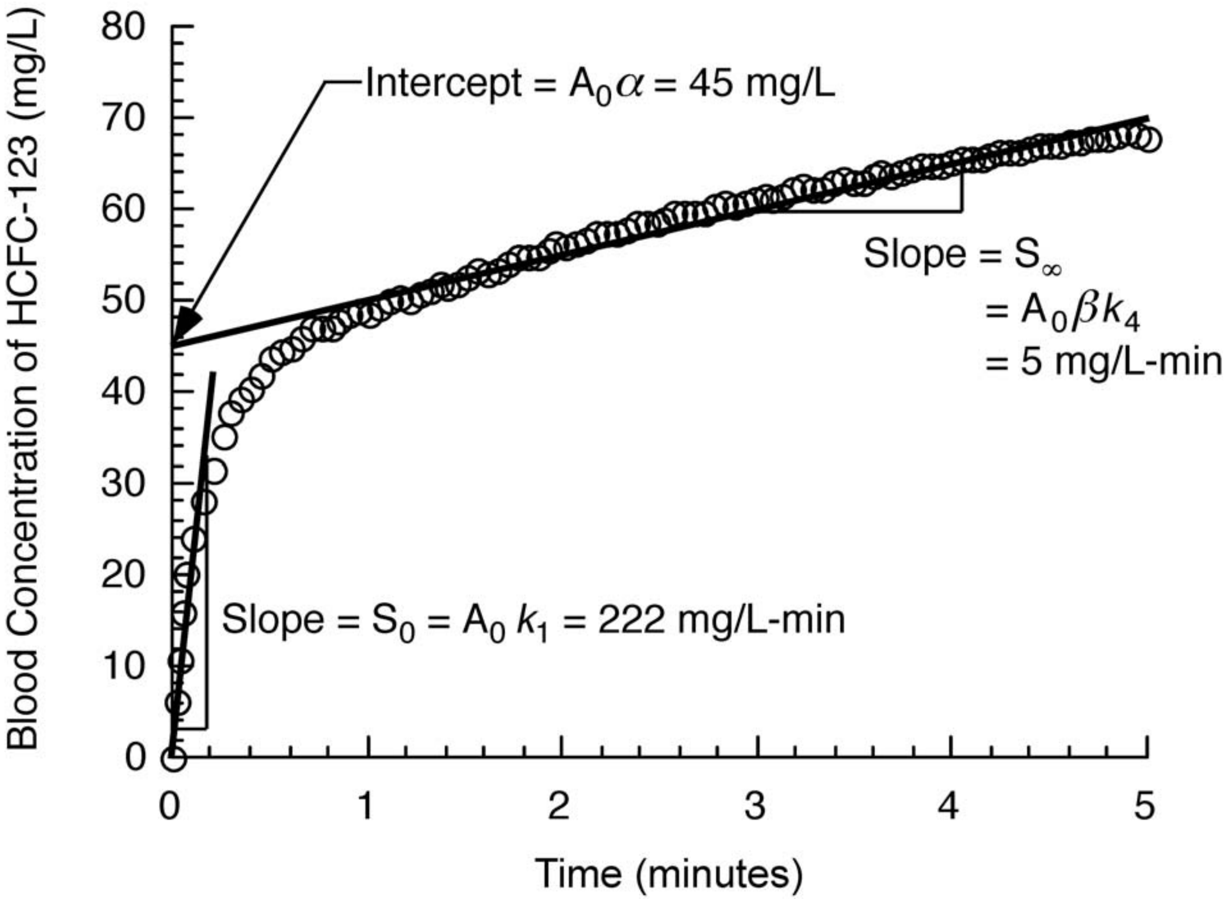
$k_3 = k_4 = 0$, $\beta = 0$, and above equation simplifies to:

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

Graphical Procedure Used as a First Estimate of Four Parameters

$$B(t) \approx A_0\left(1 - e^{-k_{23}t}\right)\left(\alpha + \beta k_4 t\right)$$

Unventilated Compartment Solution for small k_4



4 Parameters:

$$\alpha = \frac{I}{A_0} \qquad k_{23} = \frac{S_0}{I}$$

$$k_4 = \sqrt{\frac{S_\infty S_0}{A_0\, I\, P_{CA}}}$$

$$\beta = \sqrt{\frac{I\, S_\infty P_{CA}}{A_0 S_0}}$$

$$P_{CA} \equiv \frac{C(\infty)}{A_0} \approx \frac{k_3}{k_4} P_{BA}$$

A_0 = 79 mg/L (1.28%v/v)

Determination of Rate Constants

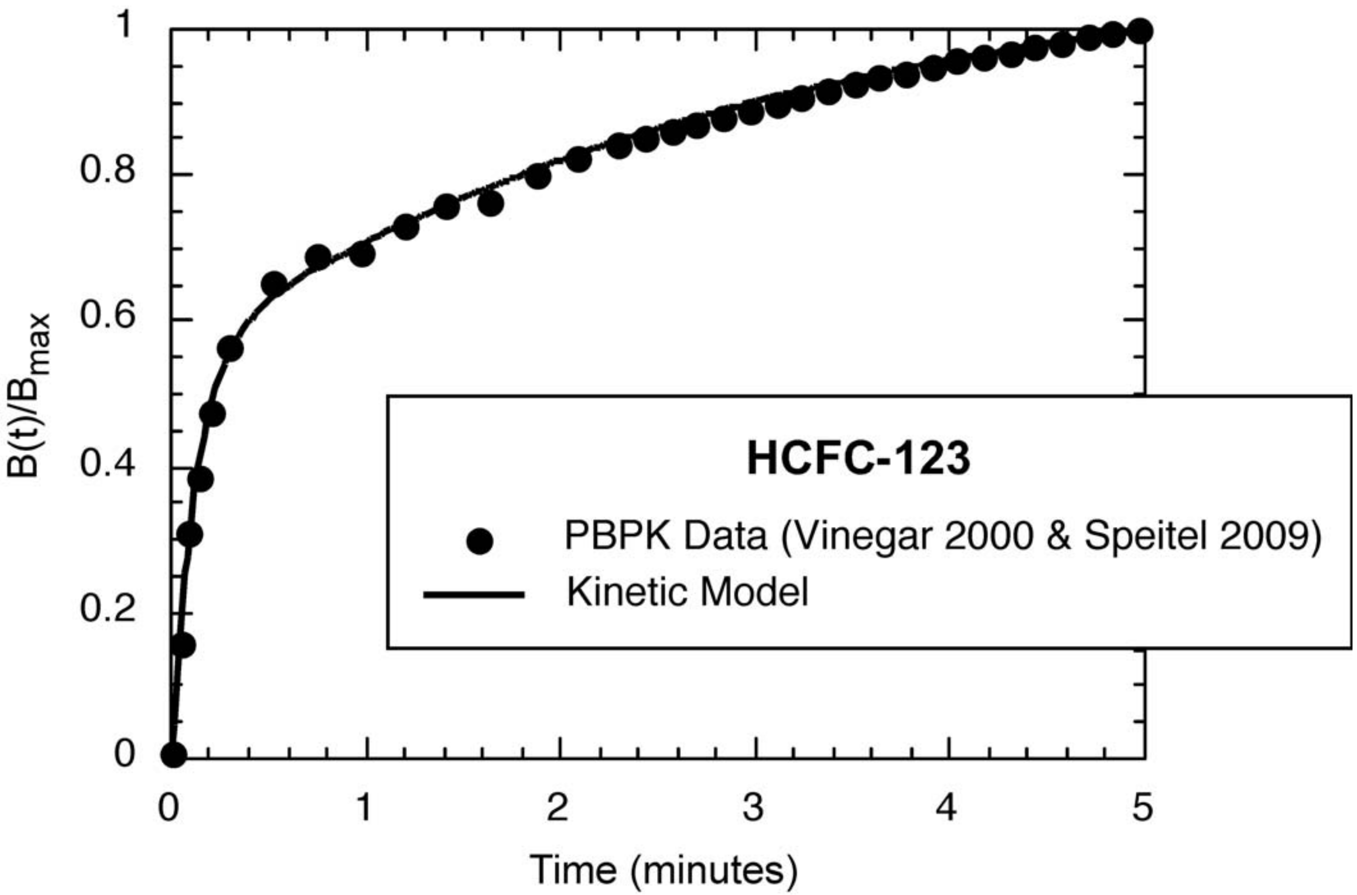
- The rate constants k_1, k_2, k_3, and k_4 for halocarbons are obtained from the initial estimates for k_4, k_{23}, α , β and the P_{BA} using the relationships:
  - $k_1 = \alpha k_{23}$,
  - $k_3 = \langle k_3 \rangle$ = average of $\beta k_{23}/P_{BA}$ and $k_{23} - \langle k_2 \rangle$;
  - $k_2 = \langle k_2 \rangle$ = average of k_1/P_{BA} and $k_{23} - \langle k_3 \rangle$ for each agent.
- *The rate constants are iterated in the formulae (ventilated compartments) until a best fit is obtained by inspection for a constant concentration of the halocarbon in air, A_0.*

