Environmentally safe medicines for farmed salmon

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BVSc, MRCVS, **managing director of Triveritas, takes a look below the surface of this highly complex subject**

RECENTLY there has been considerable media interest in salmon farming, including the potential environmental implications related to salmon farms.

Amongst the issues that have been raised has been the use of veterinary medicines for the treatment of farmed salmon. This article is a brief review to look at the work done in this area by the UK regulatory bodies and the veterinary pharmaceutical companies.

There are specific regulatory guidelines concerning the environmental safety of veterinary medicines used on fish farms. Indeed, it is a widely held view within the animal health industry that the environmental safety data packages for fish medicines are amongst the most expensive and extensive for any veterinary medicine.

There have been no active ingredients specifically developed for use in aquaculture, which is a relatively small part of the animal health market, and therefore, understandably, there is an extreme shortage of data applicable directly for use in this particular environment.

Initially the sponsors of salmon medicines will generally examine the available literature regarding the pharmaceutical concerned. This includes reviewing the physico-chemical characteristics, such as solubility in water, persistence in the environment and many other factors. Assuming that the medicine concerned appears to have suitable characteristics, then it may be considered appropriate for further development.

The environmental safety package for a salmon medicine will usually be far more expensive than the rest of the data package to assemble, and therefore it will be the first consideration in any such development project.

First steps indoors

In the absence of appropriate data, a series of laboratory studies is generally conducted initially. These studies involve selecting representative species of organisms that may typically be found in the environment of salmon farms, or that may be exposed to medicines used on salmon farms. These will include organisms dwelling both in the water column and in the seabed or sediment.

The tests performed will investigate the potential lethality of the pharmaceutical to each of these species, following strictly defined protocols that are recognised internationally. At this stage, the sponsor may also decide to perform laboratory tests on additional marine species that may be of commercial importance to, for example, fishermen or those who culture or harvest shellfish.

Expert review of this substantial quantity of laboratory data will generally reveal which particular species can be considered to be the most sensitive to the compound in question. From this information - which has been generated purely in the laboratory - the most sensitive species will be chosen to be used in the marine environment for testing in the locality of salmon farms.

Sentinel monitoring

Sensitive organisms are deployed adjacent to, and in close proximity to, salmon farms:' The exact positions of such deployments depend on the local hydrography and dispersive conditions of the site. Normally this is done in collaboration with expert hydrographical review, discussion with regulatory agencies, and with local site knowledge.

The sentinel creatures are normally deployed in several replicates per location, and there will also be control deployments where the animals will not be exposed to the discharge.

Next, the salmon cages will be treated with the medicine, and its release into the environment may then potentially impact onto the sentinel animals. Each of the latter will have been examined prior to deployment, and at a fixed time after potential exposure they will also be individually re-examined and their condition assessed using health scoring schemes.

A single study may involve the use of several hundred organisms deployed at over 20 sites; and often with deployments at multiple depths, and possibly secured at or near the seabed. Water and/or sediment samples will usually be collected from sentinel locations for chemical analyses to verify that the sentinels were exposed.

Sentinel animals are individually re-examined and their condition assessed using health scoring schemes.

Finally this type of experiment will be repeated at several sites - typically slow and fast flushing lochs, and water bodies with different dispersive: characteristics.

The sponsor may also decide to perform such studies with commercially important local species (for example, crabs, lobsters and shrimps) not only for regulatory use but also to meet the understandable concerns of local fishermen.

Environmental concerns

The fate of the veterinary medicine in the environment will also be studied extensively. Initially this will usually be by radio-labelled laboratory studies using sea water and marine sediment in systems designed to imitate the types of conditions that may occur close to, and distant from, salmon farms.

There will also follow dispersion studies actually conducted in sea lochs where the veterinary medicine is used on the salmon, and where water and/or sediment samples are taken from fixed points in the area at fixed times following use.

All of the samples will be analysed for levels of the active ingredient or its breakdown products, to gradually build up a picture of exactly where the medicine goes.

During such work, and indeed during sentinel monitoring studies, there will also be extensive recording of the local hydrographic conditions at the time of the experiment. Typically, conditions recorded will include currents, salinity, temperature, and wind speed.

Water samples can be collected from various depths using specially designed samplers, and similarly specific sediment samplers are available for use to collect appropriate samples for analyses.

