EPA Reviewer: Robert J. Mitkus, PhD **Signature:** [signature] 6/5/08
Registration Action Branch 1, Health Effects Division (7509P) **Date:**
EPA WAM: PV Shah, PhD **Signature:** [signature] 6/5/08
Registration Action Branch 1, Health Effects Division (7509P) **Date:**

TXR#: 0054227

DATA EVALUATION RECORD

STUDY TYPE: 90-Day Oral Toxicity [feeding]-[rat]; OPPTS 870.3100 [§82-1a] (rodent); OECD 408.

PC CODE: 623001 **DP BARCODE:** D335563

TEST MATERIAL (PURITY): RPA 203328 (99% w/w a.i.)

SYNONYMS: Metabolite of pyrasulfotole; metabolite of isoxaflutole

CITATION: Bigot, D. (1998). RPA 203328: 90-day toxicity study in the rat by dietary administration. Rhone-Poulenc Agrochimie, Sophia Antipolis Cedex, France. Laboratory Study No.: SA 98129, September 23, 1998. MRID 45655903. Unpublished.

SPONSOR: Rhone-Poulenc Agrochemical Company, North Carolina, USA

EXECUTIVE SUMMARY:

In a 90-day oral toxicity study (MRID 45655903), RPA 203328 (99% a.i, batch # NMI874) was administered to 10 Sprague Dawley rats/sex/dose in the diet at dose levels of 0, 1200, 4800, or 12000 ppm (equivalent to 0, 73.2/93.1, 306/371, or 769/952 mg/kg bw/day in males/females, respectively).

There were no compound-related effects on mortality, clinical signs (including reflexes), ophthalmology, body weight, food consumption, hematology, clinical chemistry, urinalysis, organ weights, or gross and histologic pathology. Urinary pH was slightly reduced ($P<0.01$) at the mid and high doses (5.45 vs. 6.11 in controls); however, the findings were not considered toxicologically significant in the absence of corroborating evidence of toxicity in any other measure. **The LOAEL was not observed. The NOAEL is 12000 ppm (769/952 mg/kg/day in males/females).**

This 90-day oral toxicity study in the rat is **Acceptable (guideline)** and satisfies the guideline requirement for a 90-day oral toxicity study (OPPTS 870.3100; OECD 408) in rodents.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

This Executive Summary was prepared for United States Environmental Protection Agency, Office of Pesticides Programs, Health Effects Division use.

The following text was generated by the Australian Pesticides and Veterinary Medicines Authority. However, this document has undergone critical scientific analysis and been modified as appropriate.

Report:	**KIIA 5.8/03, Bigot D.; 1998**
Title:	RPA 203328 (99% pure): 90-Day Toxicity Study in the Rat by Dietary Administration
Lab; Duration of study	Rhone-Poulenc Agrochimie, Sophia Antipolis Cedex, France; 20 March - 24 August 1998
Report No.:	SA98129
Document No.:	M-240662-01-1
Guidelines:	EU: Annex V Method B26; MAFF: NohSan N 4200; OECD: 408; USEPA: FIFRA 82-1
GLP/QA	yes

Materials and Methods

RPA 203328 (batch NMI874) in the diet was given to SD rats (10/sex/dose) at 0, 1200, 4800, and 12000 ppm for 90 days. These concentrations provided doses of 0, 73.2, 306, and 769 mg/kg bw/day for males and 0, 93.1, 371, and 952 mg/kg bw/day for females. Stability, concentration and homogeneity of RPA 203328 in the diet were analysed and proved to be satisfactory (100-108% of nominal concentration). The rats were 7 weeks old at the start of treatment, and body weights ranged from 219 to 249 g in males and from 159 to 189 g in females. Animals were housed individually in suspended stainless steel wire cages, with food and water available *ad libitum* except on the night prior to blood and urine collections. Clinical signs, moribundity, and mortality were checked twice daily on weekdays and once daily on weekends and holidays. Prior to the start of the study and in week 12, the grasping, righting, corneal, pupillary, auditory startle, and head shaking reflexes were tested for each animal. Body weight and food consumption were measured on a weekly basis. Ophthalmoscopic examinations were conducted on all animals prior to the start of the study and on the control and high-dose animals in week 12. Also in week 12, blood was collected for hematology (red blood cell count, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, white blood cell count, platelet count, differential leukocyte count evaluation, reticulocytes and prothrombin time) and clinical chemistry (total bilirubin, glucose, urea, total protein, albumin, total cholesterol, triglycerides and inorganic phosphate, chloride, sodium, potassium, calcium, creatinine, AST, ALT and AP) by puncture of the retro-orbital venous plexus. Urine was collected overnight on the night prior to sacrifice. Animals were then anesthetized by intraperitoneal injection of 50 or 60 mg/kg bw pentobarbital and sacrificed by exsanguination. Gross examination was conducted, selected organs were weighed (adrenals, brain, liver, kidneys, epididymis, heart, pituitary, prostate, spleen, testes, thyroid, and ovaries), and samples of organs and tissues were preserved for microscopic examination (eye and optic nercve, liver, spleen, kidney, urinary bladder, prostate, testis, epididymis, seminal vesicle, uterus, vagina, ovary, brain, spinal cord, heart, aorta, trachea, esophagus, larynth, lung, thymus, mesenteric lymph node, submaxillary gland, submaxillary lymph node, pancreas, tongue, skin, mammary gland, stomach, duodenum, jejunum, ileum, cecum, colon, rectum, anus, urinary bladder, pituitary gland, adrenal, thyroid, parathyroid, skeletal muscle, sciatic nerve, eye and optic nerve, harderian gland, bone-sternum and bone marrow-sternum).

Findings

There were no mortalities or any clinical signs during the study. There was no effect of RPA 203328 on food consumption and bodyweight. Rats in the 12000-ppm treatment group showed no ophthalmoscopic abnormalities compared to control rats at any time during the study. There were no treatment-related effects on any hematological and clinical chemistry parameters tested. Urinary pH was slightly reduced ($P<0.01$) at the mid and high doses (5.45 vs. 6.11 in controls).

Pathology

There were no treatment-related effects on organ weights at any dose in either males or females. A few macroscopic findings were noted at necropsy in some treated groups without a dose-related pattern, namely dark or yellowish color of the liver, dark kidneys, and marked lobular liver pattern (see Table below). However, there was no histopathological correlate to any of these findings and therefore they were not considered to be treatment-related. There were no histopathological abnormalities that could be attributed to treatment.

Pathology findings at necropsy

Parameter	Male (ppm)				Female (ppm)			
	0	1200	4800	12000	0	1200	4800	12000
Organ weight								
Bodyweight (g)	445	448	427	425	250	257	248	256
Liver								
Absolute (g)	10.6	10.7	9.8	10.1	6.1	6.1	6.0	6.0
Relative (%)	2.4	2.4	2.3	2.4	2.4	2.4	2.3	2.4
Kidney								
Absolute (g)	2.7	2.7	2.6	2.7	1.6	1.5	1.6	1.6
Relative (%)	0.6	0.6	0.6	0.6	0.67	0.67	0.63	0.63
Macroscopic findings								
Liver								
dark	0	2	2	2	0	0	0	0
yellowish	0	0	0	0	0	0	1	1
marked lobular pattern	0	2	1	2	0	0	0	1
Kidneys								
dark	0	0	0	0	0	0	1	1

Conclusions

Because there were no toxicologically significant effects on any of the parameters tested, the NOAEL (NOEL) for this study was 12000 ppm (769 mg/kg bw/day for males and 952 mg/kg bw/day for females), the highest dose tested.