File No. 1-100/(SP- PAR)/FSSAI/2013
Food Safety and Standards Authority of India
(Ministry of Health and Family Welfare)

FDA Bhavan, Kotla Road
New Delhi-110002
Date: 16 October 2013

Shri. B. S. Phogat,
Addl. Plant Protection Advisor
Department of Agriculture & Cooperation
Central Insecticides Board & Registration Committee
N.H. IV, Faridabad-121001, Haryana

Subject: Approved proforma for submitting data on pesticide residue and toxicity by applicants seeking registration of new pesticides for use in the country under Section 9(3) of the Insecticide Act, 1968

Sir

The Scientific Panel on Pesticides and Antibiotic Residues has drafted a proforma for submitting data on residue and toxicity by the applicants seeking registration of new pesticides for use in the country under Section 9(3) of the Insecticide Act, 1968. The said draft was an agenda item for the workshop organised by FSSAI on "Emerging issues in pesticide residue & scientific developments" conducted by FSSAI on 3rd Oct, 2012 at INSA, New Delhi in which various scientists, technical personals and representatives from Industry gave their comments on the proforma. The Panel reviewed the comments and incorporated necessary corrections and finalised the proforma. The draft proforma has been approved by Scientific Committee in its meeting held on 26.06.2013 and by Authority in its meeting held on 29.08.2013.

2. In this regard it is requested that CIB & RC may communicate to the Pesticide manufacturing industry that w.e.f. 01.01.2014, FSSAI will accept only those applications for fixation of MRL which are in the new proforma.

Yours faithfully,

(Dr. A. Madhavan)
I. I)

Encls: The approved proforma 01

Copy to:

1. PPS to Chairperson
2. PS to CEO
3. FSSAI Website

PROFORMA FOR SUBMITTING DATA ON RESIDUE AND TOXICITY BY THE APPLICANTS SEEKING REGISTRATION OF NEW PESTICIDES FOR USE IN THE COUNTRY UNDER SECTION 9(3) OF THE INSECTICIDE ACT, 1968

Format-I: SUMMARY OF GOOD AGRICULTURAL PRACTICES FOR PESTICIDE USES
(Application on agricultural and horticultural crops)

Responsible body for reporting: (name, address)		Date: - Page: Country:	
Pesticide (Common name):			
Trade name:			
Main Uses:			

Use Pattern

Crop and/or situation	F or G	Pest or group of pests controlled	Formulation		Application			Application rate per treatment			PHI (days)	Remarks (1)
			Type	Conc. of ai	method, kind	growth stage	number (range)	kg ai/hl	water l/ha	kg ai/ha		
(a)	(b)	(c)	(d-f)	(i)	(f-h)	(j)					(k)	

PHI— Pre-harvest Interval
SC - Suspension concentration
F— Field use
j— Growth stage at last harvest

I)GENERAL INFORMATION

1) Identity-

- ISO common name
- Chemical name
  IUPAC
  CAS
- CAS Registry No.
- CIP AC No.
- Synonyms and trade names
- Structural formula
- Molecular weight

2) *Active ingredient*

Physical Properties

- PHYSICAL STATE
- COLOUR
- DENSITY
- MELTING POINT
- STABILITY. (TIME AND TEMPERATURE TO BE MENTIONED)
- VAPOUR PRESSURE IN MPA

Chemical Properties

- OCTANOL WATER PARTITION COEFFICIENT
- SOLUBILITY
- HYDROLYSIS
- PHOTOLYSIS
- DISSOCIATION CONSTANT

***3.* Technical Material**

Physical Properties

- MINIMUM PURITY (IN %)
- PHYSICAL STATE
- COLOUR
- DENSITY
- MELTING POINT RANGE
- STABILITY (TIME AND TEMPERATURE TO BE GIVEN)

Chemical Properties

- REFERENCE TO FAO SPECIFICATIONS FOR TC OF TK (TC, TECHNICAL MATERIAL, TK,TECHNICALCONCENTRATES), IF APPLICABLE

***4.* Formulations**

[Provide a list of commercially available formulations]
Type of formulation: (EC, WDP, WP etc.)
Properties:

- PHYSICAL STATE
- COLOUR
- STRENGTH OF THE FORMULATION
- DENSITY
- SOLUBILITY

II) METABOLISM AND ENVIRONMENTAL FATE

A) Crop Metabolism Studies-

1) Identification and quantification of the metabolites on the registered crop and on similar crops are required.
2) Metabolic Pathways in crops.

- **B) Animal metabolism studies -** metabolism studies in livestocks such as poultry and ruminants*.

1) Live Stock Metabolism

-Determine the composition of the residue in Livestock tissues and milk

Livestock feeding studies(Poultry and ruminants)

- *Compund and purity*
- Doses-- ?? mg/kg bw/day equivalent to ?? ppm in feed dry weight.
- Method of administration- Capsule or mixed with ration.
- Dosing regime---- ? time per day, ?? number of days.

