

CONTROLLED FLOCCULATION STUDIES BY  
STREAMING CURRENT MEASUREMENT

Dipak G. Shah and Bhogi B. Sheth

University of Tennessee

Center for the Health Sciences

College of Pharmacy

Division of Drug Product Technology

Memphis, Tennessee 38163

ABSTRACT

The streaming current technique was investigated for the measurement of particle charge in aqueous dispersions. The initial phase of the investigation dealt with the study of relevant measurement parameters in order to develop a measurement procedure for obtaining reproducible charge measurements. The streaming current measurement technique was applied to the study of controlled flocculation of aqueous dispersions of microcrystalline silica and of bismuth subnitrate. A profile of streaming current as a function of added electrolyte was obtained for these dispersions. Sediment height and redispersibility measurements were also recorded for these dispersions. It was found that the sediment height and redispersibility behavior of these dispersions as a function of added electrolyte was consistent with the particle charge conditions as indicated by the streaming current profile.

### INTRODUCTION

Increasing attention has been focused in recent years upon the interfacial properties of powdered drugs. Various interfacial interactions such as controlled flocculation in suspensions and solute adsorption are being recognized as being important in pharmaceutical research. The physical stability of pharmaceutical suspensions has been the subject of a number of research and review articles. Stanko and Dekay reported that Zeta Potential (ZP) of sulfamerazine suspension changed with additives and this was related to stability (1). Haines and Martin studied the electrokinetic behavior of insoluble drugs in dispersion and were able to correlate the magnitude of ZP to the caking tendencies of pharmaceutical suspensions (2,3). Wilson and Ecanow investigated the controlled flocculation of sulfamerazine by aluminum chloride (4). They attributed the observed flocculation to the interaction of aluminum chloride with a wetting agent, dioctyl sodium sulfasuccinate used in the formulation. Matthews and Rhodes described suspensions of griseofulvin as undergoing either flocculation or coagulation on the basis of sedimentation rates (5).

In all of these studies, particle charge estimation was done by ZP measurement using the microelectrophoresis method. Recently an instrument called the Streaming Current Detector (SCD) has been developed for which the underlying principle of operation is based upon streaming potential (6). The instrument enables the measurement of streaming current, which provides a means to determine the polarity and the magnitude of a quantity related to the particle charge (7).

Earlier studies on the SCD have dealt with the investigation of the adsorption of cetyl dimethyl benzyl ammonium chloride by monoionic sodium bentonite and critical micelle concentrations of surface active agents (8), and determination of protein isoelectric points (9). It was felt that this technique offered a good method for studies dealing with solute adsorption and particle charge phenomena.

This report described studies dealing with the development of a procedure for streaming current measurements and the application of the streaming current technique to controlled flocculation studies. Measurement development studies were necessary as it was found that the procedures described in the instrument manual and in various literature reports were not sufficiently complete to provide reproducible data. Therefore, initial investigation was directed at evaluating the effect of various measurement parameters on instrument response with a view to develop a procedure which would provide reliable results. The method developed as a result of these studies was used to investigate selected solute-solid and solute-solute type interactions. In this report, the application of this measurement to controlled flocculation of suspensions of colloidal silica and bismuth subnitrate is presented.

#### EXPERIMENTAL

##### MATERIALS

The materials used were as follows: Cetyl dimethyl benzyl ammonium chloride<sup>1</sup>, microcrystalline silica<sup>2</sup>, bismuth subnitrate<sup>3</sup>, aluminum chloride hexahydrate<sup>4</sup>, and monobasic potassium phosphate<sup>5</sup>.

**INSTRUMENT:** A diagrammatic sketch of the SCD is shown in Figure 1. The detection probe of the unit is a plastic block or boot containing a sample reservoir, a dead-ended pump bore, electrodes and a piston which reciprocates in the bore to force fluid back and forth through the annular space between the bore and the piston. Gerdes has shown that the streaming current of the boot and the piston surface is linearly related to the product of its ZP and the dielectric constant of the liquid as shown in Equation 1 (6).

$$I = K \cdot ZP \cdot D \quad \text{Equation 1.}$$

Where I is streaming current, K is a constant, ZP is Zeta Potential and D is the dielectric constant of the liquid.