Dispersion studies may last six months or longer, with multiple site sampling, and collecting sediments from as deep as 130 metres in sea lochs. During these studies global satellite positioning techniques are used to ensure that repeated sampling over such long periods is performed at precisely the same sites.

Additionally, sediment traps - which will sample particulates in the water column that have not yet reached the bottom of the sea - will often be deployed, particularly if the chemical is known to have potential to adsorb particulates in the water column. The analytical results together with the hydrographical data will give an indication of the levels of the medicine that potentially will occur in the marine environment.

There are many *potential environmental* implications related to use *of medicines* on *salmon farms.*

Computer models

Generally the next step is to develop computer dispersion models. This enables computers to try to predict the likely levels of the medicine to be found in the environment at certain distances from the salmon farm, combined with the ability to mimic changes to environmental parameters.

For example, current speeds, wind speeds and other items can be adjusted by computer to see what potential impact this may have on the levels of the substance in the environment. If possible, the results of the dispersion studies will be compared to the predictions from computer dispersion models, to try to see if the computer-generated predictions do actually concur with data from the real world.

This process is known as validation. Validated computer dispersion models would have the benefit of being able to predict the likely levels of veterinary medicines in the marine environment under a whole variety of different environmental conditions.

Complete picture

From the initial laboratory data on various species of animals - the sentinel monitoring studies, the dispersion studies and the computer dispersion modelling - a picture will begin to emerge of any potential adverse effects of a veterinary medicine on any animals in the marine environment.

For a veterinary medicine to be licensed for use in salmon farming, it would have to have no detectable adverse impacts or only those that could be considered to be extremely localised, limited and reversible.

The metabolites and breakdown products of veterinary medicines used in salmon farming will also be considered regarding their potential to cause any adverse environmental effect. Often the relative toxicities of such compounds can be found in the basic toxicology package of the molecule, but sometimes further tests specific to the marine environment may be required.

Another area of investigation by the sponsor is to look at the potential of the veterinary medicine to bioaccumulate in the environment. Typically this will involve analysis of organisms that are known to bioaccumulate compounds such as the blue mussel.

Such studies will be performed both in the laboratory, and in field conditions, with the levels of any medicine accumulated in the mussels being carefully analysed, and the potential implications considered.

In the EU, the sponsor will then ensure that there is a critical environmental safety report written by an independent expert. The data, plus expert report, will further undergo a rigorous assessment by the Veterinary Medicines Directorate, followed by a second appraisal by the Veterinary Products Committee.

If the applicant should be successful regarding the environmental safety aspects - and of course all other requirements (safety, quality and efficacy) - the product may be granted a Marketing Authorisation for use on salmon farms. However, in the UK this does not mean that the medicine can be used legally because there is a second tier of protection to the marine environment.

Additional safeguards

Before the medicine can be used commercially on a UK salmon farm, the site owner must apply for a Discharge Consent from the Scottish Environmental Protection Agency (SEPA). SEPA will look in detail at the quantities of the medicine proposed to be used and all the local considerations of the site concerned. This will include not only the local hydrography, and mass of salmon, but also the interests of all other users of the water body.

The process of obtaining a Discharge Consent involves a period for public comment to SEPA so that everyone concerned has the opportunity to raise issues that may be relevant to the particular site. As might be expected in such a situation, there is also a lengthy appeals procedure for the final resolution of whether a Discharge Consent should be issued or refused.

If a Discharge Consent is granted, it will normally specify the amount of the veterinary medicine that can be used on the site, including the amounts permitted to be used per day and per annum. Additionally, the Discharge Consent is likely to have specific limitations to the level of the medicine that may be released into the environment, and these levels may be monitored.

Therefore, it appears with salmon medicines we have potentially a unique situation whereby although a product may have a Marketing Authorisation, it still may not be legally used unless the local environmental agency concerned has also approved its use.

Generally, the environmental safety standards which are used to regulate the use of medicines on salmon farms in the UK are considered to be the most stringent in the world. Indeed, this may explain why there are far fewer salmon medicines used in the UK than in most other salmon farming countries.

Studies involve selecting representative species that may typically be found in the environment of salmon farms. Above: a lobster in a holding pot and right, sea urchins.