Animals

- Breeed-
- Number of animals in each group-
- Numbe of groups(Typically three dosing grp and control grp.)-
- Body weight- ??kg
- Feed consumption- ?? kg feed dry weight per day
- Milk production- ?? liters or kg per day

Procedure

- Nature of feed ration-
- Milk collection- ?? times per day
- Milk composition-
- Interval between final dose and slaughter for tissue collection-
- List of tissue collected(note different type of fat and muscle)-
- Fat types kept separate or composited for analysis-
- Separation of cream from milk for separate analysis

(THIS INFORMATION IS ONLY REQUIRED FOR THE COMPOUNDS WHICH ARE RECOMMENDED TO BE USED IN CROPS AS ANIMAL FEED OR DIRECTLY ON ANIMAL FEED OR TO BE USED AS VETERINARY APPLICATION IN DOMESTICATED LACTATING ANIMALS. SIMILARLY IN CASE OF POULTRY STUDY , IT IS REQUIRED ONLY IF THE COMPOUND IS RECOMMENDED TO BE USED ON POULTRY FEED.

** In case of poultry similar checklist to be adopted except instead of milk egg has to be taken.

Detemine the levels of residue occurring in animal feed mateials as a result of the pesticide use following GAP-

Calculate the livestock dietary burden from residue levels and live stock diet-

Apply the dietary burden to the results of the livestock feeding studies to estimate residue levels in animal commodities-

NB:
Whereever the pesticides are used for direct application on animals for ectoparasite control, the crop metabolism/metabolic pathway studies are not required. However, the information on the animal metabolism study including absorption, distribution metabolism and excreation pattern of the pesticides to be given as per the above checklist

III) FATE AND BEHAVIOUR IN SOIL-
IV) FATE AND BEHAVIOUR IN WATER/ WATER-SEDIMENT SYSTEMS-

V) DATA ON RESIDUES-

A) INFORMATION ON SUPERVISED FIELD TRIALS FOR RESIDUE STUDIES
(FOR HERBICIDE, DATA TO BE GENERATED FOR 2 SEASONS, 3 LOCATIONS AND FOR OTHERS, DATA TO BE GENERATED FOR 1 SEASON, 4 LOCATIONS,)

Details	Season I				Season II		
	L1	L2	L3	L4	L1	L2	L3
(a) Location / Trial conducted							
Name of the institute where residue trial has been carried out							

Name of the institute where residue analysis has been carried out							
(b) Application Data							
Name of the crop including variety							
Crop planting / sowing date							
Description of the plot plan/crop lay out/cropping system							
Plot size							
Number of plants per plot / unit area							
Number of plots per treatment							
Method of application and equipment							
Number of applications and application dates							
Application details							
Dose rate							
Spray volume	Untreated /control standard dose a.l/ha Double dose a.l/ha	Untreated/ control standard dose a.l/ha Double dose a.l/ha	Untreated/control standard dose a.l/ha Double dose	Untreated/control standard dose a.l/ha Doubl	Untreated/ control standard dose a.l/ha Double dose a.l/ha	Untreated/control standard dose a.l/ha Double dose a.l/ha	Untreated/control standard dose a.l/ha Double dose

			a.l/ha	e dose a.l/ha			a.l/ha

CLIMATIC CONDITIONS	**Season I**				**Season II**		
	L1	**L2**	L3	L4	L1	**L2**	**L3**
Av. Min. temp (^{0}C)							
Av. Max. temp (^{0}C)							
Max. Relative Humidity							
Min. Relative Humidity							
Av Relative Humidity (%)							
Rainfall (mm)							
Av Relative Humidity (%)							
Other pesticides applied to trial plots with relevant details							
Growth stage at last treatment							

SAMPLING DATA
No. of samples taken per test/treatment
Sample weight and preparation
Data of sampling with time
Interval between application and sampling
Storage conditions before analysis

B) METHOD OF ANALYSIS-

Laboratory should validate the method followed for pesticide residues analysis and establish recovery in the range of 70 to 130 %, relative standard deviation (< 20%) at LOQ or at the reporting limit.

C) STORAGE STABILITY TESTS-

The result of storage stability test for residues in stored analytical samples of representative substrate should be provided for samples held in storage before analysis.

