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Introduction

The dose-response analysis is used in experiments where a treatment or chemical is applied at different rates, and the level of response to the dosage is recorded (as a percentage or count of individuals that responded). The analysis estimates the treatment rate/dosage that results in a response from a particular percentage of individuals in the study. One example is the LD50, which estimates the dosage level that results in a response of 50%, i.e. the *median lethal dose*.

*ARM provides three different Dose-Response estimation algorithms:

- Probit - Least Squares
- Probit - Maximum Likelihood
- Logit

To begin, select File – Print Reports, and select the Dose-Response Analysis report. Note that since this report requires extensive user interaction, it cannot be run as a batch process.

The estimation method, analysis type, and output format can be customized with the Dose-Response Analysis report options.

Then click Next on the Print Reports dialog to begin the analysis process.

Dose-Response Analysis Report Options

Report Options | General Summary | Report Preview

Estimation method

Probit - least squares

Probit - maximum likelihood

Logit

Estimation algorithms provided courtesy of Dr. J.J. Hubert, University of Guelph.

Analysis type

Estimate: LD 50

Simple

Time series

Output format

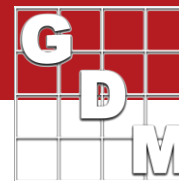
Calculation table

Analysis equations

Confidence level 95%

Line graph

Display X axis as log scale



Step 1 - Treatment Selection

Specify the treatment numbers that you wish to include in the analysis. Leave the selection empty to select all treatments by default.

Trit No.	Treatment Name	Fom Conc	Fom Unit	Fom Type	Rate	Rate Unit	Appl Code
1	Sure Kill	4	LBA/GAL	L	0.1	LB AI/A	A
2	Sure Kill	4	LBA/GAL	L	0.15	LB AI/A	A
3	Sure Kill	4	LBA/GAL	L	0.2	LB AI/A	A
4	Sure Kill	4	LBA/GAL	L	0.3	LB AI/A	A
5	Sure Kill	4	LBA/GAL	L	0.5	LB AI/A	A
6	Sure Kill	4	LBA/GAL	L	0.7	LB AI/A	A
7	Sure Kill	4	LBA/GAL	L	0.95	LB AI/A	A
8	Sure Kill	4	LBA/GAL	L	0	LB AI/A	A

Specify treatment numbers to include in report

OK Cancel

Step 2 - Data Column Selection

Next, specify the assessment data column numbers to include in the report.

Specify assessment column numbers to include in report

Clear

OK Cancel Help

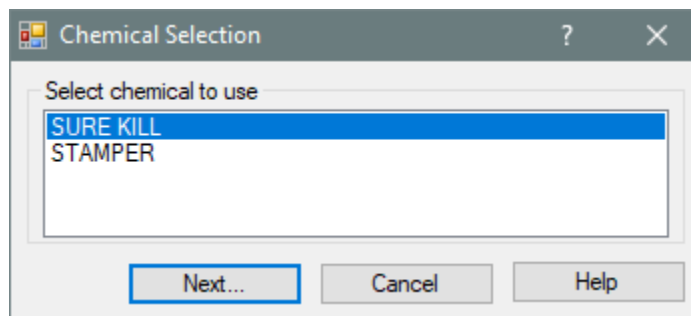
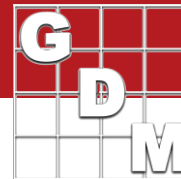
When determining which data column(s) to select for the Dose-Response Report:

- Select only the data columns that include **response** information to be included in the analysis.
- If the Analysis type (set on the report options) is **Simple**, then select only 1 data column. **Time Series** analysis calculates dose estimates from *multiple* data columns.
- Do not select data columns that are marked as non-analyzable in the ARM Action Codes field. If a non-analyzable data column is selected, ARM does not include that data column in the analysis.
- Do not select data columns that contain sample size information. Select only the data columns that contain response information. If the user selects a data column in this step and then selects the same data column during the sample size verification step, ARM issues a warning and the analysis process may need to be restarted.
 - See Step 5 - Sample Verification for further discussion of sample size data columns.
- If no valid data columns are selected, the analysis process cannot proceed, and aborts.