Rate Constants for Kinetic Model of Halocarbon Uptake

	Source							
	Partition Coefficient	Fitted Parameter				Calculated From Fitted Parameters		
Agent	P_{BA}	α	β	k_{23} (min^{-1})	k_4 (min^{-1})	k_3 (min^{-1})	k_2 (min^{-1})	k_1 (min^{-1})
Halon 1211	0.12*	0.26	0.050	1.9	0.50	0.6	1.3	0.49
Halon 1301	0.062	0.06	0.003	4.4	0.40	0.1	4.3	0.27
HFC 227ea	0.033	0.03	0.003	4.8	0.10	0.2	4.6	0.16
HFC 236fa	0.106	0.10	0.17	4.1	0.01	0.02	4.08	0.43
HCFC 123	1.16	0.48	0.48	8.5	0.33	4.2	4.3	4.08

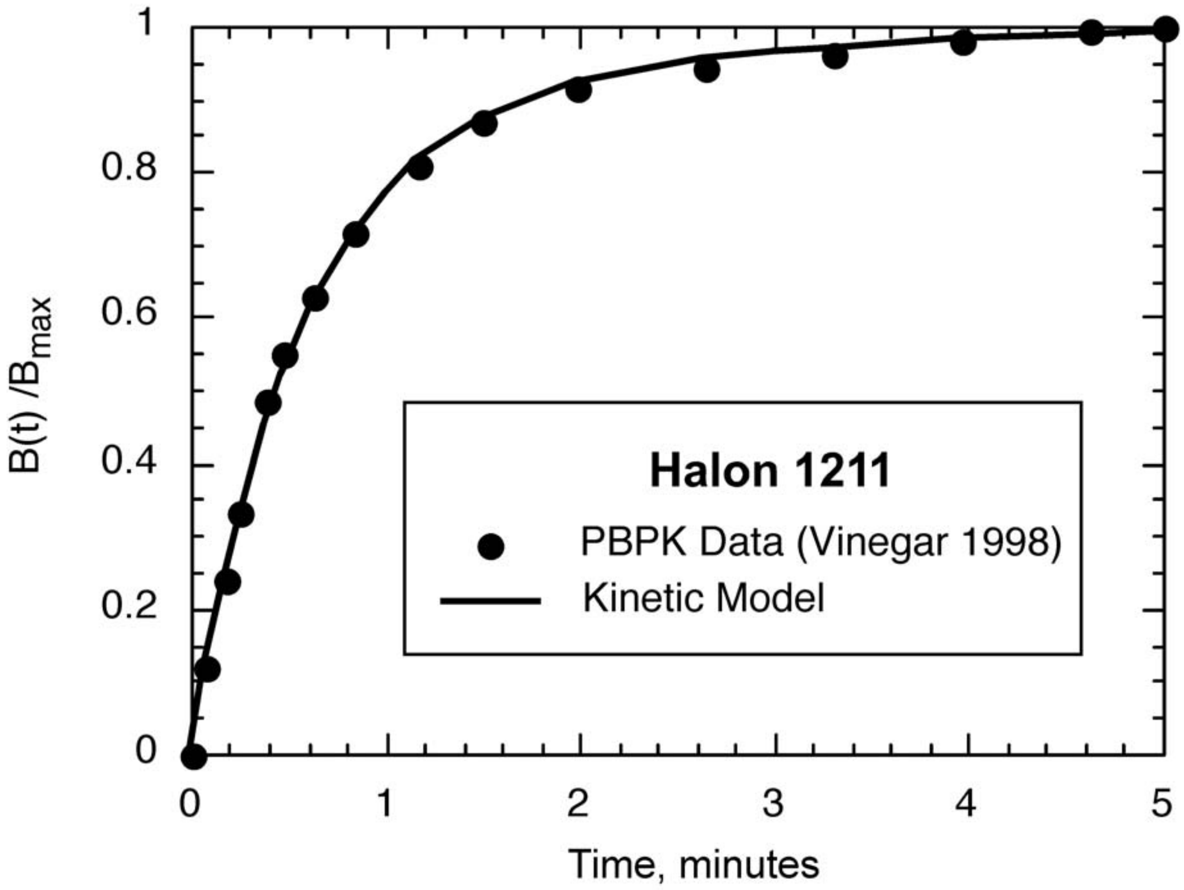
*** $P_{BA} = k_1/\langle k_1/P_{BA}\rangle$, where $\langle k_1/P_{BA}\rangle = 4.2 \pm 0.6\ min^{-1}$ is the average k_1/P_{BA} for the other 4 halocarbons**

Comparison of the Kinetic Model to PBPK Data for Simulated Exposures to HCFC-123



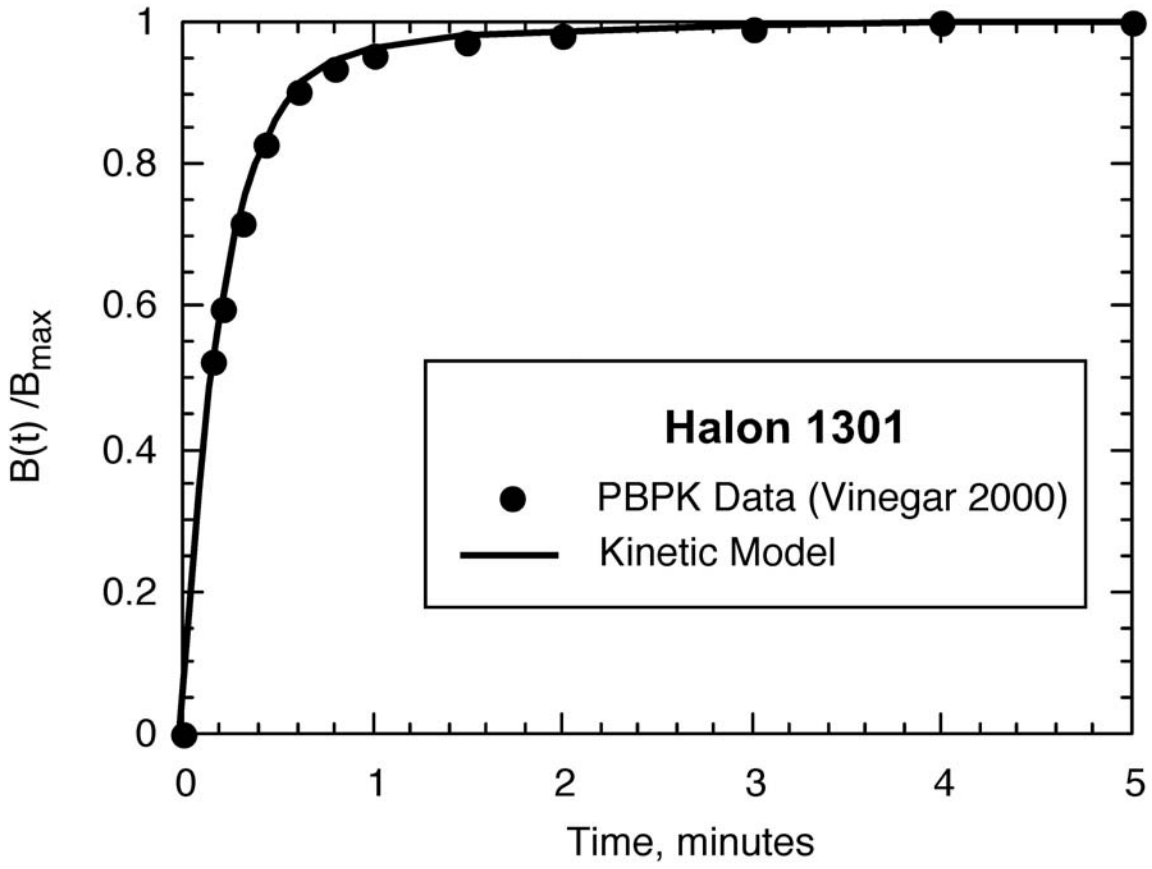
A_0 = 1.28% v/v (79 mg/L)