D)RESIDUE DATA-

In case of cereals, oil seeds, pulses, which are harvested information may be as follows:

RESIDUES	**RESIDUES ESTIMATED AT HARVEST (mg/kg)**		
	Agl Prod (Year) Soil	Agl Prod (Year) Soil	Agl Prod (Year) Soil
Control			
Replication I			
Replication II			
Replication III			
Mean+ SD			
Standard dose (a.i./ha)			
Replication I			
Replication II			
Replication III			

Mean			
Double Dose (a.i./ha)			
Replication I			
Replication II			
Replication III			
Mean+ SD			

In case of fruits and vegetables the residue data should be submitted as follows:

DAYS	NORMAL DOSE RESIDUE (MG/KG)				DOUBLE DOSE RESIDUE (MG/KG)			
	R1	R2	R3	MEAN+SD	R1	R2	R3	MEAN+ SD
0								
1								
3								
5								
7								
10								

D) EFFECT ON NORMAL PROCESSING ON THE FATE OF RESIDUE-

Processing data is not required when the plant material is used as raw and also if the residues are below the limit of quantification level.

Proposed waiting period
Proposed MRL limit
Precribed MRL registered crop in other countries
MRLs of pesticides o other crops

E) USE PATTERN-

The use pattern should be summarized from two aspects, (1) biological efficacy and (2) formulation and application. The biological efficacy should be given in the format I and information and formulation and application should be summarized in the format II

F) GAP INFORMATION-

The information should be given in the format II.

Residues resulting from supervised trials on crops:

The information should be given in the format IV. To ensure the availability of all detailed information necessary for evaluation, copies of the complete original reports on the supervised trials must be submitted.

Format II: Information on pests and diseases controlled

Crop	Pests/diseases controlled	Timing of application(s)

Format III: Registered uses on vegetables and cereals

Crop	Country	formulation	Application				PHI Days
			Method	Rate kg ai /ha	Spray conc., kg ai/hl	Number	

Format IV: RESIDUES DATA SUMMARY FROM SUPERVISED TRIALS
(Application on agricultural and horticultural crops)

Active ingredient:		Crop/crop group:	
Responsible body for reporting (name, address):		Submission date:	
Country:		Page:	
Content of ai (g/kg or g/l):		Indoor/outdoor:	
Formulation (e.g. WP):		Other ai in formulation:	
Commercial product (name):		(Common name and content):	
Producer of commercial product		Residues calculated as:	

Report-No.: Location incl. Postal code	**Crop Variety**	**Date of Sowing or planting; Flowering or Harvest**	**Application rate per treatment**			**Dates of treatment(s) or no. of treatments and last date**	**Growth stage at last treatment or date**	**Commodity, Portion analyzed**	**Residues (mg/kg)**			**PHI (days)**	**Remarks**
			kg ai/ha	**water l/ha**	**kg ai/hl**				**Days**	**g a.i. / ha (X)**	**g a.i. / ha (2X)**		

VI) TOXICOLOGY ***

.Summary of acute toxicity studies with XXXXXXXXXXX

SPECIES	**STRAIN**	**SEX**	**ROUTE**	**BATCH NO.; PURITY (%)**	**LD_{50} (MG/KG BW)**	**LC_{50} (MG/L)**	**RESULTS**	**REFERENCE**
MOUSE ***(CAN BE GIVEN IF AVAILABLE)***								
RAT								
RAT								
RAT								

SPECIES	STRAIN	SEX	ROUTE	BATCH NO.; PURITY (%)	LD_{50} (MG/KG BW)	LC_{50} (MG/L)	RESULTS	REFERENCE
RAT								
RAT								
RAT								
RAT								
RABBIT								
RABBIT								
GUINEA-PIG								
GUINEA-PIG								

Table- Results of genotoxicity studies with XXXXXXXXXXX-

Test system	Test compound Strain/species/cell line used	Concentrations	Purity (%)	Result	Reference
In vitro					
Reverse mutation study					
DNA repair test on Bacteria **(Rec assay)**					

Test system	Test compound Strain/species/cell line used	Concentrations	Purity (%)	Result	Reference
Gene mutation mammalian cells					
Gene mutation / chromosomal aberration mammalian cells					

Test system	Test compound Strain/species/cell line used	Concentrations	Purity (%)	Result	Reference
Chromosomal aberration mammalian cells					
Unscheduled DNA synthesis					
In vivo					
Micronucleus test					
Chromosomal aberration test **(Bone marrow cells)**					
Unschedule DNA synthesis(UDS)					

TABULAR SUMMARY OF PIVOTAL TOXICOLOGICAL STUDIES

STUDIES	SPECIES(STRAIN) NO.OF ANIMALS	DURATION	PURITY	DOSE LEVELS/REGIMEN AND ROUTE OF ADMINISTRATION	NOAEL (MG/KG BW/DAY)	LOAEL (MG/KG BW/DAY)	CRITICAL EFFECTS	REFERENCE
SHORTTERM STUDIES (UPTO 1 YEAR)	MOUSE							
	RAT							
	RABBIT							
	DOG							
LONGTERM STUDIES (MORE THAN 1 YEAR)	MOUSE							
	RAT							
CARCINOGENICITY	MOUSE							
	RAT							
REPRODUCTIVE TOXICITY								
TERATOGENICITY	RAT							
	RABBIT							
NEUROTOXICITY								
OTHERS								

