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COMMENTS AND SUGGESTIONS: NIOSH ROAD MAP FOR ASBESTOS

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TALK OUTLINE

- Overview of Issues
- Comments on Literature Review
- Illustrations for Potential Misconceptions
- Recommendations for Refocusing Research Efforts

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COMMENTS ON LITERATURE SUMMARY IN ROAD MAP

- The references cited suggest only limited review of the rich and extensive asbestos/cleavage fragment literature
- Moreover, many statements are left unsupported
- Thus, much more can and should be extracted from the existing literature before initiating an extensive research program to fill data gaps
- The RM needs to better distinguish between formal study findings and more general author speculation

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MISCONCEPTIONS THAT MAY MISDIRECT EFFICIENT AND EFFECTIVE RESEARCH

- That arbitrarily including a greater range of structure sizes and types in counts to determine exposure concentrations is automatically health protective
- That efficient evaluation of the effects of structure size and type requires creation of samples containing “pure” sizes or types
- That animal and cell-culture studies will be more informative than better characterizing the historical human exposures in existing studies.

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MISCONCEPTIONS THAT MAY MISDIRECT EFFICIENT AND EFFECTIVE RESEARCH (cont.)

- That can reasonably evaluate the effects of fiber size and type based on data from a single environment

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ILLUSTRATION:
WHY “COUNTING EVERYTHING” IS *NOT* AUTOMATICALLY HEALTH PROTECTIVE

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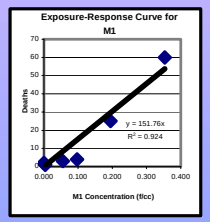
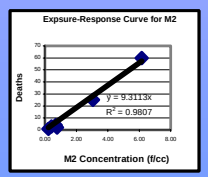
WHY "COUNTING EVERYTHING" MAY *NOT* BE HEALTH PROTECTIVE

Epidemiology Study

1 Cohort
2 Exposure Metrics





(M2 =~15M1)

Slope Factors

For M1 = 0.15
For M2 = 0.0093

Study Environments

Scenario 1	Scenario 2	Scenario 3
Exposure Concentrations M1 = 0.003 (M2 = ~ M1)	Exposure Concentrations M1 = 0.0002 (M2 = ~ 15M1)	Exposure Concentrations M1 = 0.00004 (M2 = ~ 100M1)
Estimated Risk: Using: M1 = 5E-4 M2 = 3E-5 Ratio M1/M2 = 15	Estimated Risk: Using: M1 = 3E-5 M2 = 3E-5 Ratio M1/M2 = 1	Estimated Risk: Using: M1 = 6E-6 M2 = 4E-5 Ratio M1/M2 = 0.16