Comparison of the Kinetic Model to PBPK Data for Simulated Exposures to Halon 1211



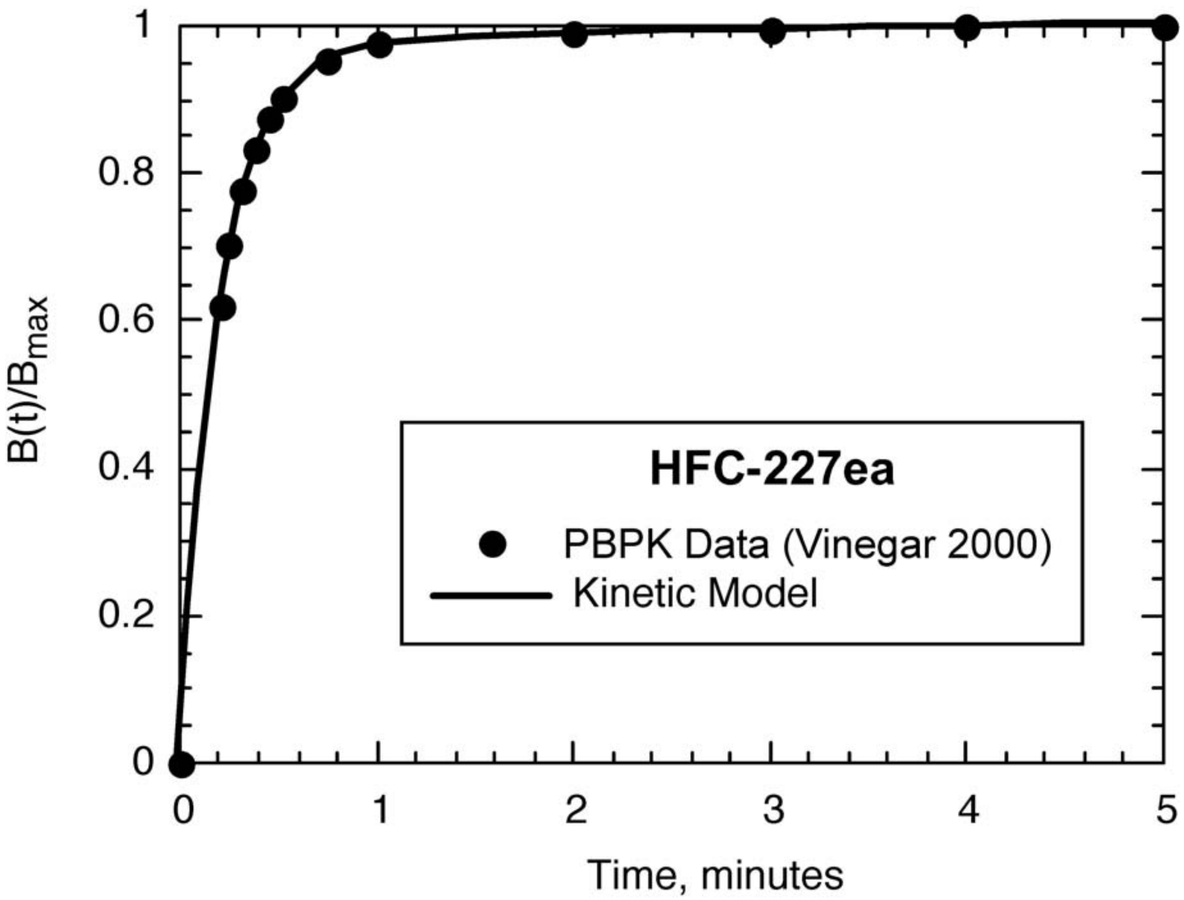
A_0 = 1% v/v (72 mg/L)

Comparison of the Kinetic Model to PBPK Data for Simulated Exposures to Halon 1301



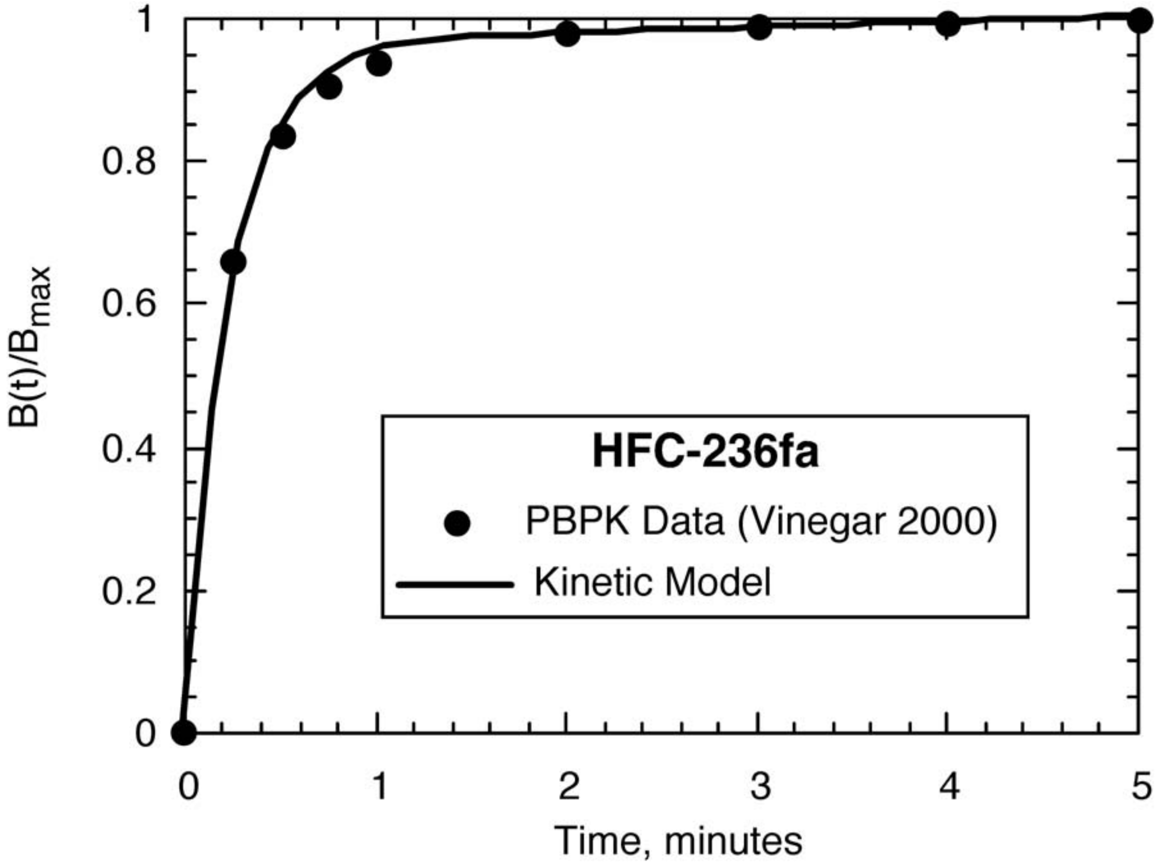
A_0 = 7.0% v/v (439 mg/L)