ADI
NATIONAL MRLS REGISTERED ON OTHER CROPS RESIDUE DEFINITION
LABELS AND LEAFLETS (COPY OF THE PROPOSED SPECIMEN TO BE ATTACHED)

***** EXAMPLES**

. Summary of acute toxicity studies with XXXXXXXXXXX

SPECIES	**STRAIN**	**SEX**	**ROUTE**	**BATCH NO.; PURITY (%)**	**LD_{50} (MG/KG BW)**	**LC_{50} (MG/L)**	**RESULTS**	**REFERENCE**
MOUSE	CRJ:ICR, SPF	M + F	ORAL	NNI-02 99.46	M: 198 F: 184		[A]	MOCHIZUKI,& GOTO,. (1992)
RAT	CRJ:CD(SD), SPF	M + F	ORAL	NNI-02;	M: 217		[B]	MOCHIZUKI,&

Species	Strain	Sex	Route	Batch No.; purity (%)	LD_{50} (mg/kg bw)	LC_{50} (mg/L)	Results	Reference
				99.46	F: 146			Kanaguchi. (1992)
Rat	Crj:CD(SD), SPF	M+F	Oral	NFG-02 99.9%	M-417 F-314		[C]	Takaori (1997 b)
Rat	Crj:CD(SD),IGS, SPF	M+F	Oral	NKP-194-07 99.9%(Suspended in corn oil)	M-195 F-140-200		[D]	Fujii (2002)
Rat	Crj:CD(SD), SPF	M + F	Dermal	N NI-02 99.46%	>2000		[E]	Mochizuki,& Fujii(1998)
Rat	Crj:CD(SD), SPF	M + F	Dermal	N FG-02 99.9%	>2000		[E]	Takaori (1997 a)
Rat	Crj:CD(SD)	M + F	Inhalation 4 h (whole body exposure)	NNI-03 99.57%	—	>0.30 (Dust; MMAD 5 μM)	[F]	Saika (1994),
Rat	Sprague	M+F	Inhalation	NFG-		>1.15	[G]	Jackson,

SPECIES	STRAIN	SEX	ROUTE	BATCH NO.; PURITY (%)	LD_{50} (MG/KG BW)	LC_{50} (MG/L)	RESULTS	REFERENCE
	-DAWLEY		4 H (NOSE ONLY EXPOSURE)	02 99.9%		(DUST; MMAD 8 µM)		(1997)
RABBIT	NEW ZEALAND WHITE	M	PRIMARY DERMAL IRRITATION/	NNI-02 99.46	—	—	NON-IRRITANT	MOCHIZUKI,&,GOTO (1993 A)
RABBIT	NEW ZEALAND WHITE	M	EYE IRRITATION	NI-25 99.46	—	—	NON-IRRITANT	MOCHIZUKI,&,GOTO (1993 B)
GUINEA-PIG	DUNKIN/ HARTLEY	F	SKIN SENSITIZATION EFFECTS (GUINEA-PIG MAXIMIZATION)	NNI-02 99.46	—	—	NON-SENSITIZER	MOCHIZUKI, (1994 A):
GUINEA-PIG	HARTLEY	M+F	SKIN SENSITIZATION EFFECTS (DELAYED CONTACT HYPERSENSITIVITY)	NFG-02 99.9	—	—	NON-SENSITIZER	COLEMAN (1997)

F, female; M, male; MMAD, mass median aerodynamic diameter

[a] In dose of 100mg/kg,crouching was observed for 20 minutes to 3 hours in males and for 20 minutes to one hour in females after administration.In 150 -400mg/kg in both sexes,most mice showed tremors for 10 minutes to 3 hours after

administration.Additionally,in 150 to 400mg/kg males and 290,400 mg/kg females,a few mice showed convulsion for 20 min to one hour after administration.All toxic signs disappeared within one day after the administration.In some surviving females of two highest dose,the body weight decreased on day 1 and recovered afterwards.Six out of 27 dead mice revealed dark-reddish lung on necropsy.

[b] No toxic signs were observed at 100mg/kg male and 80mg/kg females.In 150- 304mg/kg males and in 100-230mg/kg females,most rats showed crouching for 3hrs to one day after administration.In 150-510mg/kg males and 100-510mg/kg females,most rats showed tremors for 3hrs to one day after the administration.A few rats showed low sensitivity,lateral position,prone position,salivation,urine incontinence and ataxia for 60 minutes to one day.All toxic signs disappeared within two days after administration.Three rats out of 37 dead revealed dark-reddish lung on necropsy.

[c] Clinical signs noted in the treated rats were lacrimation(1 rat in 100mg/kg grp),mydriasis,tremor,clonic convulsion,prone position and lateral position.These signs appeared shortly after administration and their incidences reached maximum at 60 or 180 minutes.No abnormality was observed at gross necropsy..