Step 3 - Chemical Selection

ARM attempts to determine which chemical to include in the analysis by scanning the chemicals present in the selected treatments. When ARM is unable to automatically determine which chemical to analyze, ARM displays the Chemical Selection Dialog. The user should select the chemical to use in the analysis from the list of available chemicals.

Note: Treatments that are marked as untreated on the Settings Dialog - Treatment tab are used as control treatments in the analysis and are not a part of this treatment scanning process.

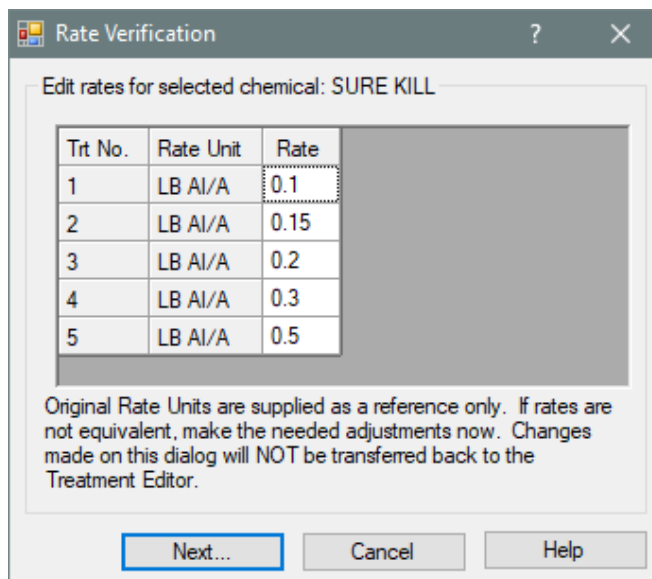


- If there is only one chemical that is present in each treatment, ARM automatically selects that chemical.
- If there is more than one chemical that is present in each treatment, ARM must prompt for the chemical to use.
- If there is not a chemical that is present in every treatment, ARM must prompt for the chemical to use.

Step 4 - Rate Verification

After the chemical to analyze has been determined, review the dosage rates. If the chemical was not found in a treatment, ARM fills the rate with "Not Present". This provides a chance to fill in any desired rate.

In some cases the selected chemical may be present more than once in a treatment. ARM defaults to the first occurrence, but the user may select the desired occurrence from a list of rates and corresponding application codes on the Rate Verification Dialog.



Note: It is the responsibility of the user to ensure that the rates listed use a consistent rate unit. To assist the user, ARM lists the original rate unit for reference. Changes made on this screen are **not** transferred back to the treatment editor.

- All treatments with a rate of "Not Present" will be dropped from the analysis.
- All treatments with a rate less than zero will be dropped from the analysis.
- All treatments with a rate of zero will be treated as a control.
- If there is more than one control treatment in the selected treatments, corresponding data will be averaged or summed depending on the data column type (percent will be averaged, response will be summed. See Step 7 - Data Preparation for further explanation).
- At least 2 valid treatments/rates are required (not counting controls) for the analysis process.