Comparison of the Kinetic Model to PBPK Data for Simulated Exposures to HFC-227ea



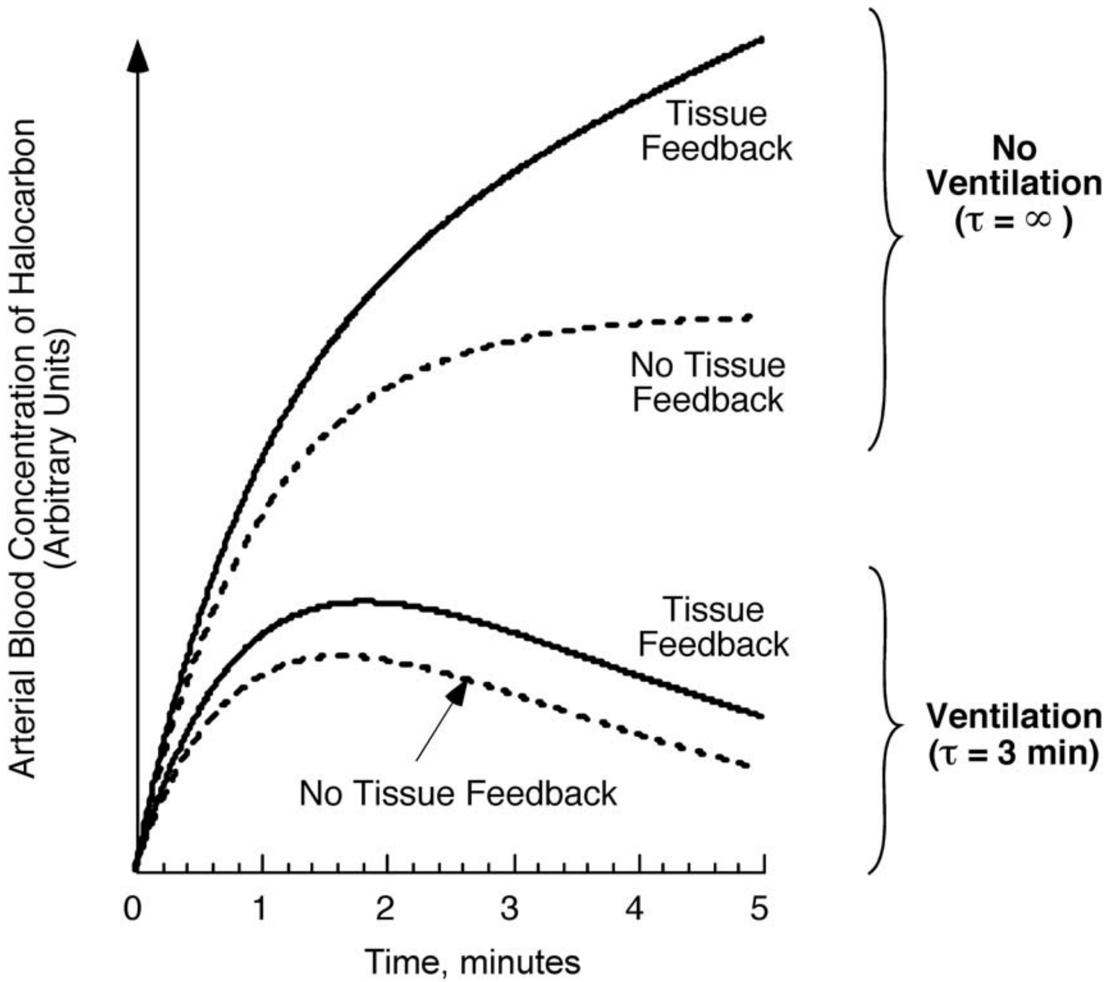
A_0 = 10% v/v (726 mg/L)

Comparison of the Kinetic Model to PBPK Data for Simulated Exposures to HFC-236fa

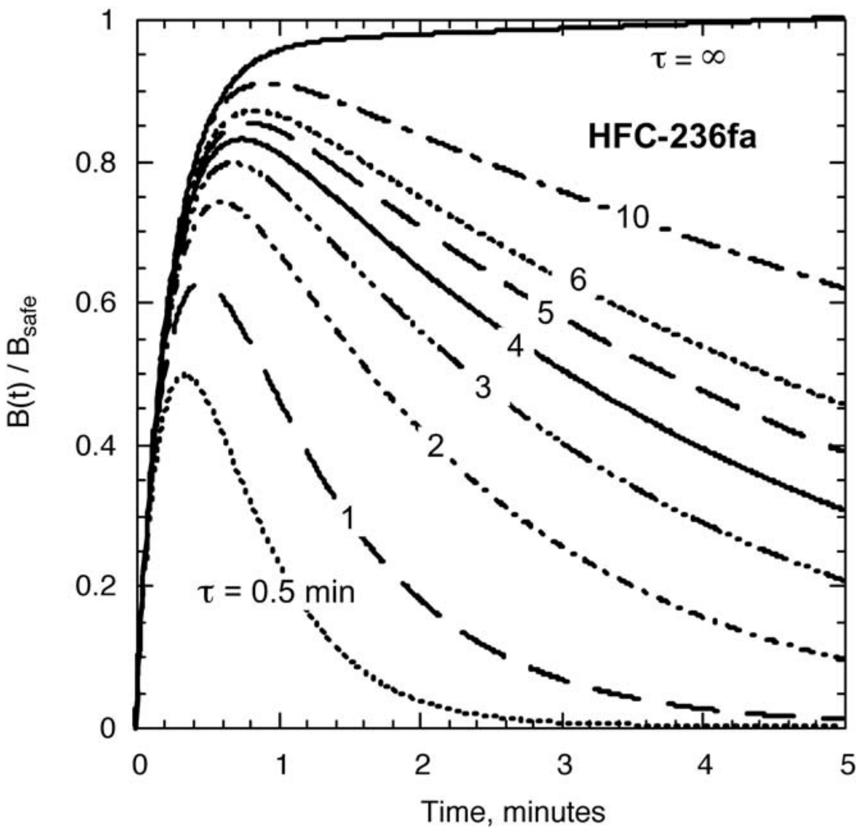


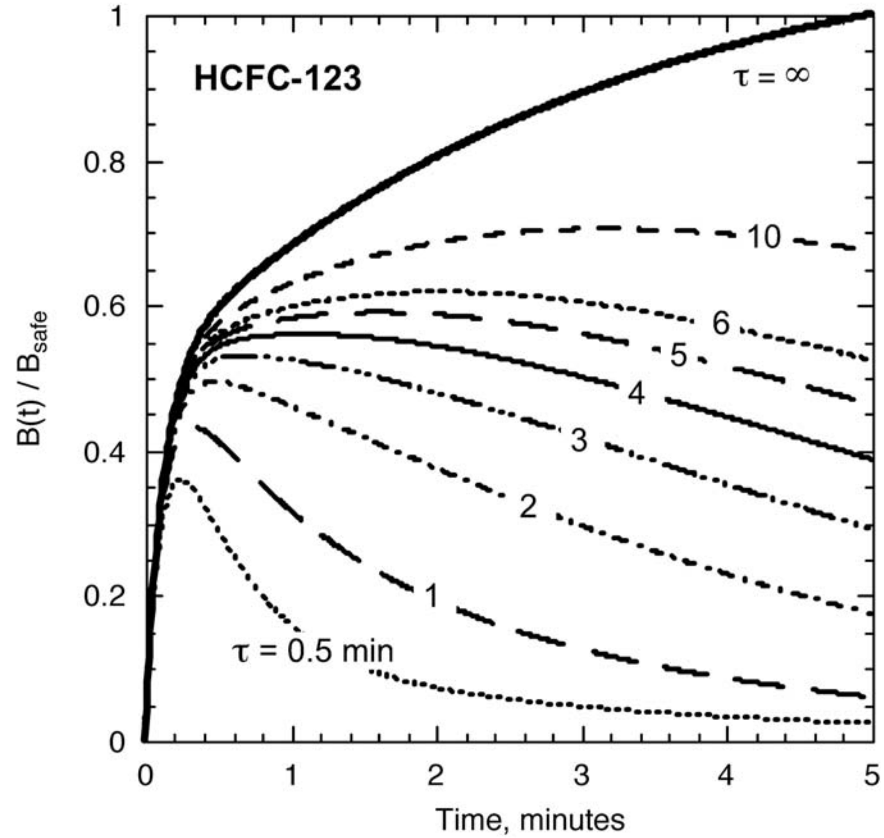
A_0 = 15% v/v (979 mg/L)

