

1 **Preliminary Comments on the REA Planning Document from Dr. Aaron Cohen**

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4 **General Structure [Section 4.2]**

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6 The overall plan for the REA Health Risk Assessment is, for the most part, clearly described. It
7 appears methodologically sound and consistent with the health evidence as reviewed in the draft
8 ISA.

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10 **Approaches for using findings from controlled human exposure studies**

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12 The choice of health endpoints appears well-justified (page 4-31), Section 4.2.1)

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14 Page 4-32, para.1: I assume that the scaling of ventilation by BSA is the appropriate way to
15 handle adult-child differences, this approach having been used in other REA, but this is not my
16 area of expertise.

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18 **Health benchmarks [Sections 3.2.2, 4.2.3]**

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20 The benchmark levels seem appropriate given the design of the controlled exposure studies.

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22 **Plans for E-R functions [Sections 3.2.2, 4.2.4]**

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24 The rationale for not including FEV₁ deserves further discussion. I am not sure I agree, given
25 the ISA review and though estimates may be less precise than for sRaw FEV₁ decrements in
26 exposed asthmatics are adverse. In any case, excluding FEV₁ seems to contradict what was said
27 in Section 4.2.1.

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29 Section 4.2.4, page 4-34, line 4: there seems to be a word (missing: "...people estimated to [have
30 experienced?] at least one...")

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32 **Variability, covariability and uncertainty [Section 4.4]**

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34 The approaches to addressing variability in the underlying exposure and health evidence and
35 characterizing uncertainty seem conceptually sound but it is not entirely clear to me what the
36 sources of variability are that will actually be addressed. Perhaps a small table would help.

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38 I understand that uncertainty will be characterized using sensitivity analysis, but I assume that
39 the risk estimates will be also presented with uncertainty intervals. This is not discussed but
40 should be, including which sources of uncertainty such intervals will include, e.g., uncertainty in
41 exposure assignment as well as in the fitted E-R functions.