

1 METHOD AND APPARATUS FOR PRODUCING UNIFORM SMALL
2 PORTIONS
3 OF FINE POWDERS AND ARTICLES THEREOF

4 This invention is directed towards the deposition of small (usually fractional
5 gram) masses on a generally electrically non-conductive substrate. One of the most
6 common methods for accomplishing the goal is practiced by manufacturers of
7 photocopiers and electrophotographic electronic printers. This involves causing
8 charged toner particles to migrate with an electric field to a charged area on a
9 photoreceptor, so-called electrostatic deposition. While electrostatic deposition has
10 been proposed for packaging powdered drugs (see US Patent Nos. 5,669,973 and
11 5,714,007 to Pletcher), electrostatic deposition is limited by the amount of mass that
12 can be deposited in a given area.

13 This limitation is intrinsic to electrostatic deposition technology and is
14 determined by the combination of the amount of charge that can be placed on the
15 photoreceptor and the charge to mass ratio of the toner particles. The mass that can be
16 deposited in an area of a substrate is limited to the charge in the area divided by the
17 charge to mass ratio of the particles being deposited. The maximum amount of charge
18 that can be deposited in an area of a substrate is determined by the substrate electrical
19 properties, the electrical and breakdown properties of the air or gas over it, and by the
20 properties of mechanism used for charging the substrate. Likewise, the minimum
21 charge to mass ratio of particles (which determines the maximum mass that can be
22 deposited) is determined by the charging mechanism. However, as the charge to mass
23 ratio is decreased, the variation in the charge to mass ratio increases even to the point
24 where some particles may be oppositely charged relative to the desired charge on the

1 particles. This variation prevents the reliable deposition of a controlled mass on the
2 substrate. Furthermore, low charge to mass ratio particles limit the overall speed of
3 deposition because the force of a particle, which sets the particle velocity, from an
4 electrostatic field is proportional to the charge carried by the particle. For these
5 reasons, higher charge to mass ratio particles are generally preferred.

6 Packaged pharmaceutical doses, in the range of 15 to 6000 μg are employed in
7 dry powder inhalers for pulmonary drug delivery. A mean particle diameter of
8 between 0.5 and 6.0 μm is necessary to provide effective deposition within the lung.
9 It is important that the dose be metered to an accuracy of $\pm 5\%$. A production
10 volume of several hundred thousand per hour is required to minimize production
11 costs. High speed weighing machines are generally limited to dose sizes over about
12 5,000 μg and thus require the active pharmaceutical be diluted with an excipient, such
13 as lactose powder, to increase the total measured mass. This approach is subject to
14 limitations in mixing uniformity and the aspiration of extraneous matter. Hence,
15 electrostatic deposition of such pharmaceutical powders is highly desirable.

16 US Patent 3,997,323, issued to Pressman et al, describes an apparatus for
17 electrostatic printing comprising a corona and electrode ion source, an aerosolized
18 liquid ink particles that are charged by the ions from the ion source, a multi-layered
19 aperture interposed between the ion source and the aerosolized ink for modulating the
20 flow of ions (and hence the charge of the ink particles) according to the pattern to be
21 printed. The charged ink particles are accelerated in the direction of the print
22 receiving medium. This patent discusses the advantages in the usage of liquid ink
23 particles as opposed to dry powder particles in the aerosol. However, from this

1 discussion it is apparent, aside from the disadvantages, that dry powder particles may
2 also be used. Furthermore, the charge to mass ratios achieved from using an ion
3 source for charging the powder particles are much higher than those generally
4 achieved using triboelectric charging (commonly used in photocopies and detailed by
5 Pletcher et al in US Patent 5,714,007), thereby overcoming the speed issue discussed
6 above. Such printers have been commercially marketed and sold. However, an
7 apparatus for depositing powder on a dielectric (i.e. a powder carrying package) using
8 the Pressman approach also suffers from the above described maximum amount of
9 powder that can be deposited on the dielectric. This is because during the deposition
10 process, charge from both the ions and the charged particles accumulates on the
11 dielectric, ultimately resulting in an electric field that prevents any further deposition.
12 In other words, the amount of material that can be deposited on the dielectric
13 packaging material is limited by the amount of charge that can be displaced across it
14 which is determined by the capacitance of the dielectric and the maximum voltage
15 that can be developed across it.

