Comments on NIOSH Asbestos Roadmap

-- Animal Bioassays --

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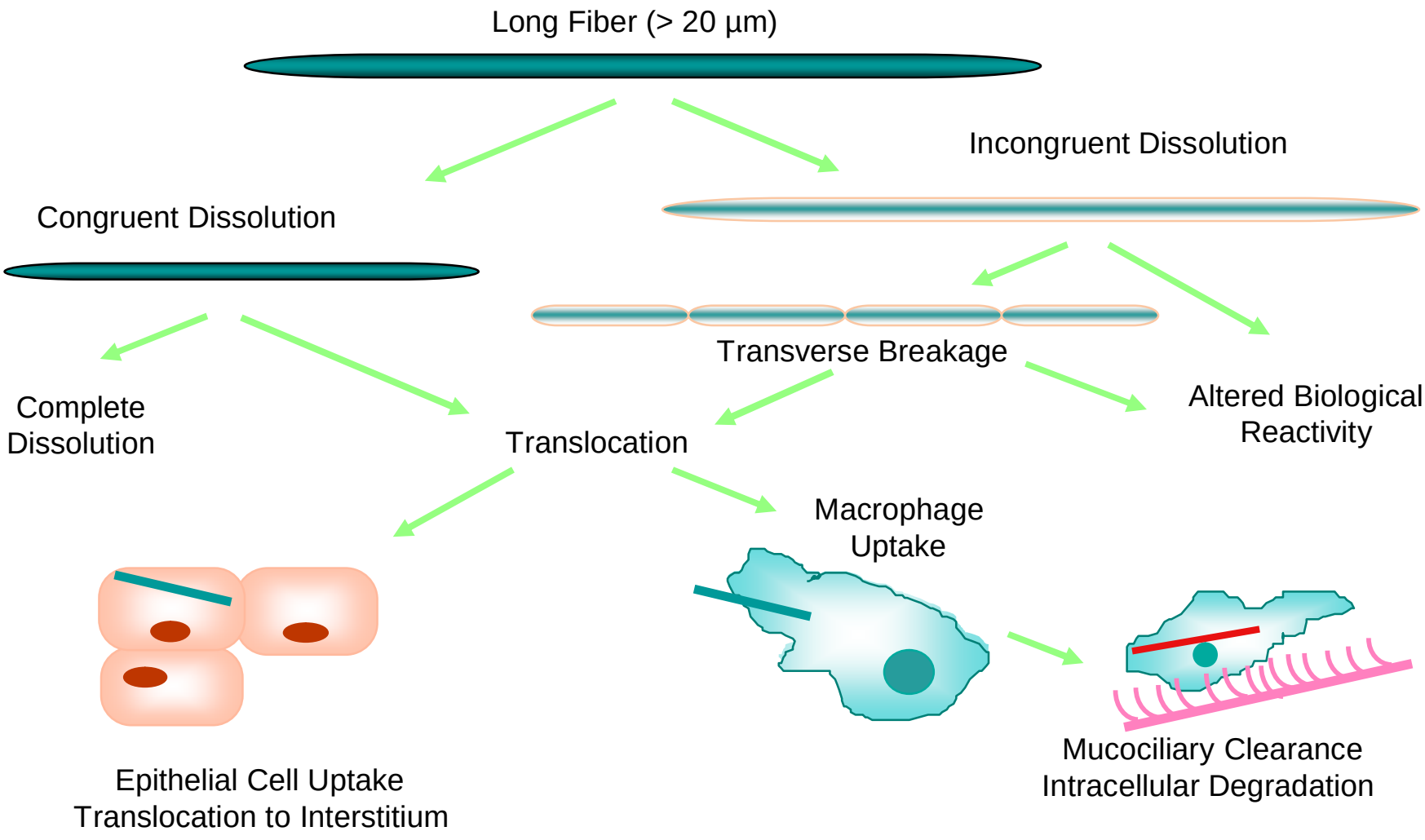
IOM-NRC Meeting on NIOSH Asbestos Roadmap
March 30, 2009
Washington, DC