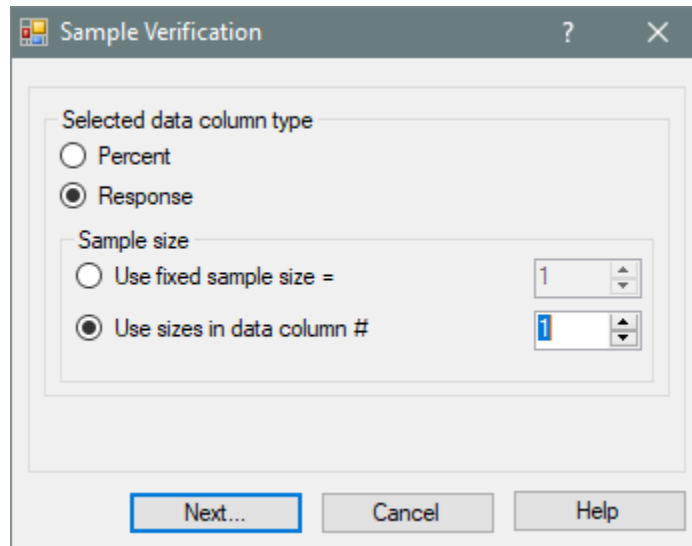


Step 5 - Sample Verification

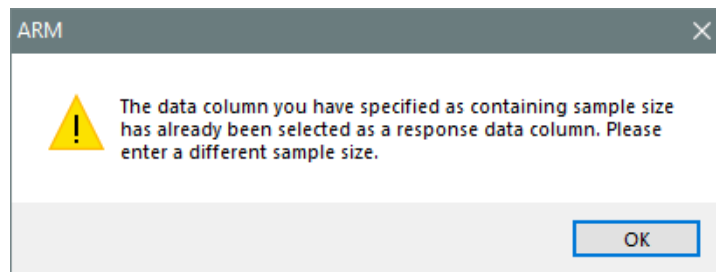
Specify how the selected data column(s) from Step 2 were assessed. Select **Percent** if assessment data is entered as percentages. Select **Response** if assessment data is entered in raw units.

Sample Size is required information for the dose-response analysis process. There are two different ways to specify this:

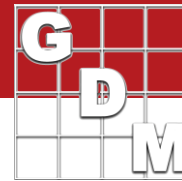
- Select **Use fixed sample size** if the sample size is the same for all observations.
- Select **Use sizes in data column #** if sample sizes differ among observations and the sample sizes to use are entered in a data column.



Note: The sample size data column may not be one of the data columns selected in step 2. If the sample size data column specified on the Sample Verification Dialog has already been selected in Step 2, ARM will display the following warning:



In order to proceed, a different sample size data column number should be specified. If the specified sample size data column number is correct but has already been included in the selected data columns, the report process must be restarted. Be sure to select only response data columns in Step 2.



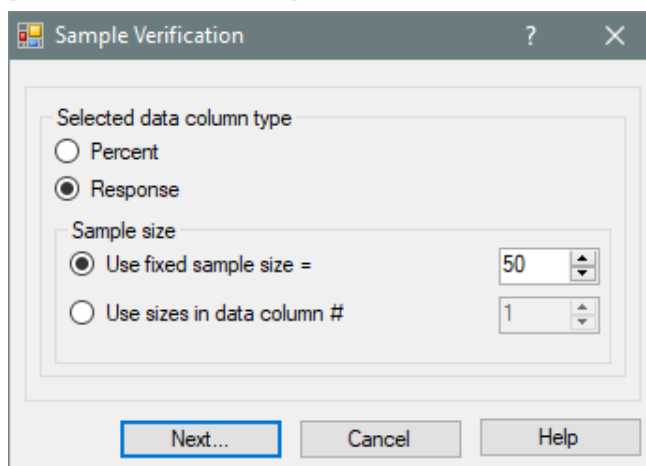
Step 6 - Data Preparation

ARM determines a sample size, response, and percent kill for each valid treatment rate in the data column, based on the choices made in Step 5. Below are four examples that illustrate these calculations, for each of the possible combinations of the Sample Verification options set in the previous step.

After ARM determines a sample size, response, and percent kill for each treatment rate, ARM validates this information according to the following checks. Data that cannot be validated is dropped from the analysis.

- Sample Size must be greater than 0.
- There must be at least one observation.
- Percent must be greater than 0 and less than 100. For Logit and Probit Least Squares estimation methods, the ARM performs the Berkson's Adjustment on percents of 0 and percents greater than or equal to 100.

Example: Fixed Sample Size with Response Data Column



If sample size has been specified as a fixed number and the selected data columns have been identified as "response" data columns ARM will calculate sample size, response, and percent based on the following formulas:

- **Response** = The sum of all assessment data for the current treatment in the current data column.
- **Sample Size** = The number of observations summed to get the Response * Fixed Sample Size
- **Percent** = Response / Sample Size

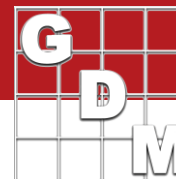
	Sub	Rep	Blk	Col	Plot	Trt	1	2	3
1	1	1	1	101	1	40	80	45	
2	1	1	1	101	1	41	79	45	
1	1	1	2	102	2	30	66	40	
2	1	1	2	102	2	31	65	40	
1	2	2	1	201	1	42	74	50	
2	2	2	1	201	1	43	70	48	
1	2	2	2	202	2	32	60	40	
2	2	2	2	202	2	33	50	41	