[d] Mydriasis and tremor were observed in all dose groups.Clonic convulsion were observed in males at 200,280 and 560 mg/kg and in females at 280,400 and 560 mg/kg.These signs appeared shortly after administration and reached maximum at 60 or 180 minutes.All deaths occurred within 1 day after administration.There were no treatment-related macroscopic observation.

[e] Neither any toxic signs observed nor any death occurred.

Results of genotoxicity studies with XXXXXXXXXXX

Test system	**Test compound Strain/species**	**Concentration**	**Purity (%)**	**Result**	**Reference**
In vitro					
Reverse mutation study	XXXXXXXXXXX Salmonella typhimurium TA98, TA100, TA1535, TA1537 Escherichia coli Strain-WP2 uvrA	313,625,1250,2500 and 5000 µg/plate	99.2	Negative with S9 mix Negative without S9 mix	Kanaguchi (1993 a)

Test system	Test compound Strain/species	Concentration	Purity (%)	Result	Reference
DNA repair test on Bacteria (Rec assay)	XXXXXXXXXXX Bacillaceae Bacillus Subtilis [M45(rec-) and H17(rec+)]	1359,2718,5435, 10870 and 21740µg/disc without metabolic activation, 679.4,1359,2718 ,5435, and 10870µg/disk with metabolic activation.	99.46	Negative	Kanaguchi (1992 b)

Test system	Test compound Strain/species	Concentration	Purity (%)	Result	Reference
Gene mutation mammalian cells #	XXXXXXXXXXX CHO cells (HPRT locus)	Without S9 mix Test-1: 500, 1000, 2000, 2500,3000,3500,4000 µg/ml Test-2: 1000,2000,2500,3000,3500,4000 µg/ml With S9 mix Test-1: 250,500, 1000,1500, 2000, 3000,3500,4000 µg/ml Test-2: 500,1000,1500,2000,2250,2500,2750 µg/ml	Not given	Negative	Adam (1997)

Test system	Test compound Strain/species	Concentration	Purity (%)	Result	Reference
Gene mutation / chromosomal aberration mammalian cells ##	XXXXXXXXXXX Mouse lymphoma forward mutation assay L5178Y Tk+/− cells (TK locus)	63.5µg/ml to 2000 µg/ml	99.57	Negative without metabolic activation. Questionable for inducing forward mutation with metabolic activation	Cifone (1994)
Chromosomal aberration mammalian cells @	XXXXXXXXXXX CHO cells	17.0,33.9,67.8,35.6, 271.3,542.5,1085 and 2170µg/ml	99.2	Induce chromosomal aberration under metabolic activation and week in without metabolic activation	Kanaguchi (1992 a)
Unscheduled DNA synthesis @@	XXXXXXXXXXX Rat primary hepatocytes	505µg/ml to 10.1µg/ml	99.57	Negative	Ham (1994)

Test system	Test compound Strain/species	Concentration	Purity (%)	Result	Reference
In vivo					
Micronucleus test $	XXXXXXXXXXX CD-1(ICR) Mice	Oral(gavage,one application)20,40,80mg/kg bw	99.57	Negative	Murli (1994 a)
Chromosomal aberration test (Bone marrow cells) $$	XXXXXXXXXXX Sprague-Dawley CD strain Rat	Single oral dose of 250mg/kg bw(gavage)	99.46	Non-clastogenic	Durward (1993)
Unschedule DNA synthesis(UDS) $$$	XXXXXXXXXXX Sprague-Dawley strain Rat(Liver cell)	75,150 and 300 mg/kg bw	99.9	Negative	San & Sly(1997)

(#) XXXXXXXXXXX was tested for its ability to induce forward mutation at the functionally hemizygous hypoxanthine-guanine phosphoribosyl transfense (HPRT) locus in Chinese hamster ovary (CHO) cells in vitro both in the presence and the absence of exogenous metabolic activation in the form of Aroclor 1254-induced rat liver S-9.Toxicity was observed after treatment with XXXXXXXXXXX in all of the tests, both in the absence and the presence of S-9 mix. No significant increases in mutant frequency were observed in cultures treated with XXXXXXXXXXX in any of the tests either in the absence or the presence of S-9 mix. The positive controls induced highly significant increases in mutant frequency in all of the tests in both the absence and presence of S-9 mix.It was concluded that XXXXXXXXXXX did not demonstrate mutagenic potential in this in vitro mammalian cell gene mutation assay.