Arterial Blood Concentrations Histories for Halocarbon in Ventilated and Unventilated Cabins With and Without Tissue Feedback to the Blood



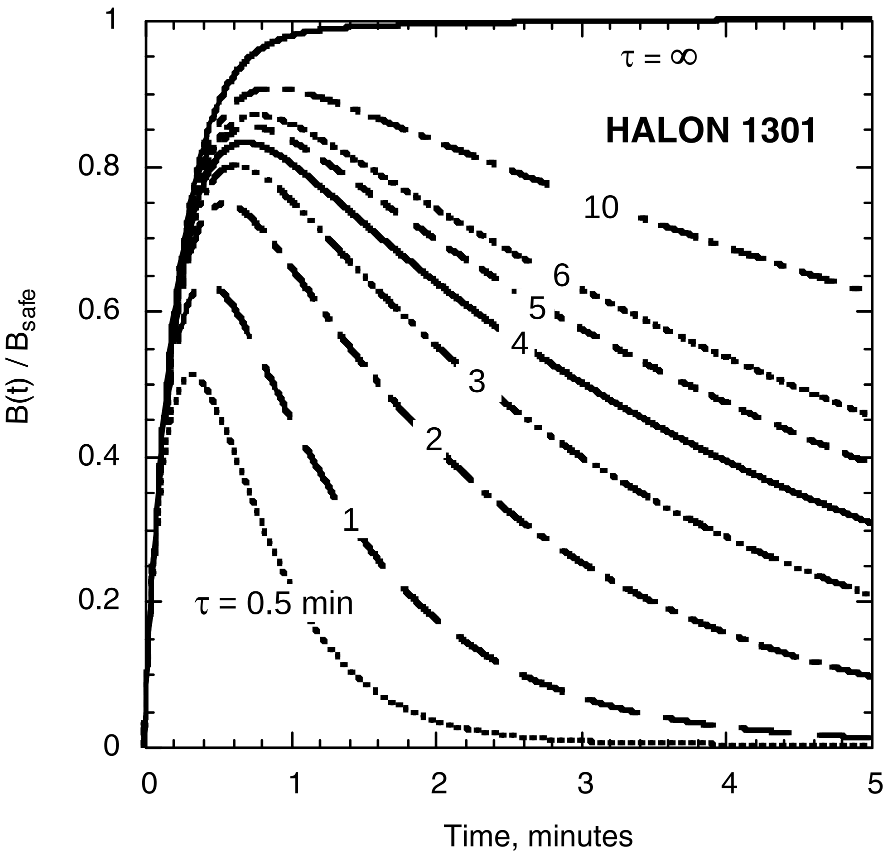
Ratio of the Arterial Blood Concentration to the Target Value B_{Safe} for Simulated Human Exposures to A_{Safe} in a Ventilated Cabin