When the sample being measured is a dispersion, there exists a double equilibrium and the relationship of Equation 1 is not

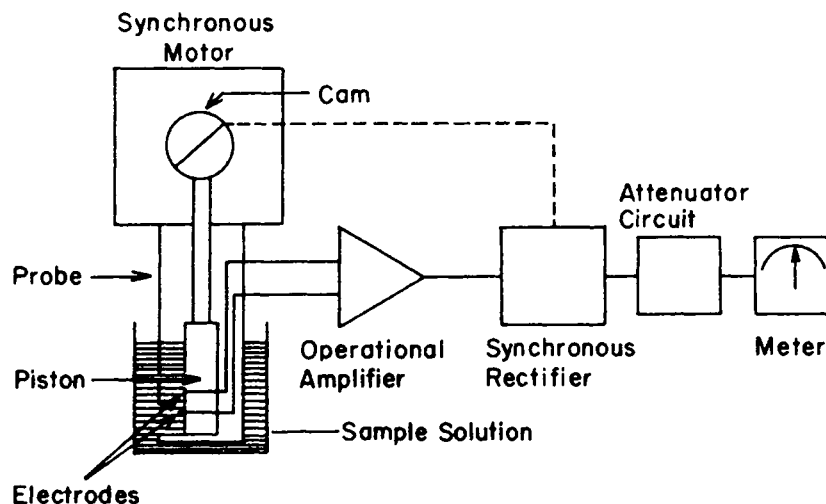


Figure 1  
Diagrammatic Sketch of Streaming Current Detector

directly applicable. In this case, the charge condition of the boot and piston surface will be a function of the charge condition of the disperse phase of the sample. Therefore, it would be expected that the charge condition of the two surfaces which are in equilibrium with the same liquid, would bear a relationship to one another. Thus the measured streaming current value would not necessarily relate to other measurements, such as electrophoretic mobility. However, it would be expected that the change in streaming current of one surface would cause the streaming current of the other surface to change in the same direction and this has always been found to be the case (6). Therefore, electrokinetic characterization of dispersions can be obtained by streaming current measurements.

#### METHOD OF MEASUREMENT

The sample to be measured was placed in a 300 ml beaker and the beaker was placed on the instrument so as to submerge the boot and piston in the sample so that the sample entered the angular

space between the boot and piston. The instrument meter scale ranged from +10 to -10 and there are six attenuator buttons to provide scale expansion. The instrument was turned on and after allowing a few seconds for the reading to stabilize, the proper scale attenuation was selected to try and get a reading between 5 and 10 scale units as far as possible. The scale readings thus obtained were in arbitrary units. It was therefore, necessary to establish a point of reference for measurements. The reference point was obtained by measuring the streaming current of deionized water. A reading for deionized water ranging from -60 to -70 was taken as the reference point indicating the boot-piston surfaces were clean with no solute adsorbed on them. The exact magnitude of the water reading is a function of specific instrument design and construction and variations in water readings between instruments may be expected. The boot and piston surfaces were cleaned and the water reading check was made prior to each measurement.

**PROCEDURE FOR CLEANING THE BOOT AND PISTON SURFACES:** Since the contaminants in the boot and piston assembly of the instrument would significantly affect the streaming current reading of a sample, it was necessary to develop a suitable cleaning procedure. The following procedure was found to be satisfactory: The boot and piston surfaces were scrubbed with Pax-Lano-Sav<sup>7</sup> soap, using a test-tube brush. Pax-Lano-Sav soap was chosen since it contains wood dust which provides an abrasive action for efficient cleaning of the boot and piston surfaces. The surfaces were thoroughly rinsed with deionized water and the final cleaning was done by placing the boot and piston assembly in a sonifier bath containing deionized water for at least five minutes.