Example: Using Treatment #1, Data Column #1 with a Fixed Sample Size of 50

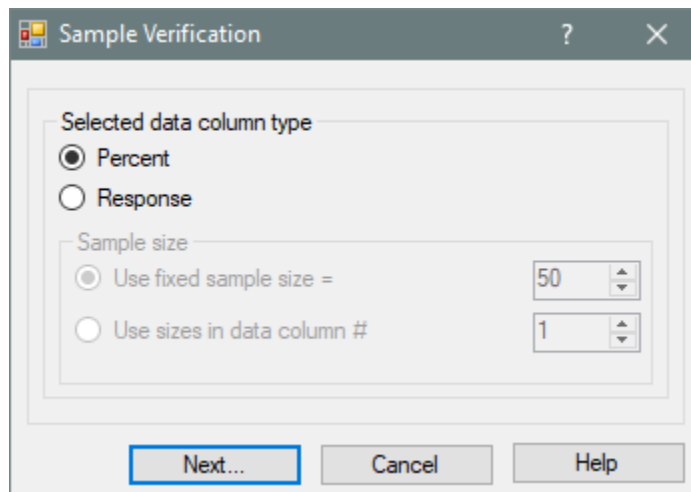
Response = 40 + 41 + 42 + 43 = 166

Sample Size = 50 * 4 observations = 200

Percent = 166/200 = 83%



Example: Fixed Sample Size with Percent Data Column



If sample size has been specified as a fixed number and the selected data columns have been identified as "percent" data columns ARM will calculate sample size, response, and percent based on the following formulas:

- **Percent** = The average of all assessment data for the current treatment in the current data column.
- **Sample Size** = The number of observations averaged to get the Percent * Fixed Sample Size
- **Response** = Sample Size * Percent

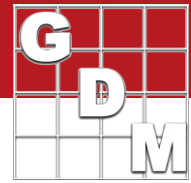
+	Sub	Rep	Blk	Col	Plot	Trt	1	2	3
🔒	1	1	1	1	101	1	40	80	45
📄	2	1	1	1	101	1	41	79	45
	1	1	1	2	102	2	30	66	40
	2	1	1	2	102	2	31	65	40
	1	2	2	1	201	1	42	74	50
	2	2	2	1	201	1	43	70	48
	1	2	2	2	202	2	32	60	40
	2	2	2	2	202	2	33	50	41

Example: Using Treatment #1, Data Column #2 with a Fixed Sample Size of 50

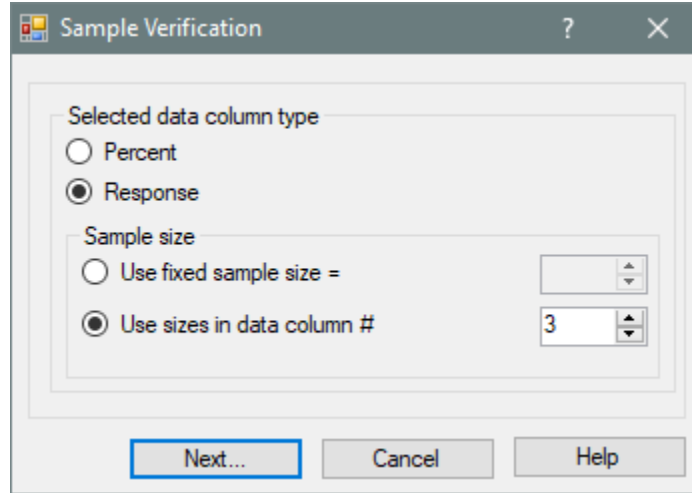
Percent = $(80 + 79 + 74 + 70) / 4 = 76\%$

Sample Size = $50 * 4 \text{ observations} = 200$

Response = $200 * 76\% = 152$



Example: Sample Size Data Column with Response Data Column



If sample size has been specified as a data column and the selected data columns have been identified as "response" data columns ARM will calculate sample size, response, and percent based on the following formulas:

- **Response** = The sum of all assessment data for the current treatment in the current data column.
- **Sample Size** = The sum of all assessment data for the current treatment in the sample size column.
- **Percent** = Response / Sample Size