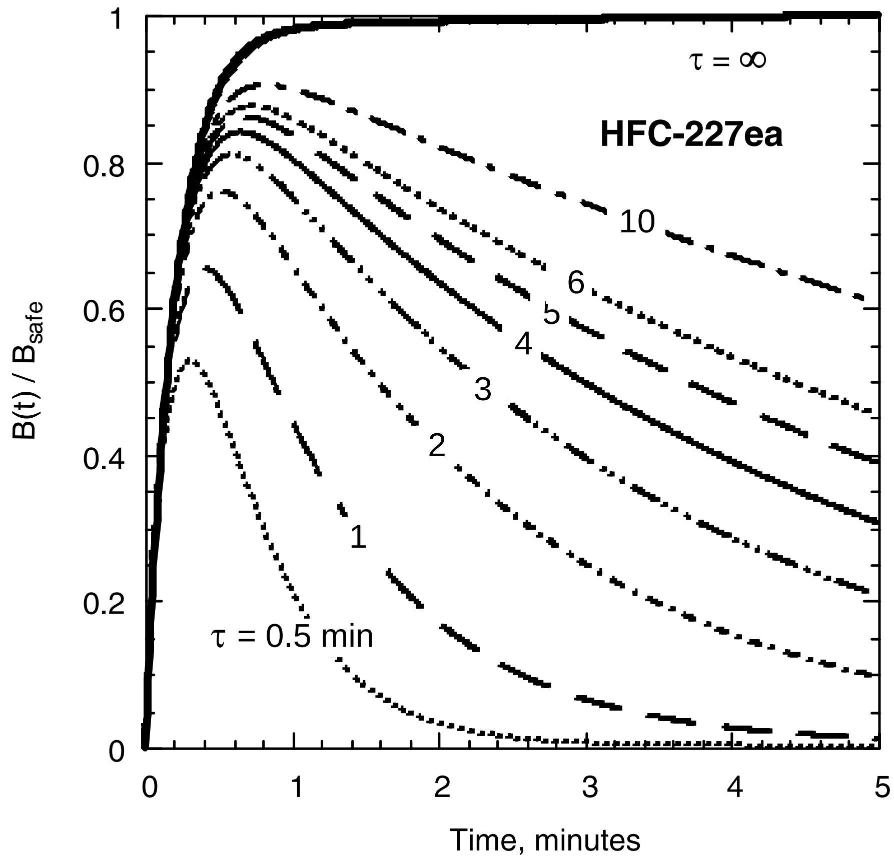




The inverse of $B(t)/B_{safe}$ at its maximum point is the ventilation benefit

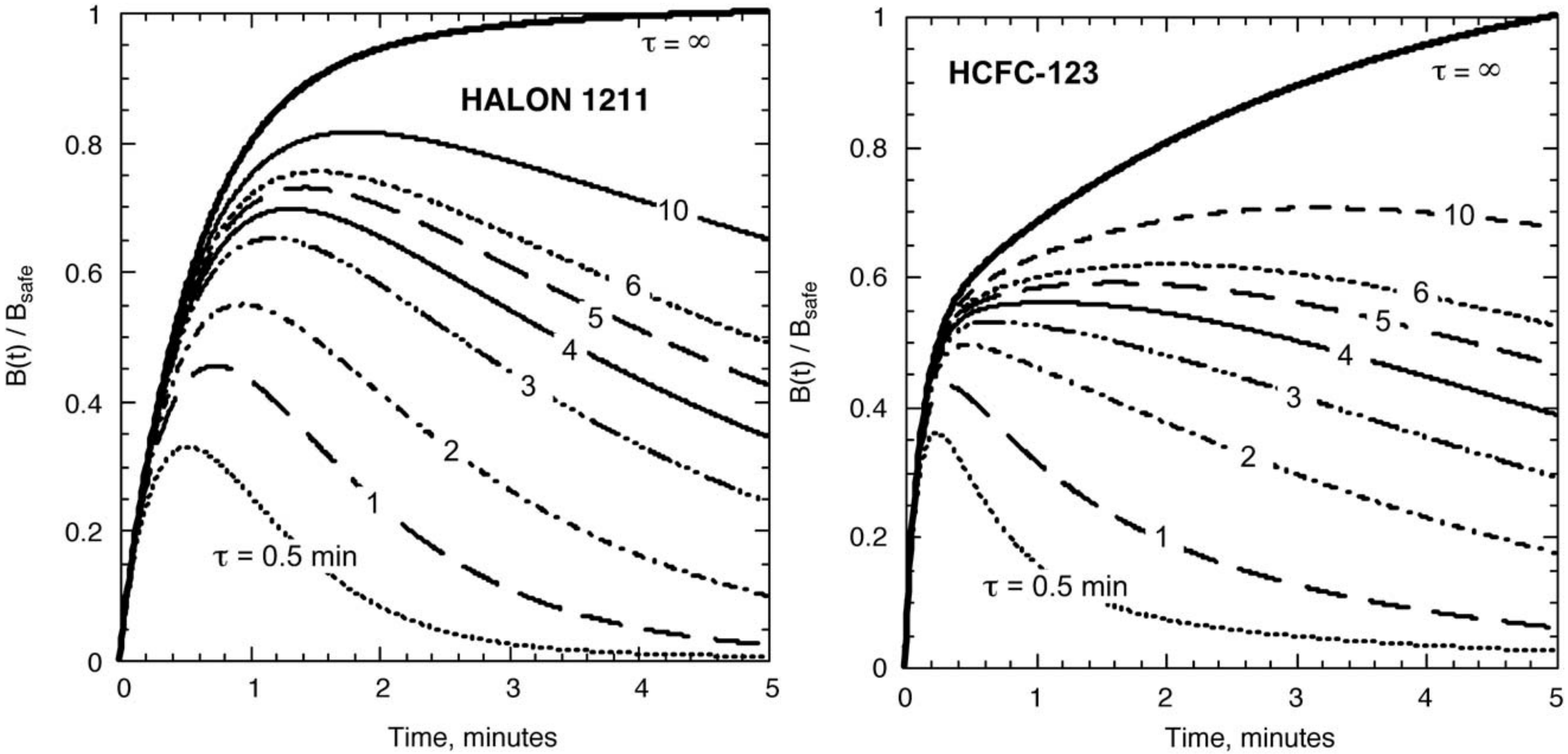
Ratio of the Arterial Blood Concentration to the Target Value B_{Safe} for Simulated Human Exposures to A_{Safe} in a Ventilated Cabin





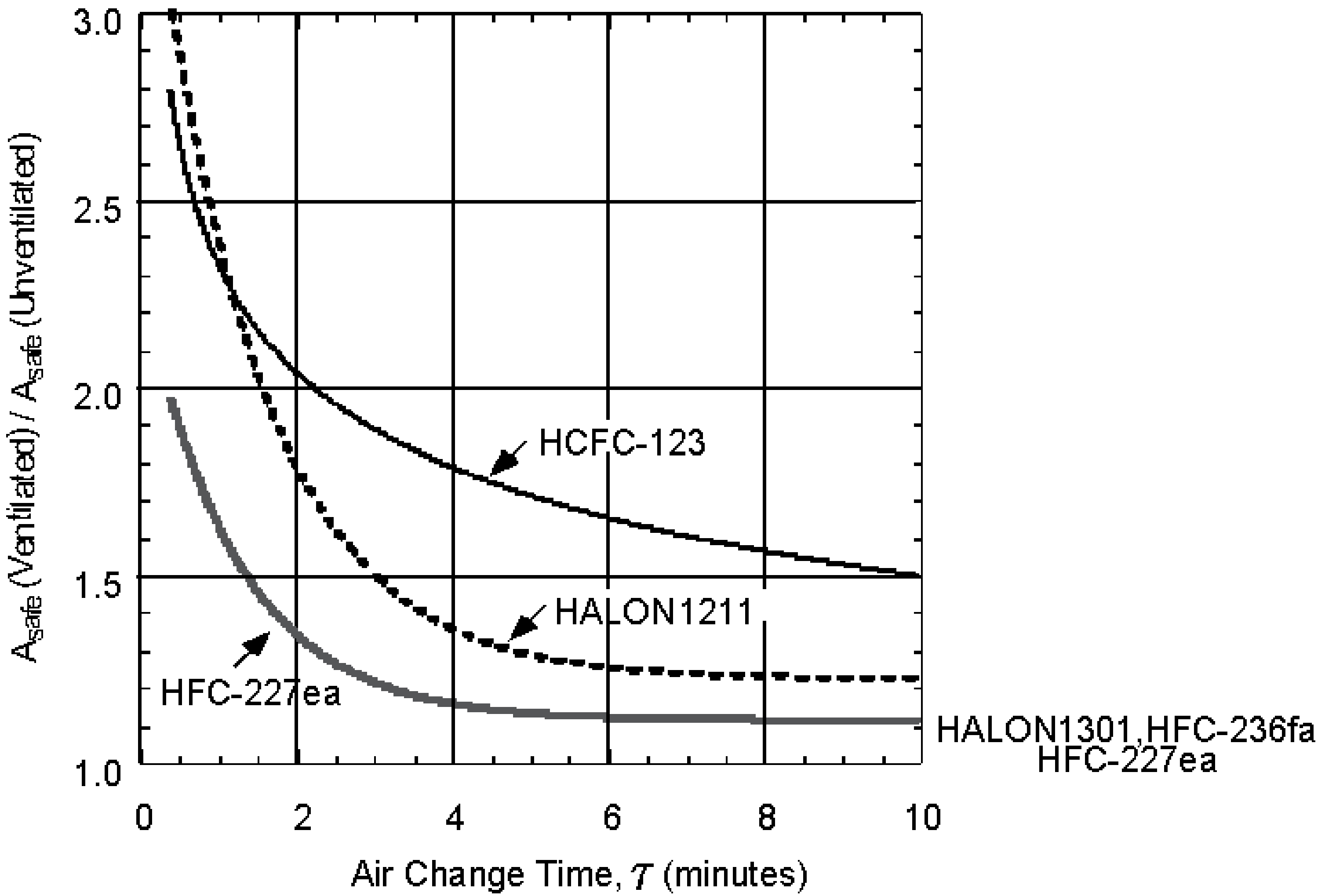
The inverse of $B(t)/B_{safe}$ at its maximum point is the ventilation benefit

Ratio of the Arterial Blood Concentration to the Target Value B_{Safe} for Simulated Human Exposures to A_{Safe} in a Ventilated Cabin