**EFFECT OF MEASUREMENT PARAMETERS:** Preliminary studies indicated that the streaming current value obtained for a sample could be significantly affected by: 1) time allowed to reach a stable streaming current reading, 2) sample volume, and 3) concentration of solute. Therefore, studies were conducted to evaluate the

effect of these conditions on the streaming current reading of a sample.

For evaluating these parameters, streaming current measurements were made of a dilute ( $5 \times 10^{-6}$  M) and a concentrated (0.01 M) solution of cetyl dimethyl benzyl ammonium chloride (CDBAC). For investigating the effects of sample volume, measurements were made using 150 ml, 250 ml, and 500 ml sample volumes. In all instances, streaming current values were measured as a function of time.

FLOCCULATION STUDIES: Silica dispersions, 2% W/V, were used as a model system for the investigation of the streaming current measurement technique for controlled flocculation of suspensions. Aluminum chloride was used as the cationic electrolyte for variation of particle charge. Suspensions of bismuth subnitrate, 5% W/V, were investigated as a typical pharmaceutical suspension, for the evaluation of this method. Bismuth subnitrate dispersions, found to be positively charged, were flocculated by the addition of varying concentrations of monobasic potassium phosphate. The procedure used for preparing suspension samples was as follows: Weighed amounts of the powder were placed in a 45 ml capacity test tube and 20 ml water was added. The powder was dispersed in water by sonification at 30 mv output for 3 minutes, using a sonifier<sup>8</sup>. The dispersion was then transferred to a 100 ml graduated cylinder. A previously determined amount of the solution of the selected electrolyte was added and the sample made up to volume with deionized water. The dispersion was then mixed on a platform shaker and allowed to stand undisturbed. The sediment height at the end of a 24-hour period was recorded. The sediment height ratio was calculated as the ratio of ultimate sediment height ( $H_u$ ) to the original sediment height ( $H_o$ ).

Observations on the appearance of the supernatant and redispersibility of the sediment were also recorded. The evaluation of

the sediment redispersibility was rated as: 1) easily redispersible sediment, 2) sediment redispersible with some difficulty, and 3) hard-caked sediment, not redispersible upon vigorous hand-shaking. Several suspensions, containing varying amounts of added electrolyte were thus prepared. Duplicate samples were prepared in each case.

### RESULTS AND DISCUSSIONS

**EFFECT OF MEASUREMENT PARAMETERS:** The results of the effect of measurement parameters on streaming current are presented in Figure 2. Examination of the data shows that an equilibration period of about five minutes was needed to obtain a stable reading for the dilute CDBAC solution. The concentrated solution was found to give a stable reading in less than one minute. This would seem reasonable since a concentrated solution may be expected to reach adsorption equilibrium in a shorter time period. Since varying solute concentrations would typically be used in a streaming current study, an equilibration period of five minutes was selected for future measurement. These results also show that a smaller degree of variation in streaming current readings was obtained with sample volumes of 150 ml and 250 ml. Further, with the 500 ml sample volume, a greater degree of variability was noted for the concentrated CDBAC solution than for the dilute solution. The reasons for this behavior are not clear. Based on these results, a sample volume of 250 ml was selected for use in future measurements.

**FLOCCULATION OF SILICA DISPERSIONS:** The effect of the addition of aluminum chloride on silica dispersions is shown in Table I and Figure 3. On the basis of the evaluation of the sedimentation and redispersibility of test samples, the sediment height ratio versus the electrolyte concentration curve in Figure 3 may be divided into three zones similar to the method reported by Haines and Martin (3). In Zone 1, A' B', referred to as the caking zone,