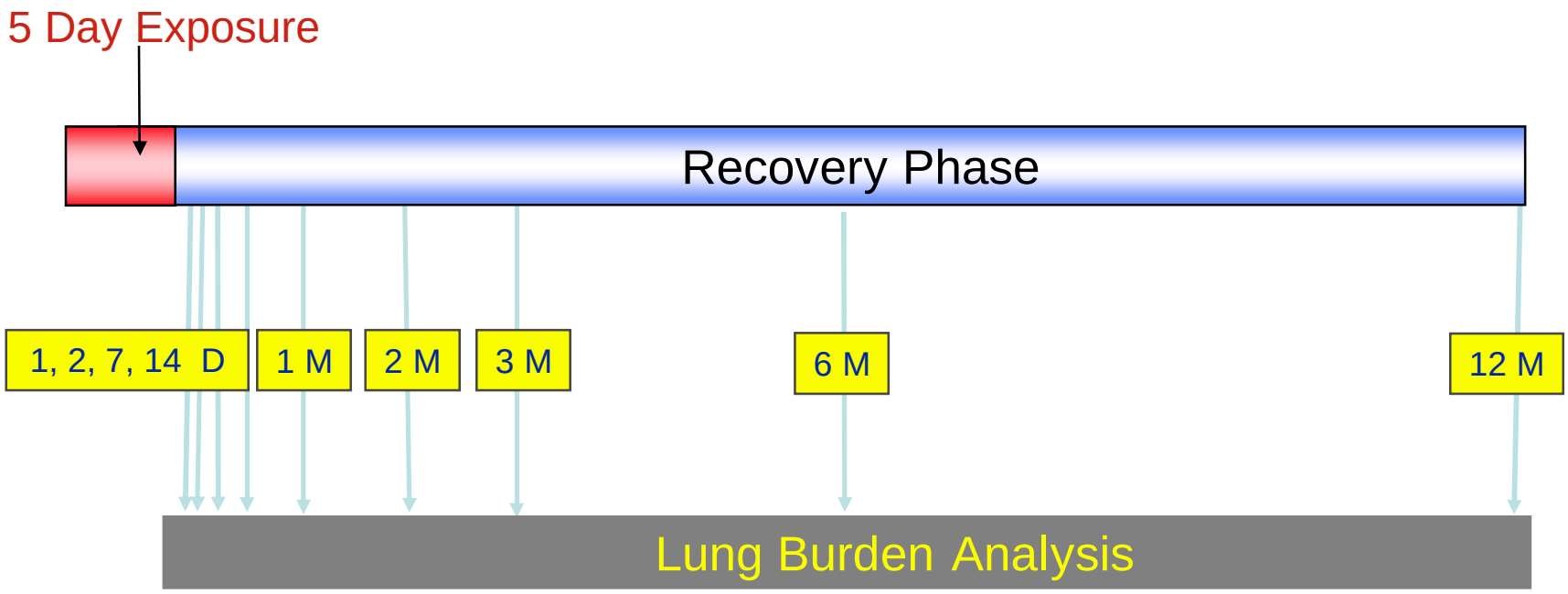
Key Issues Regarding Asbestos Roadmap

- Short-term bioassays to assess health risk
- Chrysotile vs amphibole pathogenicity
- Amphibole cleavage fragment health risk

Fiber Biopersistence is Determined by Dissolution, Leaching, & Fragmentation



Fiber Biopersistence Protocol



Fiber Biopersistence, In Vitro Dissolution, and Pathogenicity

Fiber	F/L>20um x 10^6	$WT_{1/2}$	In Vitro K_{dis} pH 7.4 (pH4.5)	Pathogenicity	
				Fibrosis	Tumors
Crocidolite	1.0	817	<1	+	+
Amosite	1.6	418	<1	+	+
MMVF32	1.3	79	9	+	+
RCF1	1.5	55	3	+	+
MMVF33	1.4	49	12	+	+/-
MMVF21	1.1	67	20	+	-
MMVF10	0.1	14.5	300	-	-
X607			9.8 (990)	-	-
MMVF11	1.0	9	100	-	-
MMVF22	0.4	9	400	-	-
MMVF34	1.5	6	59 (>600)	-	-

Hesterberg and Hart, CRT, 2001

Biopersistence of Chrysotile vs Amphibole

Table 1
Comparative clearance half-times of fibers longer than 20 μm and fibers between 5 and 20 μm for chrysotile, synthetic vitreous fibers, and amphiboles

Fiber	Type	Clearance half-time ($T_{1/2}$) (days)		Reference
		Fibers length >20μm	Fibers length 5–20 μm	
Calidria chrysotile	Serpentine asbestos	0.3	7	Bernstein et al. (2005b)
Brazilian chrysotile	Serpentine asbestos	1.3	2.4	Bernstein et al. (2004)
Fiber B (B01.9)	Experimental glass wool	2.4	11	Bernstein et al. (1996)
Fiber A	Glass wool	3.5	16	Bernstein et al. (1996)
Fiber C	Glass wool	4.1	15	Bernstein et al. (1996)
Fiber G	Stone wool	5.4	23	Bernstein et al. (1996)
MMVF34 (HT)	Stone wool	6	25[a]	Hesterberg et al. (1998a)
MMVF22	Slag wool	8.1	77	Bernstein et al. (1996)
Fiber F	Stone wool	8.5	28	Bernstein et al. (1996)
MMVF11	Glass wool	8.7	42	Bernstein et al. (1996)
Fiber J (X607)	Calcium magnesium silicate	9.8	24	Bernstein et al. (1996)
Canadian chrysotile (Textile grade)	Serpentine asbestos	11.4	29.7	Bernstein et al. (2005a)
MMVF 11	Glass wool	13	32	Bernstein et al. (1996)
Fiber H	Stone wool	13	27	Bernstein et al. (1996)
MMVF10	Glass wool	39	80	Bernstein et al. (1996)
Fiber L	Stone wool	45	57	Bernstein et al. (1996)
MMVF21	Stone wool	46	99	Bernstein et al. (1996)
MMVF33	Special-purpose glass	49	72[a]	Hesterberg et al. (1998a)
RCF1a	Refractory ceramic	55	59[a]	Hesterberg et al. (1998a)
MMVF21	Stone wool	67	70[a]	Hesterberg et al., 1998a
MMVF32	Special-purpose glass	79	59[a]	Hesterberg et al. (1998a)
Amosite	Amphibole asbestos	418	900[a]	Hesterberg et al. (1998a)
Crocidolite	Amphibole asbestos	536	262	Bernstein et al. (1996)
Tremolite	Amphibole asbestos	∞	∞	Bernstein et al. (2005b)