(##) The assay was to evaluate the ability of XXXXXXXXXXX to induce forward mutations at the thymidine kinase (TK) locus in the 15178Y mouse lymphorna cell line. The test material was soluble in DMSO at 500 mg/ml. In the preliminary cytotoxicity assay, cells were exposed to the test material at concentrations from 1.95 µg/ml to 1000 µg/ml for four hours in the presence and absence of rat liver S9 metabolic activation.The test material remained in solution in culture medium at all concentrations tested. The

test material was weakly to moderately cytotoxic with and without metabolic activation at 1000 µg/ml and lower concentrations were nontoxic. The mutation assays were initiated with treatments up to about 5070 µ9/ml in an attempt to obtain more cytotoxic dose levels.Four nonactivation and four S9 metabolic activation mutation assays were initiated. The studies were repeated several times in an attempt to clarify a response and because shifts in cytotoxicity occurred.The test material produced dose—related increases in toxicity in all mutation trials. In the nonactivation trials. the test material was lethal or excessively toxic above between 1500 µg/ml and about 3000 µg/ml. Treatments that induced less than 10% relatIve growth were not used in the analysis since these results are considered unreliable.None of the remaining treatments induced mutant frequencies that exceeded the minimum criterion for a positive response. In the presence of metabolic activation, treatments from 63.5 µg/ml to about 2000 µg/ml were evaluated, Small increases that just exceeded the minimum criterion for a positive response were observed in two trials. One trial did not have highly toxic treatments and the results were inconclusive and the last trial had one treatment that approached, but did not meet the minimum criterion for a positive response.The test material was therefore considered to have questionable activity with activation. XXXXXXXXXXX was therefore evaluated as negative without metabolic activation and questionable for inducing forward mutations at the TK locus in L5178Y mouse lymphoma cells in the presence of S9 metabolic activation and under the conditions used in this study.

(@) In the direct method, chromosomal aberration was slightly increased (p<O05) at 175 .µg/ml and 700 µg/ml in comparison with that in the solvent control. In the metabolic activation method. chromosomal aberration was significantly increased with dose-relationship at middle and high test concentrations (675 µg/m1 and 1,350 µg/m1).The frequencies of chromosomal aberration did not increase in the metabolic activation without S9mix (reference test). BP, which requires metabolic activation for expression of mutagenicity, incrcased chromosomal aberrations under the presence of S9mix, but not under the absence of S9mix.Through both methods, chromosome aberration frequencies in the negative and the solvent controls were in the range of our historical background data.On the basis of the results, the author considered that XXXXXXXXXXX induced chromosomal aberration under the metabolic activaion condition, and its activity was lower under the condition without metabolic activation.

(@@) In the Assay for Unscheduled DNA Synthesis (UDS) in Rat Liver Primary Cell Cultures, the test material, XXXXXXXXXXX, did not induce significant increases in UDS in two independent trials. In each trial described in this report, freshly prepared rat hepatocytes were exposed to NI-25 at concentrations ranging from 5000 to 0.500 µg/ml in the presence of 10 iCi/ml ^{3}HTdr (42 Ci/mMoIe). In Trial 1, fifteen treatments from 5000 to 0.500 µg /ml were initiated. The test material was insoluble in media at concentrations of 5000 and 4000 µg /mI with apparent solubility occurring at 3000 µg /mI. Five treatments from 5000 to 1000 µg /ml were not analyzed for nuclear labeling due to high toxicity. Six treatments from 500 - 10.0 µg /m1 covered a good range of toxicity (53.2% to 98.4% survival) and were selected for analysis of nuclear labeling. None of the criteria used to indicate UDS was approached by the chemical treatments in Trial I and no dose-related response was observed. A second trial was initiated to confirm these results.Based upon cytotoxicity information obtained in Trial 1, twelve dose levels from 2020 to 0.505 µg /ml were initiated in Trial 2. Treatments of 2020 to 1010 µg /ml were not analyzed due to high toxicity. Six treatments from 505 to 10.1 µg /mI covered a good range of toxicity (64.4% to 107.5% survival) and were selected for analysis of nuclear labeling. None of the criteria used to indicate UDS was approached by the chemical treatments in Trial 2. The data confrrmed the results from Trial 1 and XXXXXXXXXXX was evaluated as inactive in both trials of the Rat Primary Hepatocyte UDS Assay.

($$) Study was performed to assess the potential of XXXXXXXXXXX to produce damage to chromosomes or the mitotic apparatus of rats when administered by the oral route. The method used followed that described in the OECD Guidelines .Following a preliminary range-finding study to confirm the oral toxicity of the test material, the chromosome aberration study was conducted using XXXXXXXXXXX at the maximum tolerated dose level of 250 mg/kg.In the study groups of ten rats (five males and live females) were given a single oral dose of XXXXXXXXXXX at the maximum tolerated dose (250 mg/kg).Animals were killed 6, 24or 48 hours later, the bone marrow extracted and slide preparations made and stained.Bone marrow cells were scored for the presence of chromosome aberrations.Further groups of rats were treated with arachis oil BP or cyclophosphamide, to serve as vehicle and positive controls respectively. There was no evidence of an increase in the ncidence ol chromosome aberrations in animals treated with XXXXXXXXXXX when compared to the vehicle control groups.The positive control material produced a marked increase in the frequency of chromosome aberrations. XXXXXXXXXXX was considered to be non-clastogenic under the conditions of the test.

