Australian Government
Australian Pesticides and Veterinary Medicines Authority

Pre-application assistance (PAA) – APVMA written assistance

Applicant name:	Fisheries Research and Development Corporation
PAA ID:	136873
Assistance tier:	2
Product name:	Chloramine-T (N-chloro-4-methylbenzenesulfonamide sodium salt) / Marine and freshwater finfish. / Susceptible bacterial and parasite infections.
Date advice provided	18/10/2022

Summary of proposed application

Obtain advice on data requirement to contribute to a minor use permit application to treat susceptible bacterial and parasite infections in marine and freshwater finfish using Chloramine-T.

APVMA advice

The APVMA has reviewed your pre-application assistance application and provides the following advice under each of the relevant risk areas. Please note, advice has only been provided for technical areas requested by you in the PAA application form. Further data may be required to support a minor use permit application.

Chemistry and manufacture

As noted elsewhere in the document, chloramine-T is exempted from the requirement for active constituent approval, however products for veterinary use containing this active still require authorisation by registration or a permit. The proposed use for treatment of bacterial and parasite infections in finfish appears to involve direct use of the technical active constituent in water (the active content of the product is stated as 99%, so it appears that the product may not contain other ingredients).

Information that should be submitted for a limited chemistry assessment of the proposed permit should include specifications and a certificate of analysis for the active constituent (including limits for manufacturing impurities where available), specifications for the non-active ingredients in the product (if there are any other ingredients), the formulation details, finished product specifications, packaging specifications, and available data or argument on the product stability.

The APVMA can accept a relevant international chemistry assessment report if it is submitted with the underlying data.

A module 2.3 level assessment would be appropriate for assessment of a permit.

Human health (toxicology and worker health and safety)

For an unregistered product intended for minor permit use, a toxicology and WHS assessment will be required to establish first aid instructions and safety directions for the minor use label. This will be based on the formulation's acute hazard and repeat exposure risk from the use of the product.

You should provide formulation information, i.e., details of the formulations with toxicological information on the active constituent and each of the excipients in the formulation. You have noted the formulation is 99% Chloramine-T, therefore formulation toxicity will largely be based on the active constituent. During the toxicity assessment, the toxicity of formulation will be determined. You should also provide directions of use of the

product, i.e., use pattern, application equipment, method and rate of the application to assist in the worker exposure risk assessment.

Residues and trade

The considered use is for the immersion application of chloramine-T (N-chloro-4-methylbenzenesulfonamide sodium salt) to marine and freshwater finfish for an hour exposure on 3 consecutive days in conjunction with a re-treatment interval of 15-30 days and a zero-day WHP.

As indicated on the APVMA website, 'Any chemicals that are not approved, or exempted from approval, cannot be used as active constituents in an agricultural or veterinary chemical product, unless an application is made for approval of the active' (https://apvma.gov.au/node/4176). A residues assessment under a Module 5.5 will be required to evaluate the proposed use on fish.

For assessment, the residues definition of the considered active ingredients in fish will need to be addressed. The submission of a scientific argument and supporting literature and/or international assessments may be appropriate. In addition, the scientific argument as outlined in the current PAA submission documentation, along with full versions of all literature and/or international assessments as referenced, is considered appropriate for initial assessment of a minor use permit under a Module 5.5. The submitted information and argument will be evaluated during assessment.

A Trade Advice Notice consultation may be required should finite residues be expected at the proposed WHP.

Environment

Veterinary products are assessed using the VICH Phase I and VICH Phase II guidance[1] - if only a VICH Phase I assessment is required this will require a module 7.3 assessment, otherwise a module 7.2 is required.

The application information provided describes the treatment procedure but does not fully describe the disposal procedure for the spent treatment solutions (e.g., volume of solution to be disposed of, route of disposal). Environmental exposure is expected during disposal of the spent treatment solution, this will need to be sufficiently well described to demonstrate the routes of potential exposure and, depending on the level of assessment required (VICH Phase I/II), the concentration at disposal may need to be established. Any submission should fully describe the proposed use, any routes of environmental exposure, if relevant the environmental introduction concentration ($EIC_{aquatic}$) and any mitigation measures used to alter the $EIC_{aquatic}$. Supporting information should be provided, where needed (e.g., to demonstrate actual industrial practice or quantify actual induction concentrations).

As the proposed use is as an ectoparasiticide, unless the assessment stops in VICH Phase I (questions 1-8) a VICH Phase II assessment will be required. The information cited in the PAA application has not been evaluated for relevance/reliability as part of this PAA application. However, the sources cited can be used to address the data requirements. They appear to cover information relevant to the environmental fate and behaviour of chloramine-t and the base taxa required for risk assessment (fish, aquatic invertebrates and algae). It should be noted that original underlying studies that are critical for any risk assessment will need to be provided to the APVMA (related to environmental effects or fate and behaviour) – the review by Schmidt (2007) is a suitable international evaluation which the APVMA can use to consider the reliability of data, but copies of any critical studies need to be provided.

If the assessment does not stop at VICH Phase I, it is noted that there is potential exposure of marine and freshwater environments. Assuming this is the case any submission should consider what, if any, impact this may have on any risk assessment, including both environmental effects and fate and behaviour. Additionally, any risk assessment at VICH Phase II should consider the potential for formation of metabolites and whether any environmental exposure will result in an acceptable risk under the proposed conditions of use.

