W1 Cullen/Caldwell

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April 7, 1983

Dr. Matthew Meselson
Department of Biochemistry and Molecular Biology
Harvard University
7 Divinity Avenue
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Dear Dr. Meselson,

As discussed in our earlier telephone conversation, we have compiled the following questions relating to the "yellow rain" issue. We appreciate the opportunity to pose these questions and anxiously await the response.

I. Questions in this section are directed at the feasibility of trichothecene weapons based on their toxicity.

It has been alleged that crude extracts are more toxic than pure toxin and that such extracts constitute the actual weapon. Does the State Department concede that pure T-2 toxin, for example, would not produce lethal effects when dispersed by rockets, artillery, etc.? Assuming optimal solvent and a sensitive animal species, what is the dermal LD_{50} for T-2, DAS, deoxynivalenol, nivalenol?

The increased toxicity of crude extracts relative to pure compounds has been known for many years for various mycotoxins. However, it is generally assumed that this phenomenon is caused by the additive effects of multiple toxins in the extracts. Is the State Department suggesting that the toxicity of, for example, 1 kg of pure T-2 toxin could be exceeded by 1 kg of a mixture of T-2, DAS, zearalenone, deoxynivalenol and nivalenol? If so, what is the basis of this assertion? We know of no evidence for synergistic action among Fusarium toxins. Does the government have such data? What is it?

Do the relative proportions of Fusarium metabolites detected (T-2, deoxynivalenol, nivalenol, zearalenone) in environmental samples resemble the original chemical agent? Why is there so much zearalenone in the "ABC sample" and none in Dr. Mirocha's? Does the State Department believe that the original agent intentionally contains substantial quantities of zearalenone or is its presence viewed as a "contamination" which is not worth removing? What is the military value of zearalenone? Does zearalenone interact in any synergistic manner with other Fusarium toxins? (In our opinion, it is ridiculous to suppose that zearalenone is an unavoidable contaminant. Trichothecene

producing strains and fermentation conditions can be easily selected to avoid zearalenone production. It is absurd to think that a sophisticated technology which is mass producing these compounds would be unable to avoid zearalenone contamination.)

II. Metabolism of T-2 Toxin.

Most studies that we are aware of show rapid metabolism of T-2 to polar derivatives (HT-2, T-2 tetraol, etc). Precisely, what evidence is there to support the theory of long term (>2 weeks) tissue binding of T-2 toxin in humans? How much radioactivity in the form of T-2 toxin was detected after 2-3 weeks? What animal systems were used? What dose? How was it administered? Was any attempt made to administer radiolabelled toxin by inhalation?

III. Inhalation Toxicity.

Relative to other administration routes (i.e., IP, SC) inhalation toxicity of pure T-2 is now known to be quite low. But recently government officials suggested that pollen impregnation is a "very clever" way to deliver the toxins. How could impregnation on 10-20 μm particles make the compounds more toxic? Relative to smaller sized dust formulations, wouldn't such pollen settle more rapidly, penetrate less deeply, and dilute the toxin concentration significantly? Can substantial quantities of toxin be impregnated into pollen without its loss of structural integrity and collapse? On how many samples was pollen found?

Some investigators have identified rainforest trees as pollen sources. How does this compare with the finding of State Department experts? How many environmental samples have been found to contain substantial levels of pollen? When and where were they collected?

IV. Additional Questions.

According to an article in Nature Dec. 23, 1982 (300:678-679) an analyst for the State Department was "... sent a piece of rubber or plastic on which he was unable to detect any of the toxins." In an apparent contradiction, a government official stated (Nov. 30, 1982 State Department Press Conference) that three separate laboratories detected toxins in the samples. Please clarify. Did the analyses of gas masks involve full scan or selected ion

mass spectroscopy? If the latter, how many and which ions? What were the estimated levels in $\mu g\ cm^{-2}$?

Thank you for your patience and cooperation.

Sincerely,

Daniel Cullen

Rodney Caldwell