($$$)Tested in the UDS test with mammalian liver cells in vivo.The assay was performed in two phases. The first phase, the initial and repeat dose-finding assays, was a toxicity study used to aid in the selection of dose levels to be used in the UDS assay. The second phase, the UDS assay, was used to evaluate the potential of the test article to induce unscheduled DNA synthesis in hepatocytes of exposed male rats.In all phases of the study, test and control articles were administered at a constant volume of 10mI/kg body weight (bw) by a single oral gavage injection.In the initial dose-finding assay, male rats were exposed to 50, 100, 200, 400 and 1250 mg test article/kg bw. All five dose preparations were prepared independently, vortexed upon preparation, and vortexed again immediately before dosing the animals. Weight loss was observed at all dose levels with only the animals in the 50 and 100 mg/kg bw dose groups regaining body weight on day three. As the LD 50 (1640mg/kg)calculated in this study was different from the earlier study(217mg/kg),the dose –finding assay was repeated. In the repeat dose-finding assay, male rats were exposed to 50, 100, 200, 400 and 1250 mg test article/kg bw.Weight loss was observed in animals of the 200 and 400 mg/kg bw dose groups while the 100 mg/kg bw animals exhibited weight gain on day one and weight loss on day three. The 50 mg/kg bw animals showed minimal weight gain on days one and three . The 1250 mg/kg bw animals were found dead before a weight determination could be made on day one. . Body weights were determined prior to treatment, on day one and day three. In the UDS assay, male rats were exposed to 75, 150 and 300 mg/kg test article body weight The selection of 300 mg/kg bw as the high dose was based on the clinical signs and weight loss observed at 400 mg/kg bw, and weight loss observed at 200 mg/kg bw (in the repeat dose-finding assay). In the UDS assay, no mortality was observed in any treated or control rats. Clinical signs were normal in all dose groups following dose administration and prior to harvesting of the hepatocytes at the 2-4 hour and 12-16 hour exposures, with the exception of one animal in the 300 mg/kg bw, 2-4 hour exposure dose group exhibiting lethargy and tremors. However, this animal was not used in the hepatocyte harvest. Upon perfusion, the livers of the 300 mg/kg bw animals from the 2-4 hour and 12-16 hour exposures were observed to be much darker than the livers from any of the other dose groups.The test article, XXXXXXXXXX, did not induce a significant increase in the mean number of net nuclear grain counts (i.e., an increase of at least 5 counts over the negative control group) in hepatocytes isolated either 2 to 4 hours or 12 to 16 hours after dose administration. XXXXXXXXXXX was concluded to be negative in the unscheduled DNA synthesis (UDS) test with mammalian liver cells in vivo.

TABULAR SUMMARY OF PIVOTAL TOXICOLOGICAL STUDIES

STUDIES	SPECIES(STRAIN) NO.OF ANIMALS	DURATION (PURITY)	DOSE LEVELS	NOAEL (MG/KG BW/DAY)	LOAEL (MG/KG BW/DAY)	CRITICAL EFFECTS	REFERENCE
SHORTTERM STUDIES (UPTO 1 YEAR)	MOUSE						
	RAT						
	RABBIT						
	DOG						
LONGTERM STUDIES (MORE THAN 1 YEAR)	MOUSE						
	RAT						
CARCINOGENICITY	MOUSE						
	RAT						
REPRODUCTIVE TOXICITY							
TERATOGENICITY	RAT						
	RABBIT						
NEUROTOXICITY							
IMMUNOTOXICITY (IF AVAILABLE)							
OTHERS							

NB: All the information and data has to be submitted in form of CD.

Checklist for submission of information for fixation of MRLs for newer pesticides

For fixation of MRLs complete information/details on various parameters of residues and toxicology of pesticides are essential in the enclosed proforma by Ministry of Health and Family Welfare. The Registration Secretariat may ensure that the information received from the registrants is complete from all aspects so that MRLs are fixed correctly and without delay.