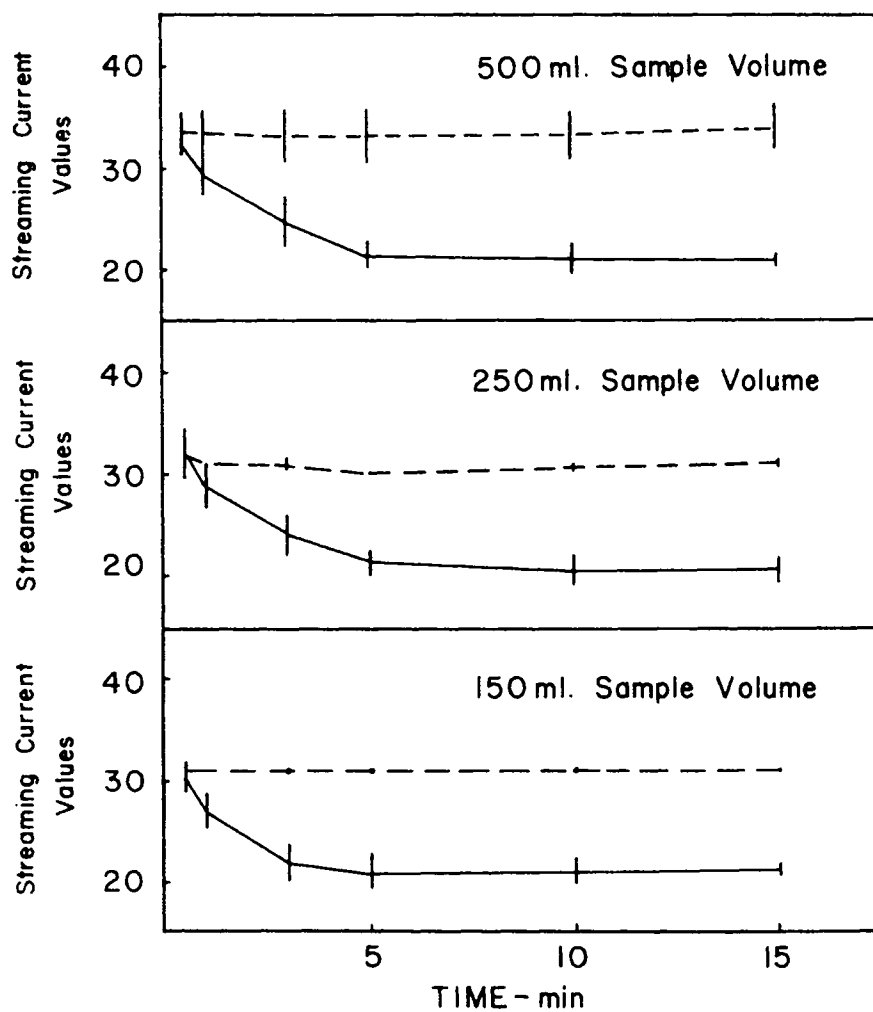


Figure 2

Effect of Measurement Parameters on Streaming Current Value

— Dilute CDBAC Solution, --- Concentrated CDBAC Solution



Table 1

Effect of Aluminum Chloride on Silica Dispersions

ALUMINUM CHLORIDE CONCENTRATION M/L	SEDIMENT HEIGHT RATIO, %	APPEARANCE OF THE SUPERNATANT	REDISPER - SIBILITY*	STREAMING CURRENT VALUES
0	0.45	Turbid	(3)	-64.4
$5 \times 10^{-5}$	1.0	Turbid	(3)	-36.6
$6 \times 10^{-5}$	3.0	Turbid	(3)	-33.6
$8 \times 10^{-5}$	5.0	Opalescent	(2)	-23.6
$9 \times 10^{-5}$	5.2	Opalescent	(1)	-21.2
$1 \times 10^{-4}$	5.15	Opalescent	(1)	-19.2
$5 \times 10^{-4}$	5.05	Opalescent	(1)	- 3.7
$1 \times 10^{-3}$	5.1	Clear	(1)	+ 1.35
$5 \times 10^{-3}$	5.0	Clear	(1)	+ 6.45
$1 \times 10^{-2}$	4.85	Clear	(2)	+ 2.6

