AccuSizer® 3.1.4.0 Software Release Notification

AccuSizer SPOS Systems

In August of 2023 Entegris released AccuSizer® software version 3.1.4.0 that includes several new features:

- DF2 search; the ability to automatically determine the optimum dilution factor for concentrated samples.
- Volume fraction calculation: this provides a calculation quantifying the percent of particle volume within a defined range.
- Scientific notation for PFAT5 calculations; this facilitates data interpretation of PFAT5 calculated results at very low concentration levels.

DF2 SEARCH

Applicability: AccuSizer APS systems two stage dilution mode only

The older PSS L2W software included the ability to automatically adjust the dilution factor (DF2) for unknown samples. In previous versions of AccuSizer software, the user needed to choose a DF2 value for all samples as shown in Figure 1, in this example the range is 11.5 – 481.

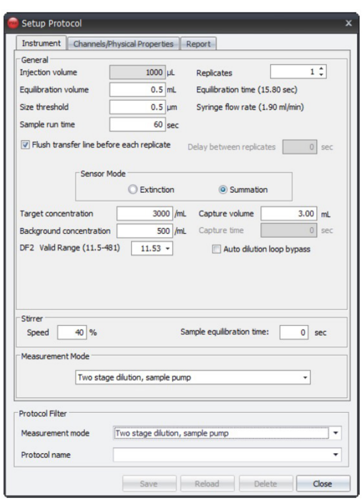

Figure 1. Legacy Setup Protocol for the APS software.

Note: DF2 is not the simple dilution ratio one might expect, but rather a calculation specific to Entegris AccuSizer systems. See Appendix I for details.

The new 3.1.4.0 release now includes the feature to automatically search for the proper DF2 value, in the Setup Protocol window shown in Figure 2.

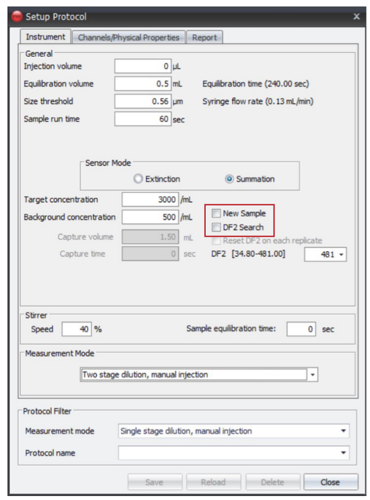

Figure 2. New Setup Protocol window for the APS software.

Select New Sample and/or DF2 Search and the system will automatically adjust the DF2 (dilution factor) and then perform the measurement using the chosen DF2 value. The measurement sequence when DF2 Search is selected in the protocol is shown below:

1. The system flushes to the selected background concentration.
2. The highest available DF2 value is used for the initial measurement.
3. The software checks if count rate (particles/mL) lies within 15% of the target (here 3000/mL).
4. If the count rate is within range, the measurement begins.
5. If the count rate is too low, the DF2 value decreases and the count rate is checked again.
6. Steps 3-5 are repeated with different DF2 values until the count rate is within 15% of the target and measurement completed.

This measurement sequence is extremely helpful when testing a new sample with unknown concentration, or a sample with known concentration that has not previously been measured on the AccuSizer APS. The operator can choose the DF2 Search feature and let the hardware/software determine the optimum dilution level.

Note: The available range of DF2 values is influenced by the syringe size and injected (loop) volume. If a protocol requests an impossible combination of values, the software will not allow the protocol to be saved.

Note: During the DF2 search sequence the highest available DF2 is used first (lowest concentration), followed by lower values until the desired count rate is achieved. This avoids cell window fouling due to elevated concentrations flowing through the sensor. The screen shot shown in Figure 3 shows how the run time data appears during the DF2 Search measurement sequence. In this example two different DF2 values were attempted before the third DF2 value achieved the desired count rate, and the measurement was performed.

