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Donald L. Ingle, Ph.D.
President
Karl A. Traul, Ph.D.
Vice President

January 15, 2001

Re: Docket No. 00D-1631

Margaret M. Dotzel
Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fischers Lane Rm. 1061
Rockville, MD 20852

Re: VICH GL23 – Comments

Dear Ms. Dotzel;

I am writing to provide some comment and input regarding the proposed draft VICH Guideline – “Safety Studies for Veterinary Drug Residues in Human Food: Genotoxicity Studies. VICH GL23.”

My principle concern lies with an apparent discrepancy within the ICH processes. The Federal Register notice (FR 65 No. 243 18-Dec-2000) states, under Section I that “One of the goals of harmonization is to identify and then reduce differences in technical requirements for drug development among regulatory agencies in different countries”. (my emphasis). The FR goes on to state, “The VICH is a parallel initiative for veterinary medicinal products”. There should also, therefore, be a goal to reduce such differences between ICH and VICH. Additionally, because FDA supports the ICH and VICH processes, this proposed guideline poses a potential conflict within the FDA. Currently the other branches of the FDA include the L5178Y tk +/- Mouse Lymphoma Assay as one of the acceptable tests for gene mutation and *in vitro* chromosomal damage. The proposed VICH Guideline presents a possible condition of non-harmonization within the ICH processes and among the branches of the FDA, rather than reducing differences and being parallel with ICH. Section 3 of the ICH Guidance (for human pharmaceuticals and biologicals) is considerably more flexible than the proposed VICH guidance for veterinary products.

The proposed Guideline states that this draft document should be read in conjunction with the VICH Guidance on General Testing Approach for the evaluation of veterinary drug residues. That document is not available. How can one effectively evaluate the proposed guideline if the full relevant guidance is not made available?

With the advent of colony sizing, the L5178Y tk +/- Mouse Lymphoma Assay has been widely accepted as an effective assay for the evaluation of both gene mutation and

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chromosomal damage potential. It is not understood why the draft Guideline has, in Section 4.2, conditional wording (“If it should become internationally accepted...”), which suggests that this assay is not widely accepted. The wording here implies that data from the assay may be considered inadequate or suspect or may not be considered for acceptability.

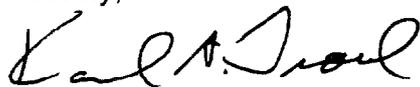
It is suggested that the sentence, in Section 4.2, that reads: “If a mouse lymphoma assay protocol is used...” should be amended to read: “When a mouse lymphoma assay protocol is used...”

The proposed changes could work a hardship upon companies that develop new drug entities for both human and veterinary use in that this could add to the burden of testing necessary to demonstrate safety. This is especially true for smaller companies with more limited product development budgets and may unfairly disadvantage these companies in comparison to larger companies.

The statements regarding the need to conform to certain OECD Guidelines in the performance of these tests are well taken. OECD Guidelines are widely accepted performance standards. Unfortunately the requirement that one must purchase the OECD guideline is onerous, especially in the U.S. where the policies and practices of open regulation prevail. If the U.S regulatory agencies, such as the FDA, are going to require product sponsors to use specific guidelines for testing of new products, then those testing requirements should be made as freely available as all of the other regulatory requirements.

Thank you for considering my comments and suggestions.

Sincerely,

A handwritten signature in black ink, appearing to read 'Karl A. Traul', written in a cursive style.

Karl A. Traul, Ph.D.

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