\*Redispersibility: (1) Sediment, Easily Redispersible.  
 (2) Sediment, Intermediate Type.  
 (3) Sediment, Not Easily Redispersible.

the sample without added electrolyte, represented by A, was found to have a turbid supernatant, a small sediment height, and the sediment was not redispersible. The addition of small incremental quantities of the electrolyte did not cause any substantial change in sedimentation behavior until point B', where the concentration of the electrolyte was  $8 \times 10^{-5}$  M. At this concentration a relatively sharp increase in sediment height and a clear supernatant were observed.

The streaming current reading versus the electrolyte concentration curve in this zone indicated particle charge status that would be expected on the basis of change in ZP that would occur due to charge neutralization. Since the streaming current reading is directly proportional to ZP (6), a value of zero for the stream-

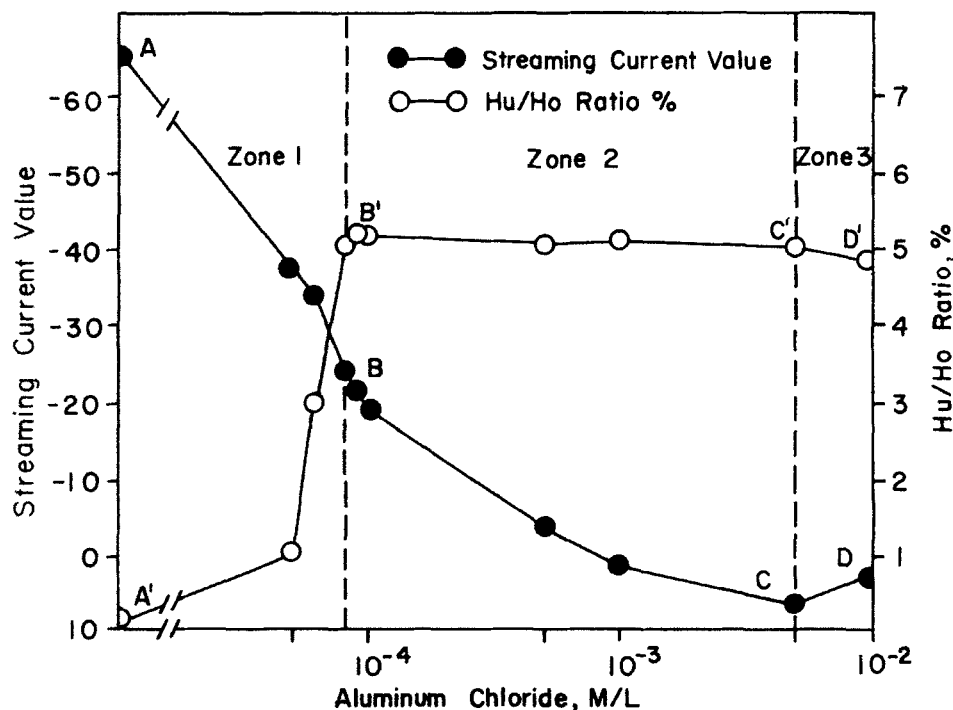


Figure 3  
Flocculation of Silica by Aluminum Chloride

ing current reading would correspond to a value of zero ZP. The streaming current value of -64.4 at point A indicates high particle charge. At point B, corresponding to the streaming current value of -23.6, initial flocculation with easily redispersible sediment was observed. Thus, initial flocculation was found to occur at particle charge status of a much reduced negative charge. This behavior is consistent with similar observations of flocculation occurring at slightly negative or positive ZP that have been previously reported (3).

In Zone 2, B'C', referred to as the non-caking zone, the sediment height ratio remained essentially the same, the supernatant was observed to be clear and the sediment remained easily

redispersible for all test samples. The value of streaming current was found to decrease, being about zero at  $1 \times 10^{-3}$  M aluminum chloride concentration.