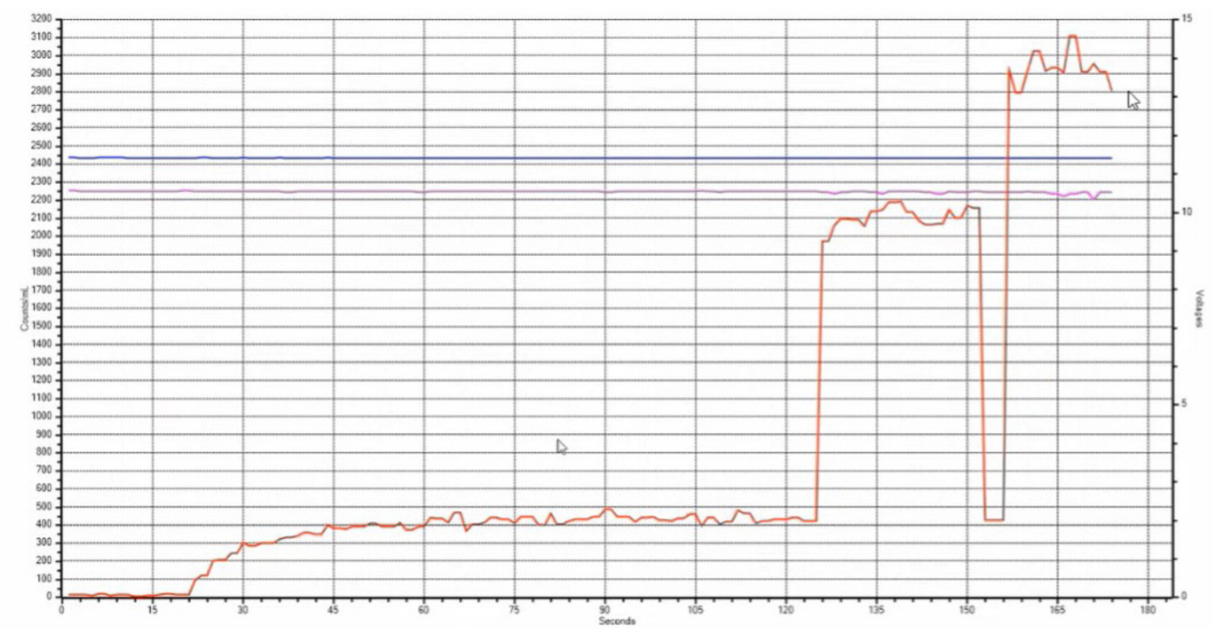

Figure 3. Run time data during a measurement.

VOLUME FRACTION CALCULATION

Applicability: All AccuSizer lab systems

The previous AccuSizer software versions only include one specific volume fraction calculation – volume % > 5 µm, or the PFAT 5 calculation. This calculation is specific to the pharmaceutical test USP <729>, Globule Size Distribution in Lipid Injectable Emulsions. The new AccuSizer version 3.1.4.0 includes the ability to calculate the volume fraction within any defined size range.

A powder metal sample was analyzed on the AccuSizer APS and the Volume Fraction calculation was performed on a size range of interest; 10 – 100 µm. The complete distribution on a volumetric basis is shown in Figure 4.

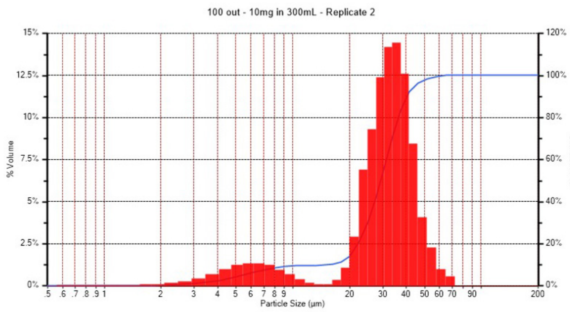

Figure 4. Volume % result for metal powder.

The volume fraction results for the defined size range are shown in Figure 5.

Flow rate: 30.0 mL/min
Number sized (≥ 0.5): 170622
Pre DF: 1.00
DF: 1.0
Sample volume: 10.0 mL
Measurement time: 20 seconds
Report date/time: 16:28, 07/17/2023

Sensor model: LE400
Sensor S/N: 20-06LAB4
Calibration file: 20-06LAB4S.SNS
Calibration date: 07-10-20
Sensor mode: Summation
Number of channels: 49

Sample: 100 out - 10mg in 300mL
Comment:
Run Date/Time: 15:22, 03/23/2021

Percent Solids (vol/vol) %	Range (µm)	Volume Fraction (%)
0.001	10.0 - 100.0	79.28612

Figure 5. Volume fraction report.

Note: See Appendix II for the PFAT5 and Volume Fraction calculation equations

SCIENTIFIC NOTATION FOR PFAT5 CALCULATIONS

Applicability: Typically AccuSizer APS systems, but the feature works for all models

The PFAT5 calculation is used for the Method II section of USP 729 testing. The volume-weighted result >5 µm (PFAT5) must be <0.05% to pass the test. Many calculated PFAT5 results are extremely low – below 0.001%, making data interpretation challenging since many software packages will just round the values to zero. The new AccuSizer version 3.1.4.0 software now reports very low PFAT5 values in scientific notation as shown in Figure 6.

Flow rate: 60.3 mL/min
Number sized (≥ 0.5): 14746
DF: 7.98
Sample volume: 4.199 mL
Measurement time: 60 seconds
Report date/time: 09:25, 06/26/2023

Sensor model: LE400
Sensor S/N: 0403905
Calibration file: 0403905S_0622_HH_60MCPA.SNS
Calibration date: 06-29-22
Sensor mode: Summation
Number of channels: 806

Sample: Trimix 2 DF2 Search
Comment:
Run Date/Time: 16:22, 06/12/2023

Fat Concentration (mass %)	Oil Density (g/mL)	$PFAT_5$ (%)
80.0	0.0050	1.83450e-6

TEST Criteria	RESULT
PFAT5 < 0.05% (PASS)	PASS

Figure 6. PFAT5 result using scientific notation.

CONCLUSIONS

Customers still using legacy AccuSizer 780 model instruments are encouraged to upgrade to the current systems to benefit from these and many other software improvements. With the addition of the automatic DF2 search and volume fraction calculations there should be no reason to remain using older, obsolete instruments that are now difficult to support.

