may be hollow or circuited so as to allow a cryogen to be introduced into the interior of the drum and to come into thermal contact with the outer surface. The drum is rotatably mounted on an axle or frame so that the drum is rotatable along its longitudinal axis in at least one direction.

[0009] As noted above, the system further includes a cryogenic component for chilling the cavities and the outers surface of the drum to a desired temperature, particularly a temperature suited for freezing the portions of liquid formulation deposited in the cavities. In some embodiments, the cryogenic component is designed to establish thermal contact between a cryogen and the outer surface. For example, the cryogenic component may deliver a cryogen to the interior of the drum such that the cryogen comes into thermal contact with the material of the outer surface via contact with interior surfaces of the drum. In some cases, the thermal contact may be indirect, such as through an intervening heat transfer fluid.

[0010] The system may further comprise a mechanism for rotating the drum during dispensing of liquid formulation. In various embodiments, said mechanism includes a motor for rotating the drum through operable connection to an axle extending through the longitudinal axis of the drum. The motor may be any suitable motor, such as a variable speed motor, and the mechanism may further include a controller for setting and/or adjusting the speed of rotation as desired.

[0010a] In some embodiments, a system for bulk manufacture of unit dosage forms comprises a drum frame having a first support structure and a second support structure; a drum coupled to the first support structure and the second support structure. The drum rotatable relative to the drum frame about a rotational axis, the drum having an outer surface with a plurality of cavities formed thereon. The system further comprises a dispenser operable to dispense a liquid formulation comprising a therapeutic or biotherapeutic agent into one or more of the plurality of cavities on the outer surface of the drum; a cryogenic component for chilling the outer surface of the drum to a target temperature capable of freezing the liquid formulation within the one or more of the plurality of cavities to form a frozen unit in the one or more of the plurality of cavities; a collection tray positioned relative to the drum to collect the one or more frozen units from the one or more of the plurality of cavities; and a dryer for drying the one or more frozen units to yield solid unit dosage forms.

[0011] In some embodiments, a method for bulk manufacture of unit dosage forms may comprise depositing a liquid formulation comprising a therapeutic agent on an outer surface of a rotatable drum or, more particularly, into defined cavities featured in the outer surface of the drum. The outer surface is chilled to an extremely low temperature, such as by exposing

the interior of the drum to a cryogenic medium, thereby providing for rapid freezing of the dispensed liquid contained within the cavities of the outer surface of the drum. The method may further comprise rotating the drum so that the deposited liquid formulation is carried through at least a portion of the rotation of the drum while in contact with its outer surface to facilitate freezing of the dispensed portions into frozen units. The method may further comprise collecting each frozen unit or a plurality thereof and drying each unit to yield a unit dosage form having a low water activity level.

[0011a] In some embodiments, a method for bulk manufacture of unit dosage forms may comprise rotating a drum around a rotational axis at a rotational speed, the drum having an outer surface with a plurality of cavities formed thereon; chilling the outer surface of the drum to a target temperature; dispensing a liquid formulation comprising a therapeutic or biotherapeutic agent into one or more of the plurality of cavities while rotating the drum about its rotational axis; freezing the liquid formulation within the one or more of the plurality of cavities to form a frozen unit in the one or more of the plurality of cavities; collecting the frozen units from the one or more of the plurality of cavities; and drying the collected frozen units to form the unit dosage forms.

[0011b] In some embodiments, a liquid formulation for preparing solid unit dosage forms comprises a therapeutic or biotherapeutic agent; a cryopreservative; a lyopreservative; and one or more excipients. The agent is homogeneously distributed throughout the liquid formulation.

[0012] As further described in detail herein, use of rapid freezing processes is important to biologic stabilization for lyophilization/freeze-drying. The controlled volumetric delivery associated with the systems and methods described herein provide rapid freezing of a controlled biological efficacious dose (e.g., probiotic stabilization) to maintain both physical shape/volume of the manufactured dosage form and its biological efficacy. Certain