

What are MRLs?

'MRLs' is a term that often crops up in discussions and articles on food safety. It is the abbreviation for 'maximum residue limits', and refers to the maximum level of named contaminants in foods that can be legally sold for human consumption.

Why do we need MRLs?

Producing enough food to sustain New Zealand's economy and feed the nation has traditionally relied on the use of pesticides and veterinary medicines (agricultural compounds). However, while the amounts used must be sufficient to control the pest or disease, residues in foods must also be minimised for a residue to be acceptable. That is, the level of residue should be as low as possible commensurate with the need to use the substance for its intended purpose. It is also a requirement that any level allowed in foods must not pose a human health risk. To ensure that any residues in foods are at acceptable levels, New Zealand has a regulatory process that sets MRLs.

Registration

Before any agricultural compound or veterinary medicine can be legally sold in New Zealand, it must be registered. The Agricultural Compounds and Veterinary Medicines Group (ACVMG) of the New Zealand Food Safety Authority (NZFSA) handles this registration.

When an application for registration is lodged, comprehensive toxicology and residues data packages must be submitted so that the acceptability of the proposed product can be established. These packages must provide data showing:

- the amount and rate of decline of any residues, and
- that the product can be used safely and pose no unacceptable risk to the human population.

Because registration allows treated foods to be sold for public consumption, possible residues in food are a major factor in the consideration of an application. If the data does not 'pass' the acceptable residue levels test, then the application for registration will not be approved.

Data assessment

Assessment of the residues data is carried out by the ACVMG and the Environmental Risk Management Authority (ERMA NZ) considers the toxicology package.

The principles of the assessment process in New Zealand are modelled on those published by the International Programme on Chemical Safety, which is administered by the World Health Organization (WHO), the International Labour Organization and the United Nations Environment Programme. These principles have been internationally refined and agreed by expert committees of the WHO since the 1950s.

How are MRLs set?

Establishing acceptable levels of residues is a complicated process. First, the toxicology data package mentioned above is used to establish an Acceptable Daily Intake (ADI) in accordance with international principles. The ADI for each substance is then used by ERMA NZ to set an Acceptable Daily Exposure (ADE) and a Potential Daily Exposure (PDE) for food. This PDE for food is compared with the Potential Daily Intake (PDI) for the substance, which is estimated from data on food consumption figures* and known residue levels in the foods. If the PDIs are less than or equal to the appropriate PDE for food, then the residue is considered acceptable and an appropriate limit can be set. Other factors take into account uncertainties in the data and in the extrapolation of the test results from animals to humans.

* provided by the Food Standards Australia New Zealand Diamond database, which used data from a recent NZ National Nutrition Survey

What information is required?

The toxicology package must contain all of the following studies:

- long-term multiple-dose feeding studies (for example, lifetime feeding studies) look for any potential for the pesticide to cause degenerative diseases (such as cancer) that develop insidiously after continuous exposure to low levels;
- developmental toxicity studies establish any potential to cause birth defects;
- reproduction toxicity studies show up any other effects on the reproduction process;
- mutagenicity studies in isolated bacterial, yeast and animal cells give information about the ability of the chemical to interact with the genetic material.

The package may also contain special studies required because of a known ability of similar chemicals to cause a particularly undesirable effect, such as nerve toxicity. Metabolism and pharmacology data are used to determine the applicability of the animal data to humans.

How are studies evaluated?

Each of the submitted studies is closely scrutinised. This includes an assessment of the quality of the data. In this regard, strict internationally agreed OECD experimental protocols have been established for toxicological testing of chemicals. These lay down such things as the minimum number of dose groups, the minimum number of animals required in each group, and how the results must be reported.

If the quality of the data is acceptable, it is then assessed to determine:

- what effects the chemical is able to elicit, and
- what dose levels are required to produce those effects.

The top dose group in each test must cause some toxicity so that the target organ for toxicity, and the nature of the toxic effect, can be identified. The other dose groups must clearly demonstrate the dose level that does not cause any observable effect at all (known as the no-observed-effect-level or NOEL) and that *any* effect is one that has a threshold.

Usually, the pesticide must be tested in more than one animal and the NOEL from the most sensitive animal in the test that demonstrates the most sensitive effect is used to calculate the ADI.

Calculating the ADI – what about ‘uncertainty factors’?

The NOEL is divided by an uncertainty factor that is usually not less than 100. The factor of 100 is made up of two factors of ten:

1. there is normally a factor of ten between the most sensitive and least sensitive animal species, and
2. there is normally a factor of ten between the most

sensitive and least sensitive individual within a species.

