Krystyna K. Locke 9/23/94

Primary Review by: Krystyna K. Locke, Toxicologist
Section I, Toxicology Branch I
Health Effects Division (7509C)

for **Secondary Review by:** Roger Gardner, Section Head Pamela M. Hurley 10/3/94
Section I, Toxicology Branch I
Health Effects Division (7509C)

DATA EVALUATION RECORD (abbreviated)

STUDY TYPE: Nonguideline: *In Vitro* Neuropharmacological

EPA IDENTIFICATION NUMBERS:

MRID No. 42337105	DP Barcode No. D182069
EPA ID No. 109101	Submission No. S424471
Case No. 819426	Rereg. Case No. 2375
P.C. Code No. 109101	Tox. Chem. No. 380 AB

TEST MATERIAL: Mepiquat chloride (Purity: 99%; Batch No. WW 285)

REPORT NUMBER: 99PO697/909018 and 91/11206

SPONSOR: BASF Aktiengesellschaft, Germany.

TESTING FACILITY: Knoll AG Research and Development, Ludwigshafen, Germany.

TITLE OF REPORT: Study on the Affinity of Mepiquat Chloride for Muscarinic Receptors.

AUTHOR: Dr. H. Weifenbach

STUDY COMPLETION DATE: September 19, 1991

EXECUTIVE SUMMARY

The purpose of this *in vitro* study was to investigate the affinity of Mepiquat chloride for subtypes of muscarinic acetylcholine receptors (M_{1-3}) in membranes of animal origin and to compare these findings with those obtained with standard muscarinic reference compounds.

The membranes, prepared in the testing facility and stored at -196°C until needed, were those of bovine cerebral cortex (M_{1+2}), rat heart (M_2) and rat submaxillary gland (M_3). The subtype-specific substances with high affinity for muscarinic acetylcholine receptors (reference compounds) were pirenzepine (M_{1+2}), methoctramine (M_2), 4-diphenylacetoxy-N-methylpiperidine methiodide [4-DAMP] (M_3) and atropine (a high affinity compound without subtype specificity). The radioligand was [N-Methyl-^{3}H]-N-methylscopolamine (^{3}H-NMS). The rats (males of Sprague-Dawley strain, weighing about 200 g) were obtained from the local supplier

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(Charles River) and the bovine brains were obtaine from the local slaughterhouse. The affinity of Mepiquat chloride for the receptors was studied by incubating membranes with ^{3}H-NMS and Mepiquat chloride (10^{-5}, 10^{-4} or 10^{-3} moles/liter) or with ^{3}H-NMS and reference compounds (10^{-10}-10^{-3} moles/liter) for 1 hour at 37°C. After incubation, the membranes were washed, the radioactivity measured and the K_i values (inhibition constants of Mepiquat chloride and reference compounds) calculated.

Compared with the reference compounds, Mepiquat chloride had very low and unselective affinity for the muscarinic receptors (^{3}H-NMS binding sites). The inhibition constants (K_i) of Mepiquat chloride were 88, 160 and 200 micromoles/liter for the receptors (M_1), (M_2) and (M_3), respectively. The K_i values for the reference compounds were in the nanomolar range. According to this submission, " there is only a small risk of side effects with muscarinic receptors with high concentrations of mepiquat chloride in animals and man ", meaning, apparently, that Mepiquat chloride is not a serious health hazard to humans and animals.

Classification of Study: Acceptable as a Nonguideline, special (neuropharmacological) *in vitro* study.