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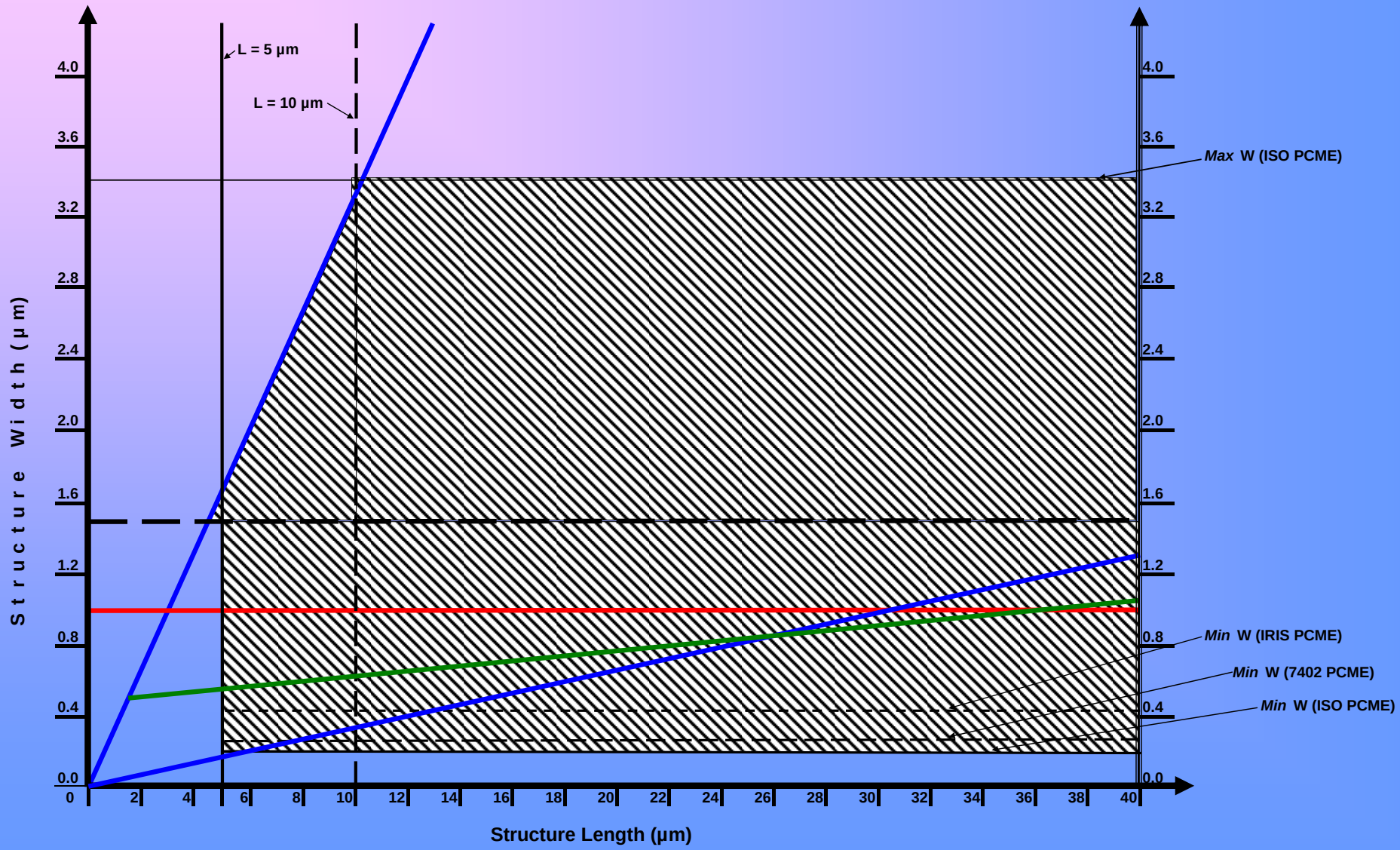
SIZE RANGE FOR THE PCME METRIC



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SIZE RANGE FOR PROTOCOL STRUCTURES