The assumption made is that humans are always ten times more sensitive than the most sensitive species tested. This is necessary because it would be impractical to test all animal species, and it also clearly errs on the side of human safety.

Other uncertainty factors can be used to take into account:

- any deficiencies in the way the data was produced,
- the possibility that the food may be eaten by particularly sensitive individuals, or
- the nature of any specific effect.

A further factor built into this process is that the NOEL is the dose level at which **no** effect is found to occur. Toxicology testing involves dosing at increasing levels, often with a factor of 10 between doses (for example, doses may be at 0, 20, 200, 2000 mg/kg body weight). The true dose at which effects begin to occur, however, must lie somewhere between the NOEL and the dose at which an effect is first observed, and so this ‘hidden’ factor could be up to a figure of 10. When this factor of 10 is multiplied by the overestimate of the potential daily intake of the pesticide (another factor up to 10) and the factor of 100 in converting the NOEL to an ADI, the overall safety factor in the process is in the order of 10,000.

Because of the nature and amount of data assessed in this process, the ADI is defined by the WHO as being “the daily intake which, during an entire lifetime, appears to be without appreciable risk on the basis of all the known facts at the time”, and “without appreciable risk” is defined as “the practical certainty that injury will not result even after a lifetime of exposure”.

The FAO/WHO convene meetings of experts who look at toxicology data as specified above to establish internationally agreed ADIs for the Codex Alimentarius Commission. For pesticides, this is the Joint Meeting on Pesticide Residues (JMPR), and for veterinary medicines it is the Joint Expert Committee on Food Additives (JECFA). The Codex Alimentarius Commission establishes internationally accepted residue limits for food products in trade. The ADIs calculated in New Zealand in the manner described above are compared with the FAO/WHO figures (where they exist, as not all pesticides and veterinary medicines registered by New Zealand have been considered by the FAO/WHO expert meetings) as a check that the process has been correctly carried out in New Zealand.

How is a withholding period set?

The residue data submitted at the time of application for registration show the level of residue in edible produce immediately after application of the agricultural compound, and also levels of residues at increasing

times after the application. This allows the construction of a 'residue decay curve'. During the registration process 'Good Agricultural Practice' is determined. This arises from a consideration of the need to use a compound, and how close to harvest or slaughter it is needed in order to achieve acceptable control of the pest or disease being treated. From this, a withholding period is set. This is the minimum amount of time that must elapse between the last use of a compound and harvest or slaughter.

The residue decay curve allows the determination of the likely residue of the compound at harvest or slaughter, and food consumption data are then used to calculate its potential human daily intake. The PDI is an overestimate of food consumption because it assumes that all food available is eaten when some of it would be wasted through storage losses etc.

This process errs significantly on the side of human safety. At no stage do we take into account those factors that reduce residues that would be present at the time of consumption. Apart from those already mentioned, these include the fact that usually far less than 100% of a type of food is treated with a particular compound, and that residues normally dissipate during storage, transport, preparation, commercial processing and cooking of the treated food.

Total diet surveys

The Ministry of Health has been involved in conducting total diet surveys for residues in the foods that the consumer can buy. Rarely do residues exceed more than 20% of the permitted levels, and so we are confident that chemical residues in food resulting from agricultural compound use do not pose any hazard to human health in New Zealand.

International aspects

Sometimes New Zealand's residue limits for a given agricultural compound are different from the international limits agreed to by the Codex Alimentarius or other countries. The reason for this lies in the fact that these

limits are not usually established on purely health grounds. Instead, they are set to ensure that Good Agricultural Practice is used by food producers, and this has the effect of keeping residues as low as possible. Each country may have a different definition of Good Agricultural Practice, which essentially establishes the need to use an agricultural compound. This is particularly true for pesticides.

If a particular pest is not found in another country, then there may be no need for the agricultural compound in question to be used and hence no need for that country to set an official residue limit. If the pest pressure is greater in another country, then there may be a need to use pesticides etc. more frequently, and/or closer to harvest than in New Zealand, and hence a need for that country to have a higher residue limit.

Where can I find out more about New Zealand MRLs?

Currently, MRLs are set in the New Zealand (Maximum Residue Limits of Agricultural Compounds) Mandatory Food Standard 1999 and its amendments. A searchable list of these MRLs can be found on the internet at <http://www.nzfsa.govt.nz/acvm/registers-lists/nz-mrl/index.htm>

For more information on the interpretation of entries in this list, or the philosophy behind the MRLs, contact:

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