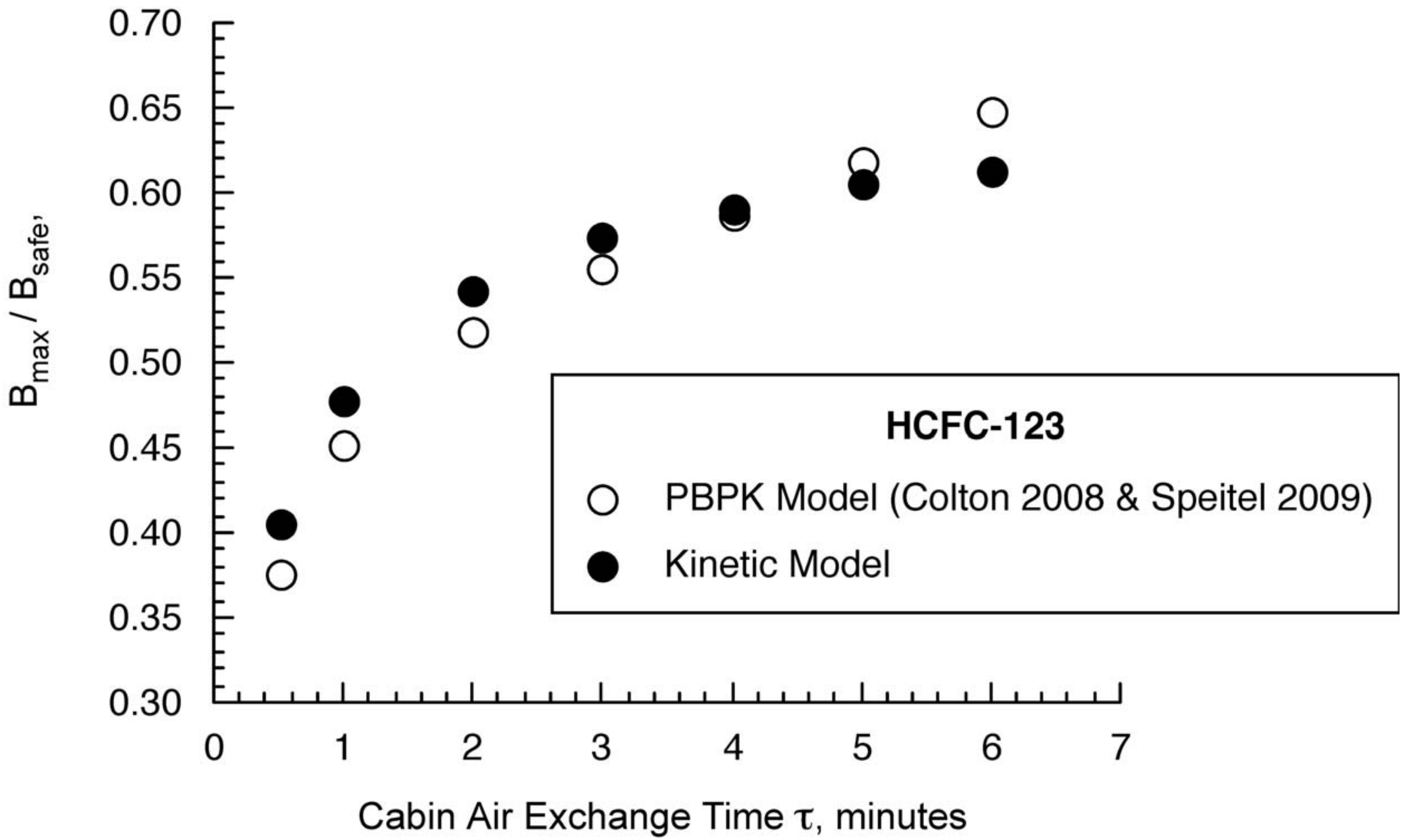


The inverse of $B(t)/B_{safe}$ at its maximum point is the ventilation benefit

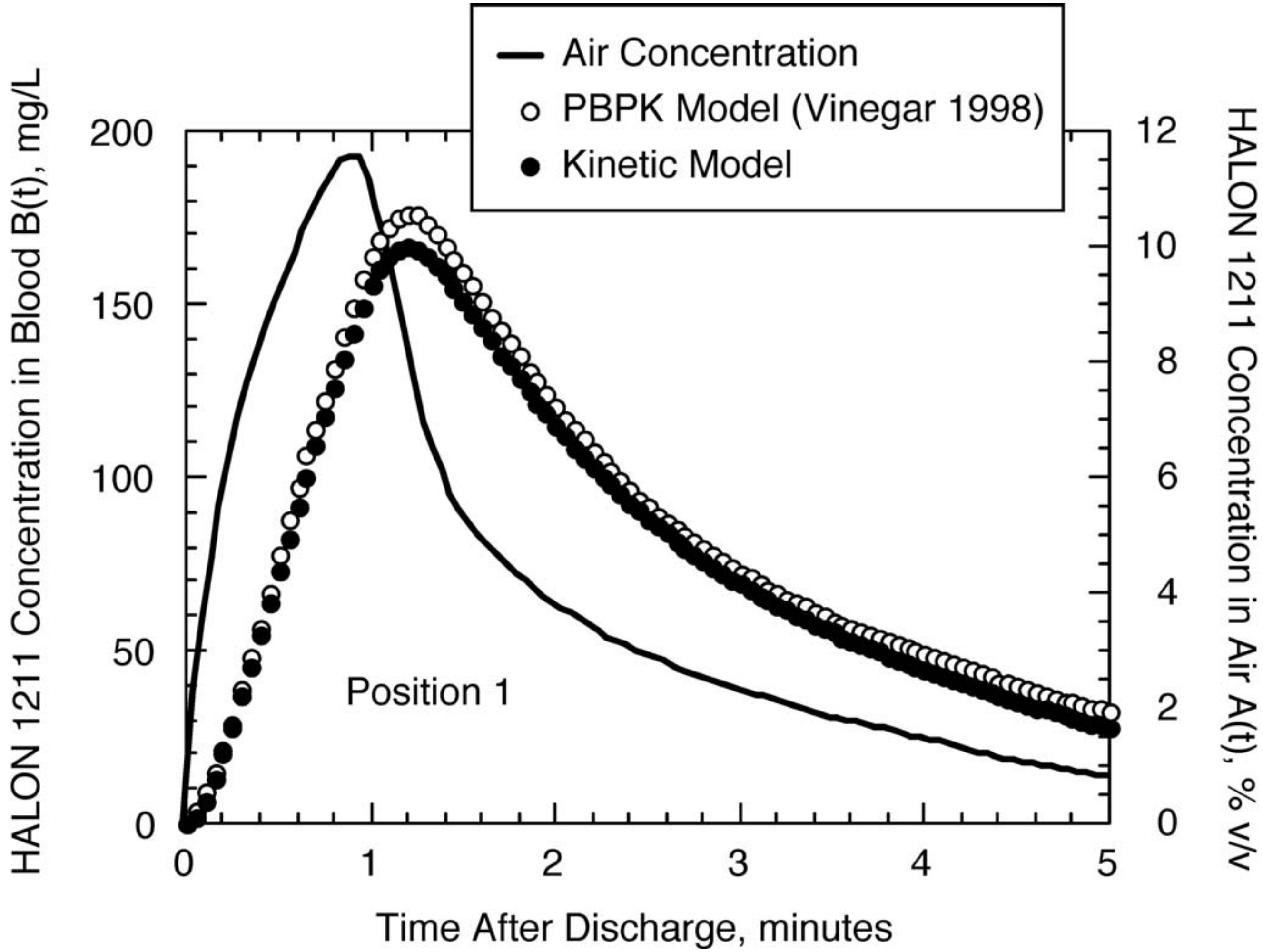
Ventilation Benefit Versus Cabin Air Exchange Time for Different Agents Using Kinetic Model