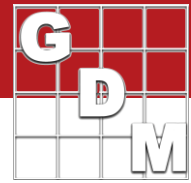
	Sub	Rep	Blk	Col	Plot	Tit	1	2	3
1	1	1	1	101	1		40	80	45
2	1	1	1	101	1		41	79	45
1	1	1	2	102	2		30	66	40
2	1	1	2	102	2		31	65	40
1	2	2	1	201	1		42	74	50
2	2	2	1	201	1		43	70	48
1	2	2	2	202	2		32	60	40
2	2	2	2	202	2		33	50	41

Example: Using Treatment #1, Data Column #1 with a Sample Size of Data Column #3

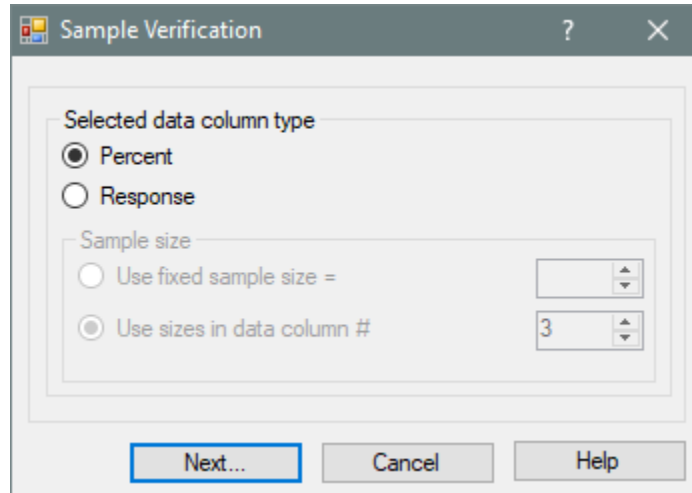
Response = 40 + 41 + 42 + 43 = 166

Sample Size = 45 + 45 + 50 + 48 = 188

Percent = 166/188 = 88%



Example: Sample Size Data Column with Percent Data Column



If sample size has been specified as a data column and the selected data columns have been identified as "percent" data columns ARM will calculate sample size, response, and percent based on the following formulas:

- **Percent** = The average of all assessment data for the current treatment in the current data column.
- **Sample Size** = The sum of all assessment data for the current treatment in the sample size column.
- **Response** = Sample Size * Percent

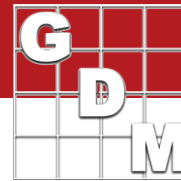
	Sub	Rep	Blk	Col	Plot	Tit	1	2	3
1	1	1	1	101	1		40	80	45
2	1	1	1	101	1		41	79	45
1	1	1	2	102	2		30	66	40
2	1	1	2	102	2		31	65	40
1	2	2	1	201	1		42	74	50
2	2	2	1	201	1		43	70	48
1	2	2	2	202	2		32	60	40
2	2	2	2	202	2		33	50	41

Example: Using Treatment #1, Data Column #2 with a Sample Size of Data Column #3

$$\text{Percent} = (80 + 79 + 74 + 70) / 4 = 76\%$$

$$\text{Sample Size} = 45 + 45 + 50 + 48 = 188$$

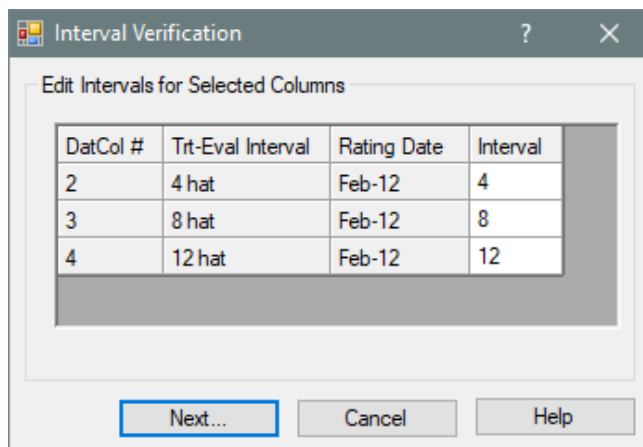
$$\text{Response} = 188 * 76\% = 143$$



Step 7 - Time Series Interval Verification

If **Time Series** is the selected Analysis Type on the Dose-Response Analysis Report Options, ARM must determine an interval for each valid data column.

