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**ENVIRONMENT DIRECTORATE
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OECD MRL CALCULATOR: USER GUIDE

**Series on Pesticides
No. 56**

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Series on Pesticides

No. 56

OECD MRL Calculator User Guide

IOMC

INTER-ORGANIZATION PROGRAMME FOR THE SOUND MANAGEMENT OF CHEMICALS

A cooperative agreement among **FAO, ILO, UNEP, UNIDO, UNITAR, WHO, World Bank and OECD**

Environment Directorate

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OECD Guidance for Industry Data Submissions on Plant Protection Products and their Active Substances-Dossier Guidance (1998, revised 2001, 2005)

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The Organisation for Economic Co-operation and Development (OECD) is an intergovernmental organisation in which representatives of 34 industrialised countries in North and South America, Europe and the Asia and Pacific region, as well as the European Commission, meet to co-ordinate and harmonise policies, discuss issues of mutual concern, and work together to respond to international problems. Most of the OECD's work is carried out by more than 200 specialised committees and working groups composed of member country delegates. Observers from several countries with special status at the OECD, and from interested international organisations, attend many of the OECD's workshops and other meetings. Committees and working groups are served by the OECD Secretariat, located in Paris, France, which is organised into directorates and divisions.

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This publication was developed in the IOMC context. The contents do not necessarily reflect the views or stated policies of individual IOMC Participating Organizations.

The Inter-Organisation Programme for the Sound Management of Chemicals (IOMC) was established in 1995 following recommendations made by the 1992 UN Conference on Environment and Development to strengthen co-operation and increase international co-ordination in the field of chemical safety. The Participating Organisations are FAO, ILO, UNEP, UNIDO, UNITAR, WHO, World Bank and OECD. UNDP is an observer. The purpose of the IOMC is to promote co-ordination of the policies and activities pursued by the Participating Organisations, jointly or separately, to achieve the sound management of chemicals in relation to human health and the environment.

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FOREWORD

With the goal of harmonizing the calculation of MRLs across the OECD, the Residue Chemistry Expert Group of the OECD Working Group on Pesticides commissioned in 2008 an expert group to propose a new MRL calculation procedure. The guiding principles of this procedure were:

- the procedure must be a practical implementation of sound statistical methods;
- it must be simple to use without requiring extensive statistical knowledge from a user;
- it should produce a clear and unambiguous MRL proposal for most residue datasets produced by field trials; and,
- it should harmonize the EU and NAFTA procedures as much as possible.

The Working Group on Pesticides approved the draft OECD MRL Calculator and its User Guide in December 2010 and recommended that they be forwarded to the Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology, for consideration as an OECD publication.

This document and the OECD MRL Calculator are being published under the responsibility of the Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology, which has agreed that they be unclassified and made available to the public.

The OECD MRL Calculator is available on the OECD public website, <http://www.oecd.org/env/pesticides> under *Pesticide Publications/Publications on Pesticide Residues*.

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The OECD MRL Calculator

1. The statistical goal of the OECD MRL calculator, in common with previous methodologies, is to produce an MRL proposal in the region of the 95th percentile of the underlying residue distribution (which we abbreviate as p95), which is conservative in the sense that it will have a much greater propensity to make errors by overestimating p95 than by underestimating it for most datasets.

2. For a statistical discussion about the methodology described in this user guide, please consult the *OECD MRL Calculator Statistical White Paper*.

How to use the OECD MRL Calculator Spreadsheet

3. To compute an MRL, the user inputs the data in the left-most blue column of the "Input-Output" sheet under "Residues (mg/kg)". Censored data (residue values that are less than the limit of quantification or LOQ) are entered by listing the LOQ value (example, 0.01) along with an asterisk in the adjacent column. The order in which the data are entered does not impact the results. If several analytical measurements have been carried out for the same sample, the average or mean value should be evaluated and used for input in the calculator. For residue trials with replicate field samples, the average or mean of the replicate values should be used for input in the calculator.

4. The spreadsheet then automatically conducts all the computations and reports all the relevant results on the same page. Above the column for the residue data, four cells with text fields are available for documenting the dataset.

5. To go back to a clean spreadsheet, the user may click on the "Reset" button. The button "Generate table" produces a table in which all the residue values are listed in ascending order. By pressing the buttons "Select frame" and "Select table" it is possible to select the details of the calculation or the residue table in order to copy them and paste them in reports.

6. The spreadsheet has been protected in order to avoid inadvertent changes to calculation formulas that may affect the results. Users who wish to look into the details of the spreadsheet programming can remove the protection by entering the password "MRL".

Explanatory messages displayed by the calculator

7. The warning "MRL calculation not possible. [Check data entry]" is displayed in case of implausible and most likely erroneous data entries such as non-numerical data, residue values ≤ 0 mg/kg or residue values > 10000 mg/kg. The same warning is also displayed if an asterisk is entered in the second column (to identify a result $< LOQ$) while the LOQ value was not entered in the left-hand adjacent cell.

8. If the dataset consists of less than 3 values the message "MRL calculation not possible. [Too small dataset]" is displayed at the bottom of the spreadsheet. The choice of 3 values was made based on the minimal requirement common among OECD countries. With a single residue value, it is impossible to compute an estimator for the standard deviation of the dataset, which is needed in the calculation procedure.

9. If the dataset consist of 3-7 residue values, the message "High uncertainty of MRL estimate. [Small dataset]" is displayed to remind the user of the considerable level of uncertainty surrounding the calculation of any statistical quantity for such small datasets. For a dataset with 8 residue values, the

estimated failure rate, i.e. the probability that the MRL is below the 95th percentile of the residue distribution, reaches approximately 25 %.

