

Preliminary Comments on the ISA from Dr. Richard Schlesinger (received May 21, 2015)

Comments on Chapter 4

Overall, the discussion of dosimetry in Section 4.2 is much improved, and the distinction between direct NO₂ reactivity in the lung and its (or its products) ability to pass beyond the ELF is well described. However, there is some room for further improvement, as noted below.

4.2.1. The information on ambient levels should be removed. There is an entire chapter that discusses this.

4.2.2

p. 4-3, line 6-10. While the ELF of the alveolar region clearly is involved in surface tension reduction, the ELF of the conducting airways is not. Thus, this sentence needs to be modified. Also, the sentence implies that the composition of the ELF throughout the lungs is similar, which it is not.

p. 4-4 Section Title Change title to “Reaction with Epithelial Lining Fluid” since the discussion goes beyond reaction merely with water.

p.4-3, line 20. Change “respiratory effects” to “toxic effects”

p. 4-4, lines 1-4. This is a bit confusing. The first sentence notes that the NO₂ dimer reacts with water, and then the next sentence notes that in aqueous solutions, NO₂ itself reacts with many solutes. This needs clarification. In fact, the entire paragraph should be rewritten as it tends to go around in circles, making the point less clear than it should be.

4.2.2.3

Some of the subsections have short summary paragraphs and others do not. It would help in evaluating the information if they all had a short conclusion at the end of each subsection.

4.2.2.4

p 4-20, line 4. Do the authors really mean O₃ or NO₂

The separation into distinct outcomes is good, but there still needs to be some additional “cleaning up” to avoid redundancy among the sections. There is the need to provide a summary for each outcome section that will allow the reader to reach some conclusion as to the role of NO_x in affecting these outcomes, especially at ambient levels.

4.3.2

There is some redundancy in discussion of effects among the sections. For example, there are CV effects noted in section 4.3.2.2. and then again in 4.3.2.9, making it difficult to obtain some overall impression of the effect on the endpoint. Thus, some restructuring and consolidation of the section should be considered. In addition, some of the subsections have summary or conclusion sentences at the end while others do not; each section should have such a paragraph or sentence and also note whether the effects occur with ambient concentrations of NO_x.

p.4-52, line 35. The term “spillover” here is not really scientific. Perhaps a better way to describe what is going on is “migration” of mediators from the lung into the circulation.

The figures provide somewhat of a summary of potential toxic pathways but otherwise do not really help with any discussions in the following chapters.

Figure 4.3 What is meant by vascular dysfunction as a result of vascular activation?