16 The above disadvantages are overcome in the present invention by providing
17 an alternating electric field for depositing particles onto a dielectric substrate. More
18 particularly, the present invention comprises a method and apparatus for depositing
19 particles from an aerosol onto a dielectric substrate wherein the method comprises and
20 the apparatus embodies the following steps: charging the aerosol particles,
21 positioning them in a deposition zone proximate to the dielectric, and applying an
22 alternating field to the deposition zone by which the aerosol particles are removed
23 from the aerosol and deposited on the dielectric substrate thus forming a deposit. The

1 alternating field provides the means to deposit charged particles and/or ions such that
2 the accumulation of charge on the dielectric substrate does not prevent further
3 deposition of particles thus enabling electrostatic deposition of a deposit with
4 relatively high mass.

5 In one embodiment of the invention, the particles are alternately charged in
6 opposite polarities and deposited on the substrate with the alternating electric field,
7 thus preventing charge accumulation on the dielectric substrate.

8 In a second embodiment, an ion source is provided in the deposition zone to
9 provide ions of both polarities for charging the particles. The alternating field
10 determines which polarity of ions is extracted from the ion source. These extracted
11 ions may be used for charging the particles and/or discharging the deposited particles
12 on the dielectric substrate.

13 In a third embodiment substantially all of the particles are removed from the
14 aerosol. In this embodiment, the mass of the deposit is controlled by measuring the
15 mass flow into the deposition zone and controlling the deposition time to accumulate
16 the desired mass of deposit.

17 In yet another embodiment, the mass of the deposit is determined by
18 measuring the mass flow both into the deposition zone and immediately downstream
19 thereof, and the difference being the amount deposited.

20 The foregoing and other advantages of the present invention will become
21 apparent from the following description taken together with the accompanying
22 drawings in which:

1 FIG. 1 depicts a schematic cross section of a deposition apparatus made in
2 accordance with the present invention;

3 FIG. 2 illustrates voltage differences in the deposition apparatus of FIG. 1;

4 FIG. 3 depicts an article made in accordance with the present invention; and

5 FIGS. 4 to 7 depict schematic views of various preferred embodiments of the
6 present invention.

7 The present invention provides a method and apparatus for depositing a
8 relatively large mass of material upon a dielectric substrate and the resulting
9 deposition product. The general apparatus for carrying out this deposition is shown in
10 FIG. 1 and includes a first electrode 5, a dielectric substrate 1 closely proximate to or
11 in contact with a second electrode 3, also herein referred to as a deposition electrode.
12 The volume between the dielectric substrate 1 and the first electrode 5 comprises a
13 deposition zone into which aerosol particles are introduced. This is indicated by the
14 horizontal arrow of FIG. 1. An alternating electric field (the deposition field),
15 indicated by the vertical arrow in FIG. 1 is created within the deposition zone by first
16 electrode 5, second electrode 3 in combination with an alternating voltage source,
17 shown in FIG. 1 as comprising batteries 9 and 11 and switch 7 wherein the polarity of
18 the field generating voltage is determined by the position of switch 7. However, any
19 suitable means for generating an alternating voltage is contemplated to be within the
20 scope of the invention. Charged particles from the aerosol within the deposition zone
21 are electrostatically attracted to the substrate 1 thereby forming a deposit 15 as shown
22 in FIG. 2. The deposit is incrementally formed from groups of particles deposited
23 from each cycle of the alternating field thereby forming a deposit with a relatively

1 larger mass than is possible if a static electric field were to be used. The process of
2 forming the deposit may be terminated by removal of the alternating field. The
3 completed deposit is shown in FIG. 3 as deposited on the dielectric substrate 1.

4 The aerosol particles may comprise a dry powder or droplets of a liquid. In
5 one particular embodiment of this invention, the particles comprise a pharmaceutical,
6 for example, albuterol. The pharmaceutical deposits made from deposited
7 pharmaceutical particles may, for example, form a dosage used in a dry powder
8 inhaler. In a second embodiment of this invention, the particles comprise a carrier
9 coated with a biologically active agent. An example of a bioactive agent coated
10 carrier is a gold particle (the carrier) coated by fragments of DNA (the bioactive
11 agent). Such particles are used for gene therapy. The prior examples are intended to
12 exemplify the applications of the invention, and not intended to limit the scope of it.

13 The aerosol gas may comprise air or any other suitable gas or gas mixture. For
14 some applications where it is desired to control precisely the environment to which
15 the particles are exposed, and/or to control ion emission characteristics (discussed
16 subsequently), pure nitrogen, or nearly pure nitrogen mixed with a small percentage of
17 another gas, e.g. carbon dioxide, is preferred.