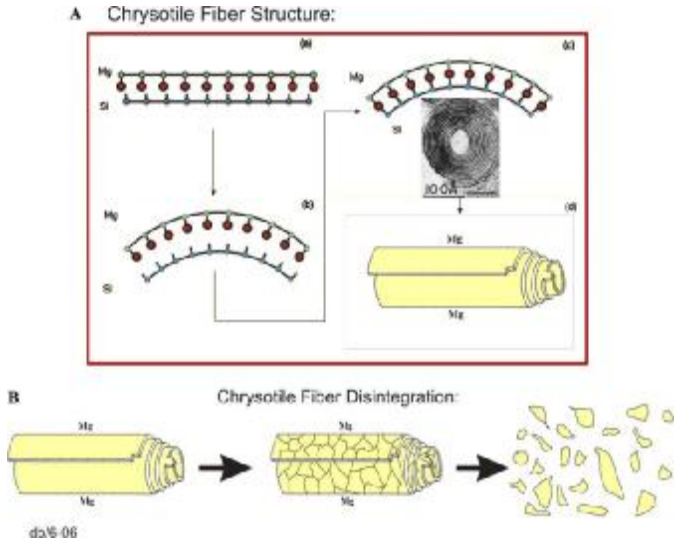
Chrysotile 90-Day Subchronic Study

- Exposure to 536 WHO fibers/cm^3
  - 5,000 times the US workplace limit
  - No lung pathology
- Exposure to 1,429 WHO fibers/cm^3
  - 15,000 times the US workplace limit
  - Minimal fibrosis observed
  - Lung overload?
- The long chrysotile fibers broke apart into shorter fibers and small particles

Bernstein et al., 2006

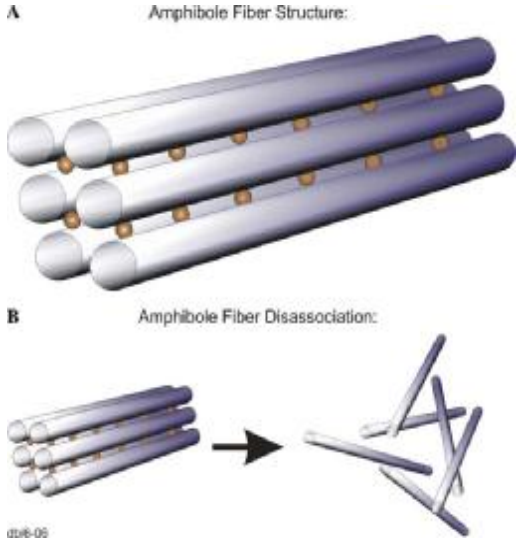
Asbestos Physical/Chemical Properties Determine Dissolution and Breakage

Chrysotile



- Sheet silicate
- Sheet is a rolled sandwich of Mg and Si
- 8 angstroms thick
- Acid soluble

Amphiboles



- Double-chain silicates
- Solid silicon cylinders
- Breaks into smaller fibers
- Not acid soluble

Amphibole Cleavage Fragments

- Amphibole cleavage fragments:
  - Thick, short fibers which break along cleavage planes without the high strength and flexibility of asbestiform fibers.
- Recent reviews
  - Addison & McConnell, 2008
  - Gamble & Gibbs, 2008
  - Mossman, 2007
- Weight of evidence suggests that cleavage fragment amphiboles do not increase the risk of lung cancer or mesothelioma

Summary and Recommendations
-- Chrysotile vs Amphiboles --

- Chrysotile is not biopersistent
- No lung pathology at 500 WHO f/cc in 90-day study
- Test chrysotile from other mines to validate bioassays
  - Biopersistence assay
  - 90-day, 3-dose subchronic inhalation bioassay
  - At least two doses below overload levels
  - Compare with amphiboles
- Develop in vitro solubility assay to screen asbestos fibers
  - Use two pHs—7.4 and 4.5

Summary and Recommendations
-- Cleavage Fragment Health Risk --

- Reviews suggest cleavage fragments not pathogenic
- Isolate cleavage fragments from bulk material
- Test isolated cleavage fragments in bioassays
  - Biopersistence assay
  - 90-day, 3-dose subchronic inhalation bioassay
  - At least two doses should be below overload levels
  - Compare with amphibole asbestos fibers
- Bulk material, containing cleavage fragments, should also be tested in a 90-day subchronic study