1. Name of pesticides and the crop on which the MRLs is to be fixed.
2. Date on which application was received by the Registration Secretariat.
3. Date on which application with data is sent to the Ministry of Health and family Welfare.
4. General information-

A)	IDENTITY	YES	NO
B)	PHYSICAL AND CHEMICAL PROPERTIES	YES	NO
C)	TECHNICAL MATERIAL	YES	NO
D)	FORMULATION	YES	NO
E)	METABOLISM AND ENVIRONMENTAL FATE	YES	NO

5. Application data on supervised trials (Information in respect of following is provided or not)

A)	TRIAL CONDUCTED	YES	NO
B)	COMMODITY	YES	NO
C)	NAME OF THE INSTITUTE WHERE	YES	NO

	SUPERVISED TRIALS WERE CARRIED OUT		
D)	NAME OF THE INSTITUTE WHERE RESIDUE ANALYSIS WERE CARRIED OUT	YES	NO
E)	CROP PLANTING/SOWING DATA	YES	NO
F)	PLOT SIZE IS MENTIONED	YES	NO
G)	NUMBER OF PLANTS PER PLOT	YES	NO
H)	NUMBERS OF TREATMENTS PROVIDED	YES	NO
I)	METHOD OF APPLICATION AND EQUIPMENT	YES	NO
J)	NO. OF APPLICATION AND DATES	YES	NO
K)	DOSE RATIO	YES	NO
L)	SPRAY VOLUME	YES	NO
M)	GROWTH STAGE AT LAST TREATMENT	YES	NO

6. Sampling data

A.	DETAILS OF NO. OF SAMPLES TAKEN PER TEST	YES	NO
B.	DETAILS OF SAMPLE WEIGHT AND PREPARATION	YES	NO
C.	DETAILS OF SAMPLING WITH TIME	YES	NO
D.	INTERVAL BETWEEN LAST APPLICATION	YES	NO

	AND SAMPLING		
E.	HAS THE DATA ON THE FOLLOWING: WAITING PERIOD PRE-HARVEST INTERVAL	 YES YES	 NO NO

7. Method of analysis:

A)	COMPLETE METHOD OF ANALYSIS AS PER BIS FORMAT	YES	NO
B)	RESULTS OF RECOVERY EXPERIMENTS INDICATING LEVEL FORTIFICATION	YES	NO
C)	DETAILS OF EQUIPMENT PROVIDED	YES	NO
D)	LIMIT OF DETERMINATION IS INDICATED	YES	NO

8. Climatic Conditions: whether details of the following provided:

A)	AVERAGE MIN. TEMPERATURE (DEGREE CELSIUS)	YES	NO
B)	AVERAGE MAX. TEMPERATURE (DEGREE CELSIUS)	YES	NO
C)	MINIMUM RELATIVE HUMIDITY	YES	NO
D)	MAXIMUM RELATIVE HUMIDITY	YES	NO
E)	AVERAGE RELATIVE HUMIDITY	YES	NO
F)	RAINFALL (MM)	YES	NO

G)	OTHER PESTICIDES APPLIED TO TRIAL PLOTS WITH RELEVANT DETAILS	YES	NO
I)	GROWTH STAGE AT LAST TREATMENT	YES	NO

9. Data on toxicity- whether information on the following is provided:

A)	ACUTE ORAL RAT LD_{50}	YES	NO
B)	ACUTE ORAL MICE LD_{50}	YES	NO
C)	ACUTE DERMAL LD_{50}	YES	NO
D)	ACUTE INHALATION LD_{50}	YES	NO
E)	MUTAGENICITY NAME OF TESTS DOSES USED RESULTS	YES	NO
F)	TERATOGENECITY RAT RABBIT	YES YES YES	NO NO NO
G)	EFFECT ON REPRODUCTION (RAT)	YES	NO
H)	CARCINOGENECITY (RAT/MICE) NOEL	YES	NO
I)	TOXICITY TO LIVESTOCK (ANIMAL NAME)	YES	NO
J)	ADI	YES	NO
K)	BASIS OF CALCULATION OF ADI	YES	NO
L)	HAS THE PESTICIDE REVIEWED BY JMPR OR ANY OTHER INTERNATIONAL ORGANISATION? IF SO	YES	NO

	WHETHER DETAILS HAVE BEEN PROVIDED?		
M)	HAS THE PROPOSED MRL OF THE PESTICIDE IN CROP BEEN GIVEN?	YES	NO
N)	HAS MRL FIXED BY OTHER COUNTRIES ON THE PROPOSED FOOD COMMODITY BEEN SUBMITTED	YES	NO
O)	HAS THE RESULTS OF THE RESIDUE ANALYSIS FOR THREE SEASONS/MULTI LOCATION TRAILS BEEN SUBMITTED?	YES	NO
P)	HAVE YOU GIVEN INFORMATION ON USE PATTERNS	YES	NO
Q)	HAVE YOU GIVEN INFORMATION ON GAP INFORMATION	YES	NO
R)	HAVE YOU GIVEN INFORMATION ON RESIDUES RESULTING FROM SUPERVISED TRIALS ON CROPS	YES	NO
S)	HAVE YOU GIVEN INFORMATION ON NATIONAL MAXIMUM RESIDUE LIMIT	YES	NO
T)	HAVE YOU GIVEN INFORMATION ON RESIDUE DEFINITION	YES	NO