18 Basic components of an aerosol generator include means for continuously
19 metering particles, and means for dispersing the particles to form an aerosol. A
20 number of aerosol generators have been described in the literature and are
21 commercially available. The most common method of dispersing a dry powder to
22 form an aerosol is to feed the powder into a high velocity air stream. Shear forces then
23 break up agglomerated particles. One common powder feed method employs a

1 suction force generated when an air stream is expanded through a venturi to lift
2 particles from a slowly moving substrate. Powder particles are then deagglomerated
3 by the strong shear force encountered as they pass through the venturi. Other methods
4 include fluidized beds containing relatively large balls together with a chain powder
5 feed to the bed, sucking powder from interstices into a metering gear feed, using a
6 metering blade to scrape compacted powder into a high velocity air stream, and
7 feeding compacted powder into a rotating brush that carries powder into a high
8 velocity air stream. A Krypton 85 radioactive source may be introduced into the
9 aerosol stream to equilibrate any residual charge on the powder. Alpha particles from
10 the source provide a bipolar source of ions that are attracted to charged powder
11 resulting in the formation of a weakly charged bipolar powder cloud.

12 Non-invasive aerosol concentration (and mass density for aerosols of known
13 particle size and specific density) may be determined optically by using right angle
14 scattering, optical absorption, phase-doppler anemometry, or near forward scattering.
15 A few commercially available instruments permit the simultaneous determination of
16 both concentration and particle size distribution.

17 Particles may be charged within or outside of the deposition zone. One
18 contemplated method of charging particles is triboelectric charging. Triboelectric
19 charging occurs when the particles are made to come in contact with dissimilar
20 materials and may be used with the particles are from a dry powder. Triboelectric
21 charging is well known and widely used as a means to charge toner particles in
22 photocopying and electrophotographic electronic printing processes. Generally,
23 triboelectric charging of particles takes place outside of the deposition zone. A

1 parameter that characterizes the efficacy of particle charging is the charge-to-mass
2 ratio of particles. This parameter is important as it determines the amount of force
3 that can be applied to the particle from an electric field, and therefore, the maximum
4 velocity that particles can achieve during deposition. This, in turn, sets an upper
5 bound to the deposition rate that can be achieved. Charge-to-mass ratios of $1\mu\text{C}$ to
6 $50\mu\text{C}$ per gram are achievable when triboelectrically charging $1\mu\text{m}$ to $10\mu\text{m}$ diameter
7 particles. Such charge-to-mass ratios are documented for pharmaceuticals by Pletcher
8 et al in U.S. Patent 5,714,007. However, other particle charging methods may achieve
9 charge-to-mass ratios at least ten times greater than is possible with triboelectric
10 charging. Accordingly, it is preferred to use such a method to maximize the velocity
11 of the particles when under influence of the deposition field and the rate at which it is
12 possible to form the deposit.

13 Generally these methods for applying higher amounts of charge to the particles
14 utilize an ion source to generate an abundance of ions of both or either positive and
15 negative polarities. Some of the negative polarity ions may be electrons. As particles
16 from the aerosol pass in front of the ion source (the charging zone), ions of one
17 polarity are accelerated away from the ion source by an electric field through which
18 the particles travel. Ions that impact the particles attach to the particles. Ions continue
19 to impact the particles until the local electric fields from the ions attached to the
20 particles generate a local electric field of sufficient magnitude to repel the oncoming
21 ions. Figures 5 and 6 illustrate two approaches for generating charging ions as well as
22 the means for providing an accelerating field.

1 In FIG. 5 ions are generated using corona wire 35. Ions are accelerated
2 through an open mesh screen 39 from an electric field created between open mesh
3 screen 39 and electrode 25. Housing 37 may be slightly pressurized to prevent the
4 migration of aerosol particles into the corona cavity. Alternatively, the corona source
5 may consist of one or more corona points at the location of corona wire 35. Aerosol
6 enters the charging zone through channel 23. Particles are charged by corona
7 generated ions that pass through the apertures of screen 39. Such a particle charging
8 method is known. A derivative of this method is described by Pressman et al in US
9 Patent 3,977,323. As shown in FIG. 5, electrode 25 is the previously described
10 deposition electrode and open mesh screen is the first electrode of the previously
11 described deposition zone. Likewise, substrate 33 is the previously described
12 dielectric substrate. Thus, in this exemplary configuration, the charging zone and
13 deposition zone are the same and the particles are simultaneously charged and made to
14 deposit. A particle trajectory is shown by path 41.