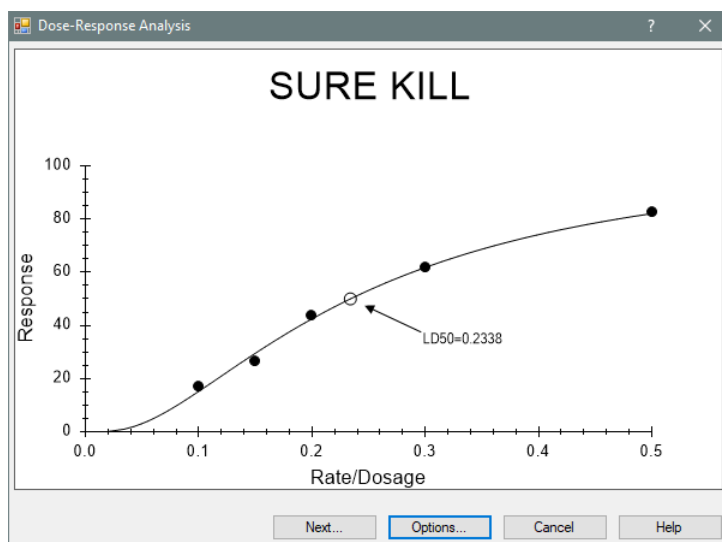
ARM first looks at the Trt-Eval Interval Field ("TEI"). If there is an entry, ARM will use that for the default interval. If there is not a Trt-Eval Interval, ARM will next look to the Rating Date Field ("EED"). If there is a rating date entered, ARM will use that date in reference to the first application date found in the site description ("ADx"). ARM will convert the intervals to the lowest common denominator.



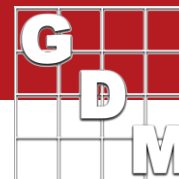
Step 8 - Analysis Graph

The analysis graph displays next, to review and customize prior to printing. Use the Options button to edit the graph properties and change the appearance of the graph. There are two types of analysis graphs, based on the selected Analysis Type option on the Dose-Response Analysis Report Options.

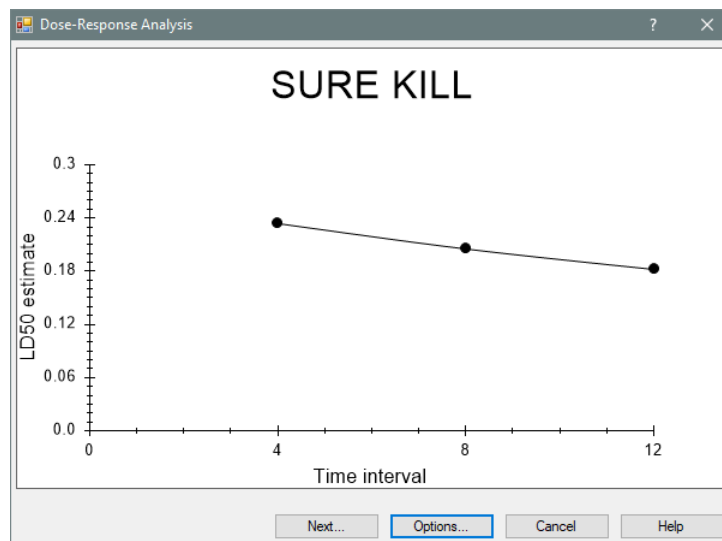
A **Simple Analysis** is performed on one data column. The Simple graph plots the original response vs. rate data used to calculate the dose estimate. ARM marks and labels the calculated dose estimate with a hollow point and the estimate abbreviation and percentage entered on the report options. ARM draws a probit or logit line based on the plotted data.



Note: For a probit estimate method, the probit line corresponds directly to the slope and intercept equations that may be printed on the report. However, when using the logit estimate method, the logit line drawn is not based on the slope and intercept equations on the report.



A **Time Series Analysis** is performed on multiple data columns. ARM calculates a simple dose estimate for each selected data column and plots the estimates against the intervals defined in Step 7 - Time Series Interval Verification. ARM draws a spline curve to connect these points.



Acknowledgements and References

*Algorithms were provided courtesy of Dr. J. J. Hubert, University of Guelph.

Other References:

Hubert, J. J. BIOASSAY. Dubuque: Kendall/Hunt Publishing Company, 1992.