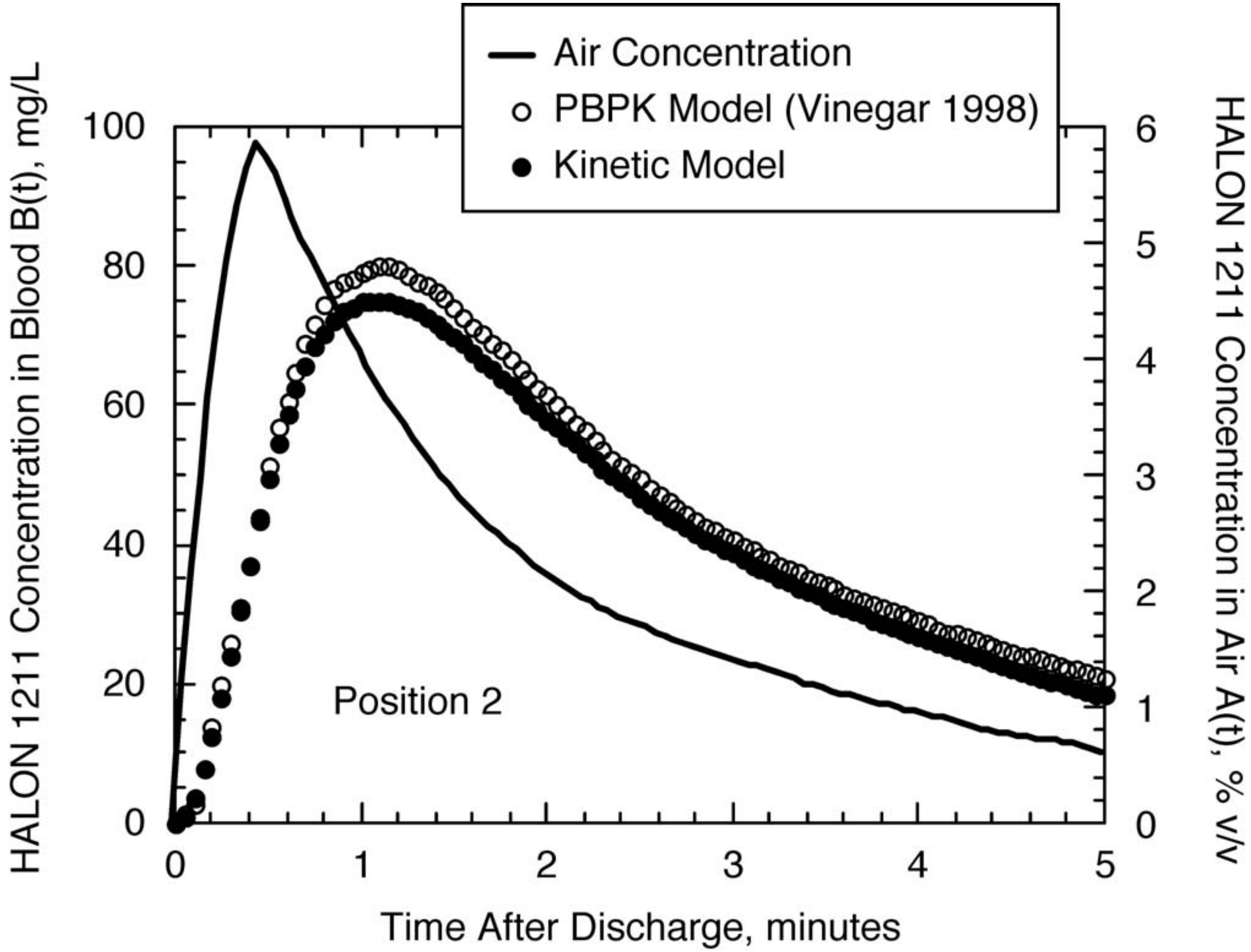
Ratio of the Maximum Arterial Blood Concentration B_{max} to the Target Value B_{safe} for Simulated Human Exposures to A_{safe} in a Ventilated Cabin



Comparison of the Arterial Blood Concentration History at Position 1 in a Small Compartment for the Indicated Time-Varying Concentration of Halon 1211



Comparison of the Arterial Blood Concentration History at Position 2 in a Small Compartment for the Indicated Time-Varying Concentration of Halon 1211



Conclusion

Properly calibrated kinetic model was found to predict human arterial blood concentration histories for time varying exposures as well as PBPK models.

Reference Report

FAA Report DOT/FAA/AR-08/3

Speitel, Louise C. and Lyon, Richard E., "Guidelines for Safe Use of Gaseous Halocarbon Extinguishing Agents in Aircraft"

See FAA Website: www.fire.tc.faa.gov

Reports

Author

Halon Replacements in Hand Fire Extinguishers - ICAO Resolution to Mandate Replacements

The Sixth Triennial International Fire & Cabin Safety Research Conference

Atlantic City, NJ
October 25-28, 2010

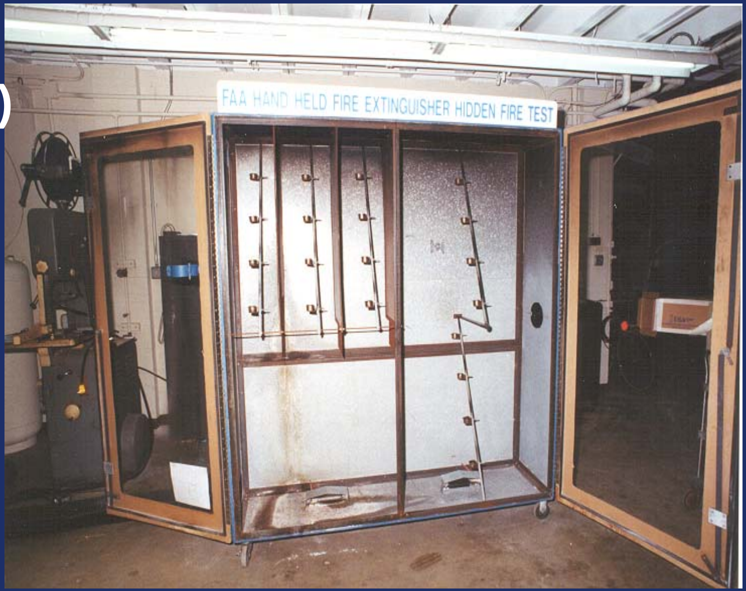
John Petrakis
FAA Aircraft Certification Service
Washington, DC

Topics

- Review of Halon Replacements in Hand Fire Extinguishers
- Hand Fire Extinguisher AC20-42D Revision
- Review Public Comments to AC
- Review Final Draft AC
- Mandatory Halon Replacement Proposed for Civil Aviation

Review of Halon Replacements

- Hand-Held MPS Developed 2002 (DOT/FAA/AR-01/37)
  - Hidden Fire Test (Effectiveness)
    - U.S. - U.L. Offers Test Approval
  - Seat Fire Extinguishing Test (Toxicity)
    - Full-Scale Tests FAATC
    - Measures Agent Decomposition Products



- Three Approved Halon 1211 Replacement Agents U.L. Listed

Review of Halon Replacements

Agent	Weight Equivalent Ratio	ODP	GWP
Halon 1211	1.0	5.1	1300
HFC-227ea (FM200)	2.2	0	3800
HFC-236fa (FE36)	1.9	0	9400
HCFC Blend B (Halotron 1)	2.2	.02	120

- Replacement Agents/Extinguishers Approved but Not Installed because of Increased Weight/Volume/GWP
- New Agents are being Evaluated

Review of Halon Replacements

- FAATC Testing Other Promising Halon Replacement Agent Extinguishers.
  - Powders
    - Powder May Be Drop-in Replacement for Cabin.
    - ODP - 0 GWP - 0
    - Clean Up Needed After Discharge.
    - Reduced Visibility
  - FK-5-1-12 (Novec 1230)
    - ODP - 0 GWP – 1
  - 2-BTP
    - Low ODP & GWP
  - Water Mist

AC20-42D Revision

- Cancel AC 20-42C, March 1984
- Provide Updated Guidance for New Installations of Required Extinguishers
- Establish Procedure for FAA Certification of Halon Replacement Extinguishers.
- FAA Approval of HCFC Blend B, HFC-227ea, and HFC-236fa as Halon 1211 Replacement
- Provide Guidance on:
  - Fire-Fighting Effectiveness
  - Relative Toxicity of Agents, but Stresses Need to Extinguish In-Flight Fires
  - Selection and Safe-Use for Approved Agents
  - Location, Mounting and Marking Provisions

AC20-42D Revision

- **Draft Guidance Developed by IASFPWG**
- **Draft AC Released for Public Comment 10/09**
  - 12 Commenters/188 Comments
- **Significant Comments:**
  - Concern Over Use of Conservative Modeling Analysis of Agent Toxicity in Aircraft Compartments.
  - No Consideration for Agent Stratification.
  - Question Logic of Recommending Replacement Agents that are Green House Gases.
- **Public Meeting Held 5/19-20/10**
- **Scheduled Issue of Final AC by 12/30/10**

Mandatory Halon Replacement Proposed for Civil Aviation

- ICAO (A36-12 & A37-xx) Proposal
- EC DG Environment Proposal

	New A/C Prod ICAO/EC	New A/C TC ICAO/EC	Existing A/C ICAO/EC
Lavatory	2012/2020	2012/2012	None/2020
Portable	2017/2025	2012/2012	None/2025
Engines/APU	None/2035	2012/2012	None/2035
Cargo	None/2035	None/2016	None/2035