15 An alternate particle charging method using an ion source employs a silent
16 electric discharge (SED) charge generator. The construction and operation of this
17 class of device is described by D. Landheer and E.B. Devitts, Photographic Science
18 and Engineering, 27, No. 5, 189-192, September/October, 1993 and also in US
19 Patents 4,379,969, 4,514,781, 4,734,722, 4,626,876 and 4,875,060. In the exemplary
20 implementation illustrated in FIG. 6, a cylindrical glass core 43 supports four glass
21 coated tungsten wires 45 equally spaced about its surface. The assembly is closely
22 wound with a fine wire 47 in the form of a spiral. A typical generator unit, available
23 from Delphax Systems, Canton, MA, consists of a 1cm diameter Pyrex glass rod

1 supporting four glass clad 0.018cm diameter tungsten wires. The assembly is spiral
2 wound with 0.005cm diameter tungsten wire at a pitch of about 40 turns per cm. Only
3 one glass coated tungsten wire is activated at any time. The other three wires are
4 spares that may be rotated into the active position if the original active wire becomes
5 contaminated. In FIG. 6, the active wire is that wire closest to the opening in channel
6 23. Ions and electrons are generated in the region adjacent the glass coated wire when
7 a potential of about 2300VACpp at a frequency of about 120 KHz is applied between
8 the tungsten wire core and the spiral wound tungsten wire. Ions and electrons are
9 withdrawn from the active region by an electric field created between spiral winding
10 47 and electrode 25. As in FIG. 5, in the exemplary configuration of FIGS. 6 and 7,
11 the aerosol particles are simultaneously charged and made to deposit.

12 Other ion sources exist that may be suitable for charging particles. For
13 example, it is possible to generate ions with X-rays or other ionizing radiation (e.g.
14 from a radioactive source). When particles are charged with an ion source, any means
15 for making available ions of both or either positive and negative polarity ions is meant
16 to be within the scope of the invention.

17 Another means for charging particles particularly applicable to liquid droplets
18 is described by Kelly in US Patent 4,255,777. In this approach, charged droplets are
19 formed by an electrostatic atomizing device. Although, the charge-to-mass ratio of
20 such particles cited by Kelly is not as high as can be achieved when charging particles
21 with an ion source, it is comparable to that achievable by triboelectric charging and
22 may be both preferable in some applications of the invention and is, in any case,
23 suitable for use with the present invention.

1 The above cited configurations are not meant to imply any limitations in
2 configuration. Rather they are meant to serve as examples of possible configurations
3 contemplated by the invention. Therefore, for example, although particle charging
4 with ion sources is shown and discussed wherein particles are charged within the
5 deposition zone, charging of particles with ion sources outside of the deposition zone
6 is also contemplated. All possible combinations of system configuration made
7 possible by the present disclosure are contemplated to be within the scope of the
8 invention.

9 The alternating deposition field preferably has a frequency between 1Hz and
10 10KHz, and most preferably, frequency between 10Hz and 1000Hz, and a magnitude
11 of between 1KV/cm and 10KV/cm. Other frequencies and magnitudes are possible,
12 depending upon the system configuration. For example, a higher deposition field
13 magnitude is possible, generally up to 30KV/cm - the breakdown potential of air and
14 other gases, but not preferred because it may lead to unexpected sparking. Lower
15 deposition field magnitudes are not preferred because the velocity of the aerosol
16 particles in response to the applied field becomes too low. Likewise, an alternating
17 frequency below 1Hz generally is not preferred for most applications because it is
18 anticipated that charge buildup on the dielectric substrate may substantially diminish
19 the magnitude of the deposition field over periods of a second or more. However,
20 there may be applications where this is not the case. Frequencies of 10KHz and
21 higher generally are not preferred because it is believed that the charged particles will
22 not have sufficient time to travel through the deposition zone and form the deposition.
23 However, for systems with very small deposition zones, this may not be a factor.

1 The waveform of the deposition field preferably is rectangular. However, it
2 has been found that triangular and sinusoidal waveforms also are effective in forming
3 deposits, although generally less so. The waveform has a duty cycle, which is defined
4 in terms of a preferred field direction. The duty cycle is the percentage of time that the
5 deposition field is in the preferred field direction. The preferred field direction either
6 may be positive or negative with respect to the deposition electrode depending upon
7 the characteristics of a particular system configuration. The duty cycle preferably is
8 greater than 50% and most preferably 90%. The preferred field direction is that
9 which maximizes the deposition rate.

10 As previously described, the deposition field is formed between a first
11 electrode and a second, deposition electrode. The first electrode may or may not be an
12 element of an ion emitter. In some configurations of the invention use of an ion
13 emitter in the deposition zone is advantageous in that it helps to discharge the
14 deposited charged particles thereby preventing the buildup of a field from the
15 deposited charged particles that repels the further deposition of particles from the
16 aerosol. This is particularly advantageous when the duty cycle is greater than 50%.
17 Of course, an ion emitter is required in the deposition zone if the aerosol particles are
18 to be charged within the deposition zone. However, it is also possible to control the
19 charging of the particles, synchronously with or asynchronously to the alternation of
20 the deposition field such that the buildup of a particle repelling field from the deposit
21 is minimized.