Customers currently using older versions of AccuSizer software are encouraged to upgrade to the newest version for the continually improving features and bug fixes.

Examples of recent fixes in version 3.1.4.0[1] include:

- Fixed DF2 validation issue which prevented saving within APS protocol
- Fixed issue where instrument specific protocol settings were not included in database export
- Fixed issue where sample explorer did not display SIS protocol mixing parameters
- Updated CFR activation links
- Added full report template to installer for user report creation reference

References

[1] Release Notes delivered with the software

APPENDIX I. DF2 DERIVATION

Let dV_S represent the small volume of prediluted sample (coming from the predilution chamber), with particle concentration C_0 which enters one input of the secondary-stage diluter at flow rate F_1 during the short time dt,

$dV_S = F_1\,dt$ *(Eq 1)*

Let dV_D represent the small volume of fresh diluent which enters the other input of the diluter at flow rate F_D during the same time dt,

$dV_D = F_D\,dt$ *(Eq 2)*

Let N_2 represent the change in the number of particles in the second stage diluter which results during dt (an increase due to fresh prediluted sample entering and a decrease due to particles/fluid leaving the chamber),

$dN_2 = + C_0\,dV_S - [(dV_D + dV_S)/V_2]\,N_2$ *(Eq 3)*

where V_2 represents the effective volume of the second stage diluter; in the case of a physically small "static" mixer, V_2 is typically < 10 ml.

Use equations (Eq 1) and (Eq 2) to rewrite equation (Eq 3),

$dN_2 = -\,[(F/V_2)\,N_2 - C_0F_1]\,dt$ *(Eq 4)*

where $F = F_D + F_1$, the flow rate of fluid/particles exiting the diluter.

Change variables: $M_2 = [(F/V_2)\,N_2 - C_0F_1]$, so that $dM_2 = (F/V_2)\,dN_2$. Use variable M_2 to rewrite equation (Eq 4),

$dM_2 = -\,(F/V_2)\,M_2\,dt$ *(Eq 5)*

Divide both sides of equation (Eq 5) by M_2 and integrate,

$\ln M_2 = -\,(F/V_2)\,t + C$ (const. of integration) *(Eq 6)*

Rewrite equation (Eq 6) in exponential form and return to variable $N_2(t)$,

$N_2(t) = (V_2/F)\,A\exp(-t/\tau_2) + C_0F_1\,(V_2/F)$ *(Eq 7)*

where τ_2 is the "residence time" of the second stage diluter (static mixer), typically less than 10 sec for a small effective volume V_2,

$\tau_2 = V_2/F$ *(Eq 8)*

Solve for constant A, to satisfy $N_2(0) = 0$, and substitute into equation (Eq 7),

$N_2(t) = (C_0F_SV_2/F)\,[1 - \exp(-t/\tau_2)]$ *(Eq 9)*

Divide equation (Eq 9) by V_2 to obtain the time-dependent particle concentration in the fluid stream which exits the second stage diluter and enters the sensor,

$C_2(t) = C_0(F_1/F)\,[1 - \exp(-t/\tau_2)]$ *(Eq 10)*

After enough time has elapsed, i.e. $t \gg \tau_2$, the particle concentration at the output of the second stage diluter reaches a steady-state, equilibrium value, designated by C_2,

$C_2 = C_0(F_1/F)$ *(Eq 11)*

This expression therefore establishes equation (Eq 12) for the second stage dilution factor, referred to as DF_2,

$DF_2 = C_0/C_2 = F/F_1 = (F_1 + F_D)/F_1 = 1 + (F_D/F_1)$ *(Eq 12)*

It is useful to rewrite equation (Eq 10), using equations (Eq 11) and (Eq 12),

$C_2(t) = C_2\,[1 - \exp(-t/\tau_2)]$ *(Eq 13)*

where $C_2 = C_0/DF_2$ *(Eq 14)*

APPENDIX II. PFAT 5 AND VOLUME FRACTION EQUATIONS

PFAT 5

$$\text{AbsVol (mL)} = \sum_{5\ \mu m}^{50\ \mu m} \text{PreDf} \times \text{count} \times \frac{4}{3}\pi\left(\frac{\text{Size}}{2}\right)^3 \times 10^{-12}$$

$$\text{TotVol (mL)} = \frac{\text{PFAT Conc}}{100} \times \frac{\text{Sample Volume mL}}{\text{PFAT Oil Density}}$$

$$\text{PFAT5} = 100 \times \frac{\text{AbsVol}}{\text{TotVol}}$$

Volume Fraction

$$\text{AbsVol (mL)} = \sum_{\text{Range start } (\mu m)}^{\text{Range end } (\mu m)} \text{PreDf} \times \text{count} \times \frac{4}{3}\pi\left(\frac{\text{Size}}{2}\right)^3 \times 10$$

$$\text{TotVol (mL)} = \frac{\text{Percent solids}}{100} \times \text{Sample Volume (mL)}$$

$$\text{VF} = 100 \times \frac{\text{AbsVol}}{\text{TotVol}}$$

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