With further addition of the electrolyte, the supernatant remained clear, but it was found that the sediment was not easily redispersible. This region is referred to as Zone 3, a caking zone. The magnitude of the streaming current values did not show substantial change in this region. The slight decrease in streaming current value and the loss of the ease of redispersibility is thought to be caused by the compaction of the double layer because of the proximity of large numbers of counterions in the vicinity of the particles. This mechanism has been suggested as an explanation for similar behaviour by Nash (10).

These results indicate that the measurement of streaming current can be employed in the evaluation of the charge status of suspensions and the stabilization of suspensions by control of particle charge.

**BISMUTH SUBNITRATE DISPERSIONS:** The effect of the addition of monobasic potassium phosphate on bismuth subnitrate dispersions is shown in Table 2 and Figure 4. The dispersed particles were found to be positively charged. Therefore, the electrolyte used was monobasic potassium phosphate. The concentration range of the electrolyte used was the same as for silica dispersions.

Examination of Figure 4 shows that the sediment height ratio versus electrolyte concentration curve can be divided into only two zones, Zone 1, a caking zone, and Zone 2, a non-caking zone. The test sample represented by A' containing no electrolyte, was found to have a small sediment height, turbid supernatant and the sediment was not redispersible. The addition of incremental quantities of electrolyte did not cause any substantial change in sedimentation behavior until B', at  $5 \times 10^{-3}$  M electrolyte concentration. At this concentration, a sharp increase in sediment height was observed, the supernatant was clear and the sediment was easily redispersible.

Table 2

Effect of Monobasic Potassium Phosphate on Bismuth Subnitrate Dispersions.

MONOBASIC POTASSIUM PHOSPHATE CONCENTRATION, M/L	SEDIMENT HEIGHT RATIO, %	APPEARANCE OF THE SUPERNATANT	REDISPERSIBILITY*	STREAMING CURRENT VALUES
0	2.0	Turbid	(3)	20.8
$1 \times 10^{-4}$	1.9	Turbid	(3)	28.6
$5 \times 10^{-4}$	1.9	Turbid	(3)	28.3
$1 \times 10^{-3}$	2.0	Turbid	(3)	21.0
$5 \times 10^{-3}$	7.0	Clear	(1)	-12.1
$1 \times 10^{-2}$	7.0	Clear	(1)	-12.6

\*Redispersibility: (1) Sediment, Easily Redispersible.

(3) Sediment, Not Easily Redispersible.