22 The dielectric substrate is closely proximate to and preferably in contact with
23 the deposition electrode. By closely proximate is meant that the separation between

1 the dielectric substrate and the deposition electrode is less than the thickness of the
2 dielectric substrate. In this way, the charged aerosol particles are directed to land on
3 the dielectric substrate in an area determined by the contact or closely proximate area
4 of the deposition electrode. Thus, it is possible to control the location and size of the
5 deposit.

6 The substrate for the deposit may consist of a dielectric material, such as vinyl
7 film, or an electrically conducting material such as aluminum foil. As previously
8 mentioned, as unipolar charged powder is deposited upon the surface of a dielectric, a
9 large electrical potential is formed which generates an electric field that opposes the
10 deposition field and deposition is thus self-limiting at rather low masses. If unipolar
11 charged powder is deposited on the surface of an electrical conductor, then again a
12 surface potential will be built up but of a lower magnitude than that of a
13 corresponding insulating substrate. The ratio of the surface voltage of a deposit on an
14 insulating layer to that of a deposit on the surface of a conducting layer is roughly
15 equal to ratio of the relative thickness of the dielectric plus the thickness of the
16 deposited powder and the thickness of the deposited powder layer. The use of
17 alternating deposition to form bipolar layers through the use of ac aerosol charging
18 and ac deposition fields allows larger masses to be deposited onto the surfaces of
19 conductors.

20 The dielectric substrate may be any material and have any structure suitable to
21 its other functions. For example, it may be a packaging medium, such as a tablet,
22 capsule or tablet, or the blister of a plastic or metal foil blister package. The dielectric
23 substrate may also be a pharmaceutical carrier, for example, a pill or capsule. It may

1 be any edible material, including chocolate. Alternatively, it may be simply a carrier
2 of the deposit for carrying it to another location for further processing.

3 We have found with the present invention that it is possible to deposit
4 substantially all of the aerosol particles that pass through the deposition zone under
5 conditions where the flow rate of the aerosol is below a maximum. This maximum
6 flow rate is determined primarily by the magnitude of the deposition field, the charge-
7 to-mass ratio of the charged particles, and their diameters. The capability to deposit
8 substantially all of the aerosol particles has been demonstrated for relatively large
9 mass deposits, much larger than is possible using prior art systems that
10 electrostatically create deposits. For example, we have deposited several milligrams
11 of lactose powder into a blister of a blister pack of 6mm diameter. A particular
12 advantage of the present invention is that there are no limits related to charge-to-mass
13 ratio of the charged particles nor the amount of charge laid down on a substrate as
14 there are with prior art systems. The use of an alternating deposition field enables
15 deposition of charge of either polarity on the combination of substrate and deposit,
16 whether the charge is carried by ions or charged particles. The net deposited charge
17 may be therefore neutralized if necessary. As such, the limits to the mass of the
18 deposit become mechanical in nature rather than electrical.

19 The ability to deposit substantially all of the aerosol particles that pass through
20 the deposition zone provides a new method for controlling the mass of the deposit. In
21 this method the mass flow of the aerosol particles that pass into and out of the
22 deposition zone is measured over time by means of sensors 60, 62 located upstream
23 and downstream of the deposition zone. The results could be recorded for

1 manufacturing control records and adjustments in flow rate; etc., made as need be to
2 maintain a desired deposition amount. As previously mentioned there are various
3 known means for measuring the velocity of an aerosol. In combination, these means
4 enable the measurement of the mass flow rate. The integration of the mass flow rate
5 over time gives the total mass. Accordingly, the mass of a deposit may be controlled
6 by measuring the mass flow of aerosol particles into the deposition zone and upon
7 reaching a desired deposit mass, removing the presence of the alternating deposition
8 field. In circumstances wherein a portion of the total aerosol is not deposited as it
9 passes through the deposition zone, a second measuring instrument may be positioned
10 immediately after the deposition zone. The difference between the two measurements
11 represents the total mass deposited from the aerosol as it passes the deposition zone.
12 The deposit may be controlled by removing the presence of the alternating deposition
13 field as described previously. Even in cases wherein substantially all of the aerosol
14 particles are deposited in the deposition area, the existence of a second measuring
15 instrument provides confirmation of the actual mass deposited, and is of particular
16 interest in applications where the reliability of the mass deposited is of commercial
17 interest such as pharmaceutical dosages. The mass of deposits formed by the present
18 invention is relatively larger than deposits that can be formed with prior art methods
19 that electrostatically create deposits. On the other hand, they may be much smaller
20 than masses conveniently created using prior art methods that mechanically weigh or
21 otherwise mechanically measure or control the mass. As such, the present invention
22 provides a unique means to address a hitherto unaddressed need.