10. Similarly, for the same reason the warning message "High uncertainty of MRL estimate. [High level of censoring]" is displayed if more than 50% of the dataset is censored (residues below the limit of quantification or LOQ). Although the methods selected for the MRL calculation are very robust to the presence of non-detected residues, uncertainty is considerable for residue datasets for which the majority of residues values are below the LOQ.

How the OECD MRL calculator works

11. The results of the computation are displayed in a frame at the right of the input data. The first few fields provide some general information about the dataset, including the number of data, the percentage of censored data, the highest residue, the lowest residue, and the median residue. Please, notice the range of the residue values by comparing the lowest residue with the highest residue; the larger that range is, the greater the variability present in the data. This variability is taken into account when computing the MRL and may lead in some cases to MRL proposals significantly greater than the highest residue.

12. The calculator distinguishes fully censored residue datasets (sample sets with all measurements below one or several limits of quantification) from not fully censored datasets (datasets with at least one measurement at or above the LOQ of the corresponding analytical method).

Not Fully Censored Datasets

13. For not fully censored datasets, the maximum of three calculated results is put forward as the MRL proposal by the calculator:

- the highest residue value is used as a "floor" to guarantee that the MRL proposal is always greater than or equal to the highest residue;
- the mean and the standard deviation values of the dataset are computed; the "mean + 4* standard deviation" value is evaluated as the base proposal (referred to as "Mean + 4*SD" method); and,
- the "3*Mean*CF" method (see next paragraph).

Note: for the calculation of the mean and standard deviation, all values less than the LOQ are to be introduced into the calculator with a value equal to the LOQ.

14. The "3*mean" value is computed to provide another "floor" to the calculation; in this case to guarantee that the sample coefficient of variance ($CV = \text{standard deviation} / \text{mean}$) used in the calculation is at least 0.5, a condition verified by most residue datasets. This is necessary given the tendency of small datasets to underestimate the standard deviation. A correction factor CF has been added because it was observed that the mean of a dataset is overestimated for censored datasets. The correction factor CF is equal to $1 - \frac{2}{3} * \text{fraction censored data in the dataset}$. This calculation is referred to as the "3*Mean*CF" method.

So the MRL proposal for not fully censored datasets is,

Maximum (Highest Residue, Mean + 4*SD, 3*Mean*CF).

15. The case of almost fully censored datasets but with several LOQ value is more complicated, especially when there are quantified values below the largest LOQ value. The above procedure is still used and will produce an MRL proposal but the user may consider reviewing this proposal on a case-by-case basis.

Fully Censored Datasets

16. The MRL proposed by the calculator for fully censored datasets is the level of the highest LOQ present in the dataset.

Rounding

17. To facilitate the setting of harmonized MRLs in the global environment, MRL proposals are rounded as a last step in the calculation. For numbers between 1 and 10, they are rounded to a single digit; for 10 to 100, they are rounded to multiples of 10; for 100 to 1000, they are rounded to multiples of 100 and so on. Intermediate values of 0.015, 0.15, 1.5, 15, etc, were introduced to avoid doubling of MRLs on rounding. So for example: 0.12 rounds up to 0.15, 0.16 rounds up to 0.2; and 12 rounds up to 15 instead of 20. The possibility for rounding down exists if a particular MRL level is surpassed by a specified amount.

To be more precise, the rounding possibilities are (in mg/kg):

0.001	0.0015	0.002	0.003	0.004	0.005	0.006	0.007	0.008	0.009
0.01	0.015	0.02	0.03	0.04	0.05	0.06	0.07	0.08	0.09
0.1	0.15	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
1	1.5	2	3	4	5	6	7	8	9
10	15	20	30	40	50	60	70	80	90
100	150	200	300	400	500	600	700	800	900
1000	...								

18. If it is not desired to set MRLs below 0.01 mg/kg, smaller MRL proposals may be rounded up to that value. If the 0.015 mg/kg is not desirable due to limitations in the analytical methods, the MRL may be rounded up to 0.02 mg/kg.

19. MRLs are displayed without decimal zeroes after the last significant figure, to avoid giving the impression of having more accuracy than in reality. So, for example, a MRL is displayed as 2 mg/kg but not 2.0 mg/kg; 0.1 mg/kg is possible but 0.10 mg/kg is not.

20. Rounding down will happen if the MRL proposal exceeds the lower MRL rounding possibility by less than 10% of the difference between the upper and lower MRL rounding possibilities. For example:

MRL Class	10% of Difference	Cut off Point for Rounding Down
0.02	0.001	0.021
0.03	0.001	0.031
0.09	0.001	0.091
0.1	0.005	0.105
0.15	0.005	0.155
0.2	0.01	0.21
0.3	0.01	0.31
0.9	0.01	0.91
1	0.05	1.05
1.5	0.05	1.55
2	0.1	2.1
3	0.1	3.1

Some rounding examples:

Unrounded proposal:	1.04 mg/kg	→	Rounded proposal: MRL:	1 mg/kg
Unrounded proposal:	1.12 mg/kg	→	Rounded proposal: MRL:	1.5 mg/kg
Unrounded proposal:	1.53 mg/kg	→	Rounded proposal: MRL:	1.5 mg/kg
Unrounded proposal:	1.58 mg/kg	→	Rounded proposal: MRL:	2 mg/kg
Unrounded proposal:	2.07 mg/kg	→	Rounded proposal: MRL:	2 mg/kg
Unrounded proposal:	2.12 mg /kg	→	Rounded proposal: MRL:	3 mg/kg
Unrounded proposal:	21.0 mg/kg	→	Rounded proposal MRL:	30 mg/kg