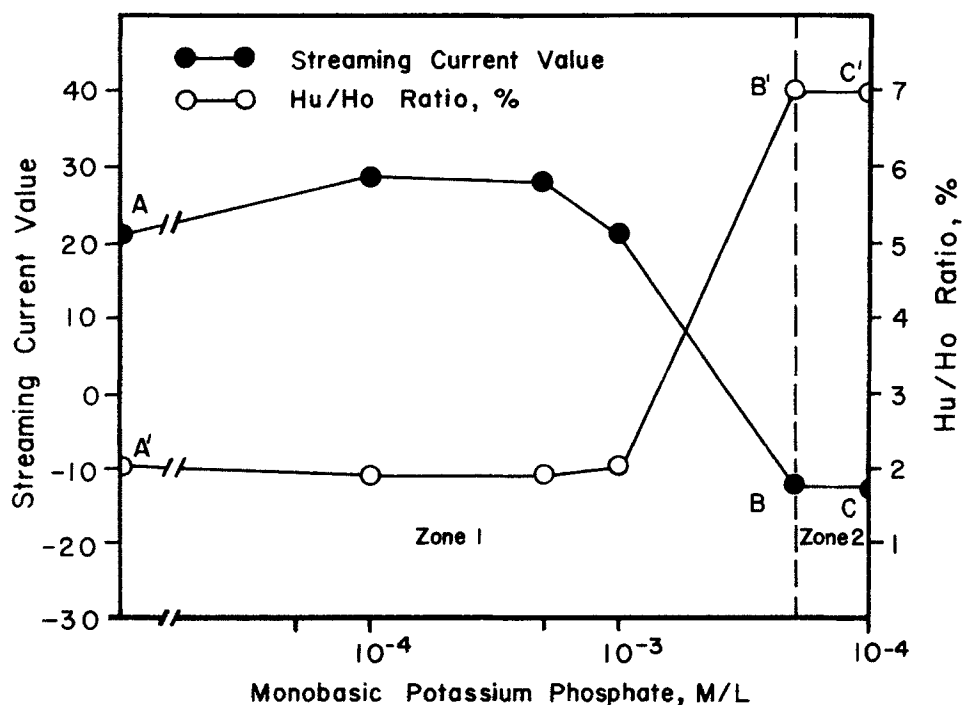


Figure 4

Flocculation of Bismuth Subnitrate by Monobasic Potassium Phosphate

The streaming current versus electrolyte concentration curve in this zone showed that the dispersion with no electrolyte had a streaming current value of 20.8, a relatively high positive charge. The addition of electrolyte caused initially a slight increase in the streaming current value and then a decrease with further electrolyte addition. The reasons for the increase in charge are not clear, but might possibly be due to the interaction of the electrolyte with soluble contaminants of the dispersed drug. The aqueous dispersion of the drug was found to have a pH value of about 1.4 indicating the presence of some soluble contaminants. The initial flocculation was found to occur at -12 streaming current value. This behavior is similar to that observed for silica dispersions and for other suspension systems reported in the literature. In the non-caking zone, the sediment height remained essentially unchanged. The streaming current values were also found to remain essentially unchanged. The occurrence of a third zone, a caking zone, on further addition of high concentrations of electrolyte to bismuth subnitrate suspensions has been reported (3). However, such high electrolyte concentrations were not used in this study.

The above results demonstrate the applicability of the streaming current measurement to the formulation of stable bismuth subnitrate suspensions by control of particle charge.

#### SUMMARY AND CONCLUSIONS

This study was concerned with the evaluation of the application of the streaming current technique to study particle charge effects in suspensions. The initial phase of the study dealt with the investigation of measurement parameters directed at developing a suitable procedure for obtaining reproducible measurements. The method resulting from these studies was utilized for the investigation of controlled flocculation of aqueous dispersions of microcrystalline silica and of bismuth subnitrate by

addition of appropriate electrolyte. Measurements were made of streaming current, sediment height and redispersibility as a function of electrolyte concentrations. It was found that the particle charge status of the dispersions as indicated by the streaming current values was consistent with sediment height and redispersibility behavior of the dispersions. Therefore, it was concluded that streaming current measurements made using the technique developed in this study can be useful in formulation of suspensions by particle charge control.

The streaming current technique can also be applied to adsorption titrations for the evaluation of solute-adsorbent interactions. It is also applicable to solute-solute interactions where the surface of the measuring head of the instrument serves as the adsorbent. Studies relevant to these types of evaluations have been conducted in our laboratories and will be presented in future reports.

#### ACKNOWLEDGEMENTS

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#### FOOTNOTES

1. Lot #89509 K & K Laboratories, Inc., Plainview, N.Y.
2. Min-U-Sil 5. Pennsylvania Glass Sand Corp., Pittsburgh, Pa.
3. Lot ALX. Mallinckrodt Chemical Works, St. Louis, Mo.
4. Lot #735366. Fisher Scientific Co., Fair Lawn, N.J.
5. Lot #PX1565. Mathison, Coleman & Bell, Norwood, OH.
6. Hydroskan<sup>TM</sup> Streaming Current Detector, Leeds & Northrup Co., North Wales, PA.
7. Pax-Lano-Sav Soap. Calgon Corp., St. Louis, Mo.
8. Model W185 Sonifier. Heat Systems-Ultrasonics, Inc., Plainview, N.Y. 11803.

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