1 The details of the invention may be further examined by considering FIG. 5.
2 Here, an aerosol generator 17 forms an air borne particle dispersion that is carried by
3 enclosed channel 19 to aerosol concentration monitoring station 21. Channel 23 then
4 carries the aerosol through a region where charging device 31 charges the powder. An
5 electrostatic field is provided between the charging device 31 and deposition electrode
6 25. Deposition electrode 25 corresponds to electrode 3 shown in FIG. 1. A dielectric
7 substrate 27 shown here as a blister pack pocket that collects charged particles
8 deflected by the electrostatic field. A second concentration monitoring station 29 is
9 employed to determine how much of the particles have been removed from the
10 aerosol. Under conditions whereby essentially all of the particles are removed from
11 the air stream, this second concentration monitor may not be required. The air stream
12 then moves into collector 30. This collector might consist of a filter or an electrostatic
13 precipitator or both. Alternately, the air may be recirculated through the aerosol
14 generator.

15 EXAMPLE

16 A filling device was set up according to the schematic of FIG. 6. The channel
17 was fabricated of 1/4-inch thick polycarbonate sheet. The channel width was 40-mm
18 and its height was 6-mm. A blister pack pocket, formed of 6-mil polyvinyl chloride,
19 having a depth of 4-mm and a diameter of 6-mm was supported on a circular electrode
20 25 having a diameter of 4-mm.

21 The charge source, consisting of glass core rod 43, spiral wire electrode 47 and
22 four glass coated wire 45 spaced at intervals around the periphery of the core rod, was

1 obtained from Delphax Systems, Canton, MA. Delphax customers employ these rods
2 in discharging (erasing) latent images on Delphax high-speed printer drums.

3 Spiral winding 47 was maintained at ground potential and glass coated
4 tungsten wire 45 was excited using 2300 volt peak-to-peak ac at a frequency of 120
5 kHz. A Trek high voltage amplifier was employed to provide square wave switching
6 of deposition electrode 25 at a frequency of 35 Hertz. The output voltage was
7 switched between +5kV and -5kV. The duty cycle was set so that negative charges
8 were extracted for 10% of the square wave period leaving positive charge extraction
9 to occur over 90% of the duty cycle.

10 An aerosol consisting of lactose powder, having a particle size in the range of
11 about 3 to about 7 microns, was suspended in a flowing stream of nitrogen gas. The
12 lactose was aerosolized by the turbulent action of pressurized nitrogen in a Wright
13 Dust Feed aerosolizer manufactured by BGI Inc., Waltham, MA. The aerosol
14 concentration was about 1 microgram/cm³ and the channel flow velocity was adjusted
15 to 30 cm/sec.

16 Charging and deposition potentials were applied for a period of two minutes
17 during aerosol flow. A well-defined mass of powder, measured and found to be 1 mg,
18 was formed at the bottom of the blister pack pocket. No powder deposition was found
19 at the blister pack walls or on the bottom of the channel.

20 Subsequent experimental runs established that the mass deposited was
21 proportional to the deposition time over the time intervals of ½ to 5 minutes.

22 With the present invention, it is also possible to multiplex the operation of two
23 or more deposition zones served from a single aerosol source by configuring

1 deposition zones along the aerosol path and selectively applying an alternating
2 deposition field at one deposition zone at a time. Aerosol particles passing into a
3 deposition zone where no alternating deposition field exists simply pass through the
4 deposition zone whereupon they can pass into a next deposition zone.

5 Although various embodiments which incorporate the teachings of the present
6 invention have been shown and described in detail herein, many other varied
7 embodiments that still incorporate these teachings may be made without departing
8 from the spirit and scope of the present invention. For example, the aerosol particles
9 may comprise carrier particles which may comprise inert substrates including
10 biocompatible metal particles coated with a bioactive agent.

11



1 1. A method for depositing particles from an aerosol onto a dielectric
2 substrate comprising the steps of charging said aerosol particles, positioning said
3 charged aerosol particles in a deposition zone proximate to said dielectric substrate,
4 and applying an alternating electric field in said deposition zone by which said
5 charged particles are removed from the aerosol and deposited on said dielectric
6 substrate thus forming a deposit.

