

Waters® Millennium³² Software: Automate Custom Calculations

Question: The “routine” test for impurities in our pharmaceutical manufacturing plant involves calculating the percent area of active versus minor contaminants in a batch of incoming raw material. Unfortunately, a simple percent area calculation is not possible. We must first remove all peaks with less than 0.05% of the total area before the final calculation is made. Must we rely on other software packages, such as Microsoft® Excel, to perform these series of calculations on our collected data?

Answer: “Custom Calculations” have traditionally been performed using external, third party software programs. Most chromatography software programs are designed to only collect, process, and store data. Few provide tools to assist chromatographers and managers reduce the raw data into a format required to make critical decisions (e.g., whether to accept or reject a particular lot of material). As indicated in Figures 1 and 2, Waters® Millennium³² Chromatography Software addresses this need. **This Performance PerSPECTive demonstrates how a “Custom Calculation” (Percent Purity) can be performed without relying on external calculations or third party software programs.**

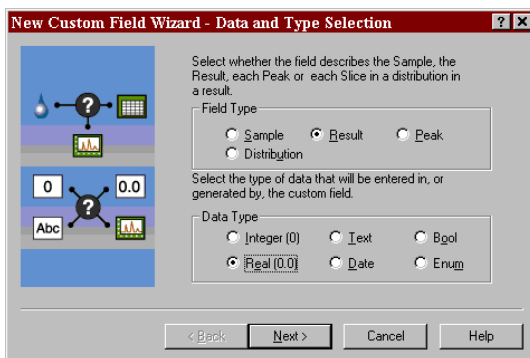
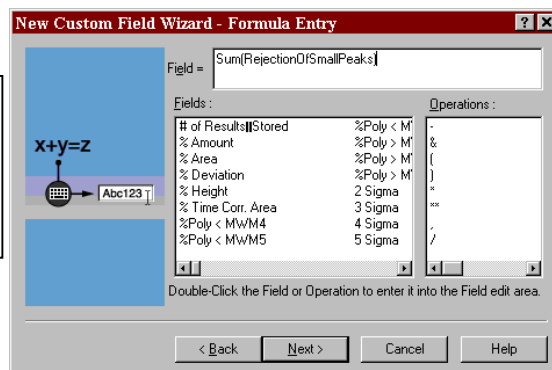


Figure 2: Get the flexibility to create simple or sophisticated Custom Calculation Fields without having to export the collected data to third party spreadsheet software such as Microsoft Excel or Lotus® 1•2•3.

Figure 1: Millennium³² Wizard technology can assist you in creating “Custom Calculations.”



Automate purity calculations: Chromatographic purity determinations from incoming raw material are frequently performed by industrial and pharmaceutical organizations before the material is released to production. The purity calculation measures the percent area of the active component in the mixture. Frequently, a batch of incoming raw material is accepted if the peak area of active component exceeds a certain percentage (typically 95%) from the total areas obtained. Difficulties arise when determining which peaks qualify for inclusion in the “total peak area” calculation. Some measurement protocols require that only peaks with areas greater than 0.05% of the “total peak area” be included in the final calculation. In this situation, peaks whose areas are less than 0.05% of the total must be eliminated before the final percent purity calculation is determined. Millennium³² Software Versions 3.2 and 4.0 provide “Custom Calculation Tools” that minimize the time, cost, and potential errors associated with manual calculations or use of spreadsheet calculations from exported chromatography data files.

Millennium³² software helps you get the right answer faster: How can a chromatography data system eliminate from the final purity calculation all “minor peaks” whose areas are less than 0.05% of the total peak area? As indicated in Figure 3, Millennium³² Custom Calculations using various Field Types and Formulae can be used to help you get the right answer faster. Using the new Boolean Logic calculation feature of Millennium³² Software Version 3.2 and 4.0, the **First Field (“RejectionOfSmallPeaks”)** tests the “percent area” for each peak against the 0.05% area rejection threshold. When the calculated area for an individual peak is greater than 0.05% of the total peak area, the formula returns that component’s peak area to the new field, labeled **“Area After 0.05% Area Rejection”** in **Table 1**. When the component’s peak area is less than or equal to the 0.05% area threshold, the formula calculates a value of -50,000. This is a reserved “null” value in the Millennium³² database that causes the removal of that component from further calculations. The **Second Field (“SumOfRemainingPeaks”)** is a Result Field that sums all the areas of the components selected after the first calculation. This gives the total area of all peaks which passed the 0.05% area threshold limit. The **Final Field (“RemainingAreaPercent”)** is another Peak Field that calculates the percent area for each of the peaks that have passed the 0.05% threshold limit test. This last field contains the values that are reported in the final report. Table 1 shows the results of these calculations as they appear in a Millennium³² report. This Table compares the percent areas prior to the Millennium³² Custom Calculation (**Blue Box**) with those after 0.05% area rejection calculations (**Red Box**).

Figure 3: Millennium³² Field Types and Formulae used for Percent Purity Custom Calculation

Name	Field Type	Type	Source	Formula
1 RejectionOfSmallPeaks	Peak	Real (0.0)	Calculated	GT(% Area,0.05)*Area+LTE(% Area,0.05)*2*-25000
2 SumOfRemainingPeaks	Result	Real (0.0)	Calculated	SUM(RejectionOfSmallPeaks)
3 RemainingAreaPercent	Peak	Real (0.0)	Calculated	RejectionOfSmallPeaks/SumOfRemainingPeaks*100

Table 1: Millennium³² Percent Purity Custom Calculation Report

Peak Results with 0.05% Area Rejection

	Peak Name	Retention Time	Area	% Area	Area after 0.05% Area Rejection	% Area After 0.05% Area Rejection
1		2.630	3889	0.0443		
2		2.866	8653	0.0986	8653	0.0987
3		2.965	12311	0.1403	12311	0.1404
4		4.670	3571	0.0407		
5	Imp A	5.648	79956	0.9110	79956	0.9117
6		5.970	6397	0.0729	6397	0.0729
7		6.655	8274	0.0943	8274	0.0943
8		6.983	7996	0.0911	7996	0.0912
9	Imp B	7.899	34906	0.3977	34906	0.3980
10	Imp C	9.138	43688	0.4977	43688	0.4982
11	Active	10.482	8567564	97.6115	8567564	97.6946
Sum			8777204	100.000	8769744	100.000

Summary:

- Millennium³² software Versions 3.2 and 4.0 provide the “Custom Calculation Tools” necessary for final result calculations without the time, cost, or potential errors associated with manual calculations or the use of spreadsheet calculations from exported chromatography data files.
- Wizard technology contained in Millennium³² software helps you generate “user definable” calculation criteria to produce validated results without the need to qualify and maintain “specialized home grown” or other third party application software.

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