[1] Available from https://vichsec.org/en/guidelines/pharmaceuticals/pharma-safety/environmental-safety.html

Efficacy and target animal safety

The proposed minor use involves treatment of susceptible bacterial and parasitic infections in marine and freshwater finfish using an unregistered product, Chloramine-T (N-chloro-4-methylbenzenesulfonamide sodium salt) which is an exempt active.

It is noted that you have summarised some literature you have available to support the proposed application. This literature cannot be assessed as part of the PAA process. However, some things you will need to consider and provide to satisfy the efficacy criteria include:

- Evidence to support the recommended dose rate, duration of treatment and route of administration.
- Evidence to support the efficacy of the product for all proposed indications in the target species.

Similarly, target animal safety can be addressed by a scientific argument supported by the literature references outlined in this PAA. This will be assessed when the full application is before the APVMA.

It is noted that you are seeking to use Chloramine-T in marine and freshwater finfish which is a wide group covering various species. Target animal safety will have to be demonstrated in all the target species as you have defined them, unless you can justify not doing so. If data is available only for a single species, you will have to include a scientific argument in your submission justifying why efficacy in a single species should be extrapolated to the whole group.

The APVMA recommends that in your submission you should consider any genus/family differences and environmental conditions and production systems differences which may impact the target animal safety. This is particularly important if you are providing data/literature based on studies conducted overseas.

To satisfy the target animal safety aspect of the safety criteria, you should:

- ensure the studies in the literature you submit include appropriate target animal safety assessment parameters
- demonstrate the safety of the product in target species following repeated dose administration via the proposed route
- demonstrate the safety of the product for the proposed length of treatment, or longer than via the proposed route. The dosage of a veterinary medicinal product (as in mammals) is principally a function of treatment concentration and exposure period
- address possible adverse effects on development (malformations) if the medication is applied to young fish (embryos, larvae and juveniles) and the product can easily interfere with growth.
- consider the range of sizes and weights of fish recruited for studies in the literature you are submitting, as the same treatment might not have the same effect in fish of different sizes.
- determine the safety of excipients and justify any lack of appropriate data. Excipients normally used in pharmaceutical products for terrestrial animals might not be well tolerated by aquatic species.

When submitting published scientific papers, you should explain their role in an executive summary so that the relevance of such data is explained to the reviewer.

Special data

When applying for a permit, for use of a product containing an approved antibiotic active constituent in a new species, a special data module 10.2 may be required. Determination of the risk to antibiotic resistance and whether a module 10 would not be required cannot be made in this PAA as more information would be required before making a decision. An assessment on whether the off label use in this application could increase in the use of the antibiotics or increase the risk to public health will be undertaken when the permit application is received by the APVMA.

International assessments

The APVMA will consider relevant international assessments, provided the data supporting the assessment are also provided. Guidance for the submission of international data can be found on the APVMA website at apvma.gov.au/node/14186.

Resulting application

The likely item number for this application is Item **21**. The likely modules, timeframes and fees applicable, based on the current fee structure, for the proposed application are:

Chloramine-T (N-chloro-4-methylbenzenesulfonamide sodium salt) / Marine and freshwater finfish. / Susceptible bacterial and parasite infections.			
Module level	**Module type**	**Timeframe***	**Fee**
1	Preliminary assessment	(1 month)	
2.3	Chemistry	6 months	
3.3	Toxicology	5 months	
5.5	Residues	4 months	
6.3	Work health and safety	4 months	
7.3**	Environment	4 months	
8.3	Efficacy and crop safety	3 months	
10.2	Special data	7 months	
11.1	Finalisation	3 months	
Total		**10 months**	**$350**

**The timeframe for the application commences when the application passes preliminary assessment and all fees are paid. The total timeframe is the timeframe of the longest assessment module plus the timeframe of the finalisation module. The APVMA has up to one month to undertake preliminary assessment once the application has been lodged.*

*** Refer to advice on environment above*

Please note: Applications may still be subject to recategorisation under section 70B of the Agricultural and Veterinary Chemicals Code. If recategorisation is required, you will be given the reasons why the modules are to be changed and the opportunity to respond.

If additional information is requested under section 159 of the Agricultural and Veterinary Chemicals Code during the assessment of the application, an extended timeframe as outlined in Schedule 6 of the Agricultural and Veterinary Chemicals Code Regulations will apply.

The assistance provided by the APVMA is based on the information provided in your pre-application assistance request. If the information you have provided is not complete or correct, that could limit the effectiveness of the assistance provided by the APVMA.

The APVMA gives no undertaking that any application lodged after receiving pre-application assistance will be approved.

Outcome

If you require clarification of any issues addressed in this request for pre-application assistance, please contact your case manager. If you are seeking advice on additional/new questions, you will need to apply for further pre-application assistance under a new application. More information is available at apvma.gov.au/node/108.

When submitting this record in support of an application please ensure you include it in your information list.

Feedback

The APVMA welcomes your feedback on our PAA service and the assistance provided to you throughout this process.

If you would like to provide feedback, please complete the *pre-application assistance feedback form*, available at apvma.gov.au/node/97841 and return it via email to casemanagement@apvma.gov.au.