7 2. The method according to claim 1, wherein said deposit has relatively
8 more mass than a deposit that can be formed using a static electric field.

9 3. The method according to claim 1, wherein said aerosol particles are
10 charged.

11 4. The method according to claim 1, wherein said aerosol particles
12 comprise particles of dry powder.

13 5. The method according to claim 1, wherein said aerosol particles
14 comprise liquid droplets.

15 6. The method according to claim 4, wherein said dry powder particles
16 are triboelectrically charged.

17 7. The method according to claim 5 wherein said liquid droplets are
18 charged by a charge injector during droplet formation.

19 8. The method according to claim 1, wherein said aerosol particles
20 comprise a pharmaceutical.

21 9. The method according to claim 4, wherein said dry powder particles
22 comprise carrier particles coated with a bioactive agent.



- 1 10. The method according to claim 3, wherein said aerosol particles have a
2 higher charge to mass ratio than is achievable using triboelectric charging.
- 3 11. The method according to claim 10, wherein said charged aerosol
4 particles achieve a relatively higher velocity than that achievable with triboelectrically
5 charged particles thereby forming said deposit more quickly.
- 6 12. The method according to claim 1, wherein said aerosol particles are
7 charged within said deposition zone.
- 8 13. The method according to claim 1, wherein said aerosol particles are
9 charged outside of said deposition zone.
- 10 14. The method according to claim 1, wherein said alternating electric field
11 has a magnitude between 1KV/cm and 30KV/cm.
- 12 15. The method according to claim 1, wherein the frequency of said
13 alternating electric field is between 1Hz and 100KHz.
- 14 16. The method according to claim 1, wherein the duty cycle of said
15 alternating field is substantially different than 50%.
- 16 17. The method according to claim 16, wherein said duty cycle is 90%.
- 17 18. The method according to claim 1, wherein said alternating electric field
18 is formed between a first electrode positioned at an end of said deposition zone
19 opposite to and facing said dielectric substrate and a second electrode in contact with
20 said dielectric substrate on the opposite side of where said deposit is formed.
- 21 19. The method according to claim 18, wherein said first electrode is an
22 element of an ion emitter.

- 1 20. The method according to claim 19, wherein said aerosol particles are
2 discharged after being deposited.
- 3 21. The method according to claim 18, wherein the contact area of said
4 second electrode with said dielectric substrate determines the location of said
5 deposition.
- 6 22. The method according to claim 1, wherein substantially all of said
7 aerosol particles are removed from said aerosol to form said deposit.
- 8 23. The method according to claim 1, wherein the gas of said aerosol is
9 predetermined.
- 10 24. The method according to claim 1, wherein said dielectric substrate
11 comprises a packaging medium.
- 12 25. The method according to claim 24, wherein said packaging medium
13 comprises a blister, tablet, capsule or tublet.
- 14 26. The method according to claim 25, wherein the blister comprises a
15 plastic or metal foil blister package.
- 16 27. The method according to claim 1, wherein said dielectric substrate
17 comprises a pharmaceutical carrier.
- 18 28. The method according to claim 1, wherein said dielectric substrate
19 comprises a carrier for carrying said deposit from said deposition zone to another
20 location for further processing.
- 21 29. The method according to claim 1, wherein said dielectric substrate is
22 edible.



1 30. The method according to claim 3, wherein said ion emitter comprises a
2 corona wire or corona point.

3 31. The method according to claim 3, wherein said ion emitter comprises a
4 silent electric discharge device.

5 32. The method according to claim 3, wherein said ion emitter comprises
6 an ionizing radiation source.

7 33. The method according to claim 12, wherein said aerosol particles are
8 charged by an ion emitter.

9 34. The method according to claim 22, wherein the mass of said deposit is
10 controlled by integrating the mass of said aerosol particles over a period of time.

11 35. The method according to claim 34, wherein said period of time is
12 determined by the measured mass of said aerosol particles.

13 36. The method according to claim 22, wherein multiple deposits may be
14 made using multiple deposition zones supplied from a single aerosol source by
15 multiplexing the application of the alternating deposition field between the deposition
16 zones.

17 37. A controlled quantity of powder carried on a substrate, comprising a
18 plurality of layers of said powder in which adjacent layers carry opposite charges.

19 38. A controlled quantity according to claim 37, wherein said powder
20 comprises a pharmaceutical.

21 39. A controlled quantity according to claim 37, wherein said substrate
22 comprises a packaging medium.



