

# Global data requirements for vertebrate testing of pesticides: Opportunities for best practice and harmonisation

Natalie Burden (NC3Rs), Samuel K. Maynard (Syngenta), Lennart Weltje (BASF SE), Michael Fryer (UK Chemicals Regulation Directorate) and James R. Wheeler (Dow AgroSciences).

Corresponding author: natalie.burden@nc3rs.org.uk

Most new pesticide active substances and their products are developed for global use. Consequently, environmental data packages are developed to meet the data requirements of all the regions and countries for which registration is intended. These different geographies often require different and sometimes duplicative testing. Such requirements can greatly increase the number of vertebrate animals used without necessarily increasing the quality or utility of information for decision making. Here we review the global vertebrate data requirements for some major regions with the aim of highlighting opportunities for best practice under current legal requirements and to promote further harmonisation.

## Systematic review:

- Shorter term - identify good practice within the current requirements to enable immediate Reduction.
- Longer term - identify opportunities for better harmonisation and mutual data acceptance across regions.

Study type	Descriptor	Test guidelines	Estimated animal numbers	Europe			North America			LATAM				Asia						Others				
				EU28	US	Canada	Argentina	Brazil	Chile	Uruguay, Paraguay, Bolivia	China	India, Pakistan	Indonesia	Japan	Malaysia	Philippines	Thailand	Vietnam	Australia, New Zealand	Russia	Andean, Caribbean, Central America			
Birds	Acute oral toxicity	Bobwhite quail	OPPTS 850.21 or OECD 223 or JMAFF 2-8-3	14.3-43.7*	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x				
		Passerine	OPPTS 850.21 or OECD 223	14.3-43.7*		x																		
		Mallard duck	OPPTS 850.21 or OECD 223	14.3-43.7*																				
		Crawling species††	OECD TG233	14.3-43.7*																				
		Flying species†††	OECD TG233	14.3-43.7*																				
	Acute dietary toxicity	Bobwhite quail	OPPTS 850.22 or JMAFF 2-8-4-2	80		x	x	x	CR	x	x	x			x			x	CR		x	x		
		Mallard duck	OPPTS 850.22	80		x	x																	
		Passerine	OPPTS 850.22	80		CR	CR																	
		Crawling species††	OPPTS 850.22	80											x									
		Flying species†††	OPPTS 850.22	80											x									
Chronic reproductive dietary toxicity	Bobwhite quail	OCSPP 850.2300 or OECD 206	2560	x	x	CR		CR												x				
	Mallard duck	OCSPP 850.2300 or OECD 206	2560		x	CR																		
Chronic multi-generation endocrine toxicity	Japanese quail	TBC	Too little experience to predict	CR	CR																			
Mammals	Acute oral toxicity	Rat or mouse	OECD 420, 423 or 425	0**	x	x		x	x	x	x	x	x	x	x	x	x	x	x	x	x			
	Long term and reproductive toxicity	Rat or mouse	OECD 407, 408, 414 or 416	0**	x	x		x		x	x	x	x	x	x	x	x	x	x	x	x			
	Wild species	Variable	OPPTS 850.24	42-120		CR																		
	Simulated or actual field testing	Variable	OPPTS 850.25	42-120	CR	CR															CR			
Aquatic vertebrates	Acute fish toxicity	Coldwater	OECD 203 or OPPTS 850.1075	42-120	x	x	x	x		x	x			CR		x	x	x	x	x	x			
		Warmwater	OECD 203 or OPPTS 850.1075 or Gaitonde or JMAFF 2-7-1	42-120			x	x		x			x			x								
		Other	OECD 203 or OPPTS 850.1075	42-120					CR															
		Saltwater	OECD 203 or OPPTS 850.1075	42-120		x	CR																	
	Acute amphibian toxicity	Clawed frog	ASTM E729 - 96	42-120									x											
	Salinity fish challenge	Salmon smolts	TBC	?			CR																	
	Chronic fish early lifestage	Freshwater	OECD 210 or OPPTS 850.14	420	CR§§	x	CR	x	x	x	x										CR§§	x	x	
		Saltwater	OECD 210 or OPPTS 850.14	420		CR																		
	Chronic fish full lifecycle bioconcentration	Freshwater	None	1680	CR	CR	CR															CR		
		Saltwater	None	1680		CR																		
	Fish bio-concentration	Bluegill sunfish, carp or rainbow trout	OECD 305, OPPTS 850.1730 or JMAFF 2-9-17	300	CR	CR	CR	x	CR	x	x				CR	CR					CR	x	x	
	Endocrine fish screening	Screening assay	OECD 230	80-96***	CR																		CR	
		Short term reproduction	OECD 229 or OPPTS 890.1350	120-240 #	CR	CR																	CR	
	Endocrine amphibian screening	Meta-morphosis Assay	OECD 231 or OPPTS 890.1100	320	CR	CR																	CR	
	Endocrine fish definitive testing	Sexual development test	OECD 234	480-720†	CR																		CR	
Medaka extended one generation reproduction test (MEOGRT)		OCSPP 890.2200	1224 - 2064§	CR	CR																	CR		
Endocrine amphibian definitive testing	Larval amphibian growth and development assay (LAGDA)	OCSPP 890.2300	480	CR	CR																	CR		

CR = Conditional Requirement  
? = Too variable to estimate

\* Maynard S, Edwards P, Wheeler J. 2014. Saving two birds with one stone: using active substance avian acute toxicity data to predict formulated plant protection product toxicity. *Environmental Toxicology and Chemistry* 33:1578-1583.

\*\* Conducted for human health assessment  
\*\*\* Species dependent  
# Typically 2x as many used to ensure sufficient reproductively compatible groups

† Depending on screening or definitive mode  
†† Uncertain if bobwhite quail are acceptable  
††† Uncertain if mallard duck or passerine are acceptable

§ Depending if F2 reproduction is required  
§§ In practice most PPP active substances require

## Birds:

- Key species choices and acceptability of OECD test species and guidelines.

## Aquatic vertebrates:

- Key species choices (e.g. acute rainbow trout, chronic fathead minnow).
- Where second fish species required (warm water) choose species accepted in other regions (e.g. carp).
- Reconsider relevance/need for saltwater fish testing.
- Species consistency can reduce the need for range finding at different test levels (e.g. acute – chronic).
- Bridging data where appropriate (fish as surrogates for aquatic amphibians).

## Endocrine testing:

- Establish clear triggers and evaluation criteria.
- Employ exposure levels that avoid confounding factors such as systemic toxicity.
- Investigate alternative options to a bird multi-generation testing.

## Next steps:

- Complete evaluation for active substance requirements globally.
- Expand the analysis to include formulated product and metabolite testing.