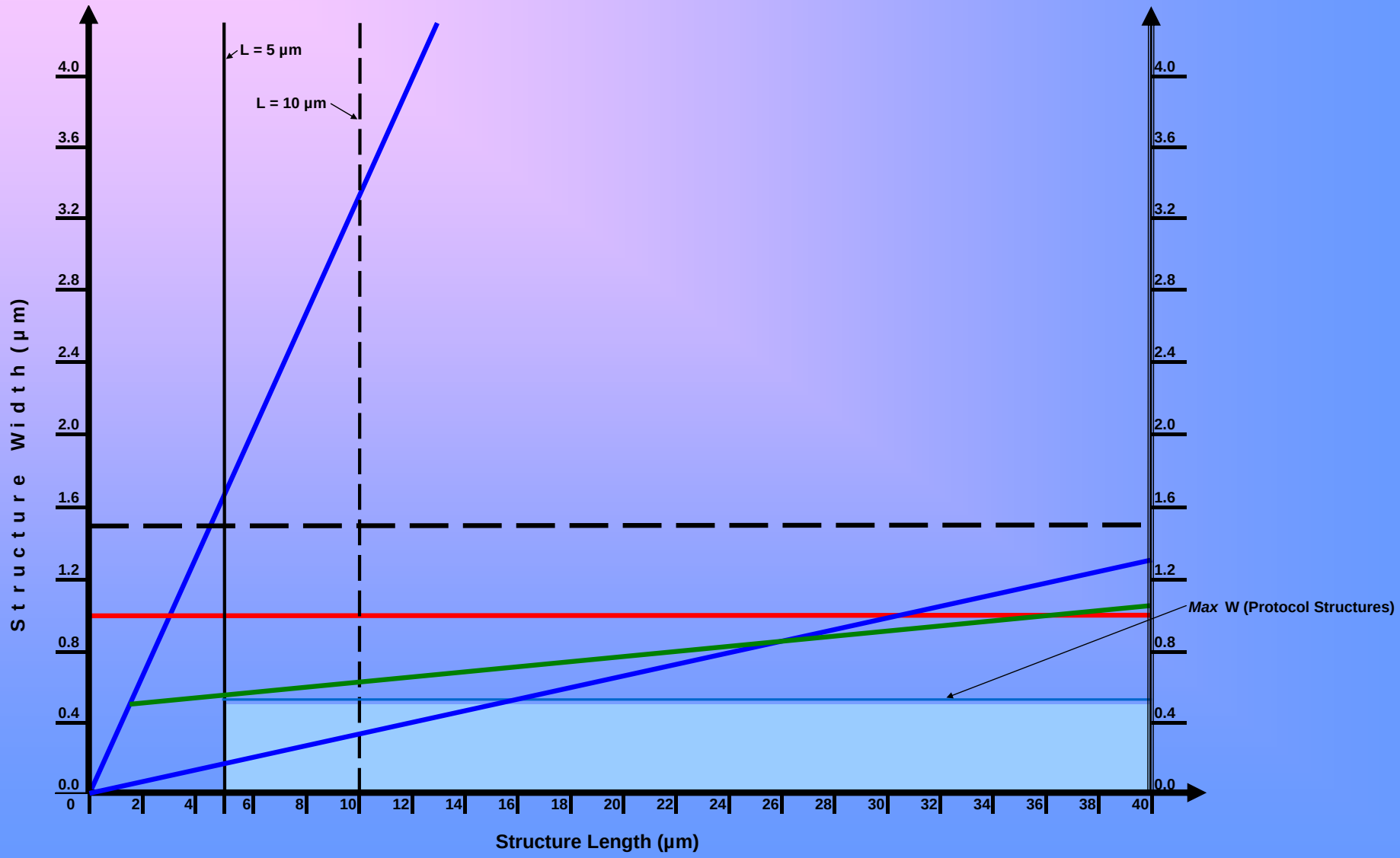

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ILLUSTRATION: WHY IT IS NOT NECESSARY TO CREATE SAMPLES CONTAINING “PURE” SIZES AND TYPES

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SYSTEM OF SIMULTANEOUS EQUATIONS TO SOLVE FOR RELATIVE POTENCY OF FOUR STRUCTURE CATEGORIES

$$P_1 = 1 - \exp[Q - B_i(A_1X_{11} + A_2X_{12} + A_3X_{13} + A_4X_{14})]$$

$$P_2 = 1 - \exp[Q - B_i(A_1X_{21} + A_2X_{22} + A_3X_{23} + A_4X_{24})]$$

$$P_3 = 1 - \exp[Q - B_i(A_1X_{31} + A_2X_{32} + A_3X_{33} + A_4X_{34})]$$

$$P_4 = 1 - \exp[Q - B_i(A_1X_{41} + A_2X_{42} + A_3X_{43} + A_4X_{44})]$$

$$P_5 = 1 - \exp[Q - B_i(A_1X_{51} + A_2X_{52} + A_3X_{53} + A_4X_{54})]$$

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SYSTEM OF INDEPENDENT EQUATIONS TO SOLVE FOR RELATIVE POTENCY OF FOUR "PURE" STRUCTURE CATEGORIES

$$P_1 = 1 - \exp[Q - B_i(A_1X_{11})]$$

$$P_2 = 1 - \exp[Q - B_i(A_2X_{22})]$$

$$P_3 = 1 - \exp[Q - B_i(A_3X_{33})]$$

$$P_4 = 1 - \exp[Q - B_i(A_4X_{44})]$$

$$P_5 = 1 - \exp[Q - B_i(A_1X_{51})]$$

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WHY IS RECONSTRUCTION OF HISTORICAL EPIDEMIOLOGICAL EXPOSURES MORE DIRECTLY USEFUL THAN ANIMAL AND CELL-CULTURE STUDIES

- Provides most direct and expedient information on human dose response
- Provides validation for linking animal and cell studies to human disease end points especially for proposed screening procedures

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WHY ONE CANNOT REASONABLY EVALUATE EFFECTS OF FIBER SIZE AND TYPE FROM A SINGLE EXPOSURE ENVIRONMENT

- Occurrence of varying size and type categories tend to be highly correlated or confounded in single environments (thus, no power to distinguish)
- Negative environments are equally important to consider
- Can only reasonably evaluate size and type effects by comparing across environments exhibiting disparate mixtures of exposures
- Can only meaningfully extrapolate to environments containing studied structures

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SUGGESTIONS FOR RE-FOCUSING RESEARCH EFFORT

- Emphasize human (epidemiological) studies and an effort to improve characterization of the associated, historical exposures
- Use TEM for research while developing less expensive alternatives to support routine analysis under new regulations
- Consider studies to automate TEM analysis
- De-emphasize quest to produce “pure” samples
- Need to recognize that adequacy of PCM metric and need to distinguish asbestiform fibers from cleavage fragments are confounded issues