- 1 40. A controlled quantity according to claim 39, wherein said packaging
2 medium comprises a blister, tablet, capsule or tablet.
- 3 41. A controlled quantity according to claim 40, wherein said blister
4 comprises a plastic or metal foil blister package.
- 5 42. An apparatus for depositing onto a substrate controlled quantities of
6 particulate material from a source of said material, said apparatus comprising a charge
7 generator for applying a predetermined electrostatic charge to particles of said
8 material upstream of a deposition zone in which said substrate is located, and a
9 controller for repeatedly varying the polarity of charge being applied to said material
10 and to said substrate.
- 11 43. The apparatus according to claim 42, wherein the controller comprises
12 a switch oscillator.
- 13 44. The apparatus according to claim 42, wherein the controller includes a
14 clock for varying the polarity of charge over time.
- 15 45. The apparatus according to claim 42, wherein said controller is adapted
16 to switch polarity applied to said powder and to said substrate in synchronization.
- 17 46. The apparatus according to claim 42, and including sensors for
18 measuring the mass flow of aerosol particles that pass into and out of the deposition
19 zone.
- 20 47. A method for depositing particles from an aerosol onto a substrate that
21 comprises moving an aerosol through a deposition region, providing means for
22 electrically charging said particles, and providing an alternating electric field between



1 said substrate and said aerosol particles whereby said particles are deposited on the
2 surface of said substrate.

3 48. The method according to claim 47, wherein said particles are solid.

4 49. The method according to claim 47, wherein said particles are liquid.

5 50. The method according to claim 47, wherein said particles comprise
6 carrier particles coated with a bioactive agent.

7 51. The method according to claim 47, wherein said particles comprise a
8 pharmaceutical.

9 52. The method according to claim 47, wherein said aerosol carrier is
10 nitrogen gas.

11 53. The method according to claim 47, wherein said substrate comprises a
12 blister pack.

13 54. The method according to claim 47, wherein said substrate is
14 comprised of an electrically insulating material.

15 55. The method according to claim 47, wherein said substrate is comprised
16 of an electrically conducting material.

17 56. The method according to claim 47, wherein said electrically charging
18 means employs a corona wire.

19 57. The method according to claim 47, wherein said electrically charging
20 means employs corona emitting points.

21 58. The method according to claim 1, wherein said electrically charging
22 means includes a charge source comprising a solid dielectric member, a first electrode
23 substantially in contact with one side of said solid dielectric member, a second



1 electrode substantially in contact with an opposite side of said solid dielectric
2 member, with an edge surface of said second electrode disposed opposite said first
3 electrode to define an air region at the junction of said edge surface and said solid
4 dielectric member, and means for applying an alternating potential between said first
5 and second electrodes of sufficient magnitude to induce ion producing electrical
6 discharges in the air region between the dielectric member and the edge surface of
7 said second electrode.

8 59. The method according to claim 47, wherein said electrically charging
9 means includes triboelectric charging of said aerosol particles.

10 60. The method according to claim 47, wherein said electrically charging
11 means includes induction charging of said aerosol particles.

12 61. The method according to claim 47, wherein said aerosol particles are
13 charged outside of said deposition region.

14 62. The method according to claim 47, wherein said aerosol particles are
15 charged within said deposition region.

16 63. The method according to claim 47, wherein said electrically alternating
17 field has a magnitude between about 1 kV/cm and about 30 kV/cm.

18 64. The method according to claim 47, wherein said electrically alternating
19 field has a frequency of oscillation between about 1 Hz and 100 kHz.

20 65. The method according to claim 47, wherein the duty cycle of the
21 alternating field is adjusted to provide maximum efficiency of said particle deposition.

22 66. The method according to claim 47, wherein said electrically alternating
23 field is formed between a first electrode positioned at one side of said deposition



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1 region opposite and facing said substrate and a second electrode contiguous to said
2 substrate.

3 67. The method according to claim 47, wherein the pattern of deposited
4 material is defined by the geometry of said alternating electric field.

5 68. The method according to claim 47, wherein the pattern of deposited
6 material is defined by an electrically conducting mask disposed adjacent said charging
7 means.

8 69. The method according to claim 47, wherein the aerosol particle mass
9 flow is monitored whereby the mass of deposited particles is controlled.

10 70. The method according to claim 47, wherein multiple deposits may be
11 made using multiple deposition regions supplied from a single aerosol source by
12 multiplexing the application of the alternating deposition field between the deposition
13 regions.

14 71. A pharmaceutical unit dose medicament powder package wherein the
15 powder is deposited using electrostatic means to form alternately charged layers of
16 said powder.

17 72. The package of claim 71, wherein said electrostatic means includes
18 moving an aerosol through a deposition region, providing means for electrically
19 charging said medicament powder, and providing an alternating electric field between
20 said powder package and said aerosol.

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