

ARTICLE COMPRISING A MICRONEEDLE**CROSS REFERENCE TO RELATED APPLICATIONS**

5 **[0001]** This application claims priority to U.S. Provisional Patent Application No. 61/846,909, filed July 16, 2013, the disclosure of which is incorporated by reference in its entirety herein.

BACKGROUND

10 **[0002]** Transdermal and topical drug delivery can be used for therapeutic treatment, but the number of molecules that can be effectively delivered using these routes can be limited by the barrier properties of skin. The main barrier to transport of molecules through the skin is the stratum corneum (the outermost layer of the skin).

15 **[0003]** A number of different skin treatment methods have been proposed in order to increase the permeability or porosity of the outermost skin layers, such as the stratum corneum, thus enhancing drug delivery through or into those layers. The stratum corneum is a complex structure of compact keratinized cell remnants separated by lipid domains. The stratum corneum is formed of keratinocytes, which comprise the majority of epidermal cells that lose their nuclei and become corneocytes. These dead cells comprise the stratum corneum, which has a thickness of only about 10-30 microns and protects the body from invasion by exogenous substances and the outward migration of endogenous fluids and dissolved molecules. Various skin treatment methods include the use of microneedles, laser ablation, RF ablation, heat ablation, sonophoresis, iontophoresis, or a combination thereof.

20 **[0004]** Devices including arrays of relatively small structures, sometimes referred to as microneedles or micro-pins, have been disclosed for use in connection with the delivery of therapeutic agents and other substances through the skin and other surfaces. The devices are typically pressed against the skin in an effort to pierce the stratum corneum such that the therapeutic agents and other substances can sequentially or simultaneously pass through that layer and into the tissues below. Microneedles of these devices pierce the stratum corneum upon contact, making a plurality of microscopic slits which serve as passageways through which molecules of active components can be delivered into the body. In delivering an active component, the microneedle device can be provided with a reservoir for temporarily retaining an active component in liquid form prior to delivering the active component through the stratum corneum. In some constructions, the microneedles can be hollow to provide a liquid flow path directly from the reservoir and through the microneedles to enable delivery of the therapeutic substance through the skin. In alternate constructions, active component(s) may be

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coated on the microneedle array and delivered directly through the skin after the stratum corneum has been punctured.

[0005] Microneedle arrays can be used in conjunction with an applicator device capable of being used several times or as a single-use device. The microneedle arrays are generally used once and then discarded.

SUMMARY

[0006] It has now been found that an interaction between an article comprising a plurality of hollow microneedles and a skin surface against which the article is urged can result in undesirable effects on the penetration of at least one microneedle of the plurality into the skin. It has further been found that, when the article comprises an array of microneedles, one of the effects can be significant variability in the depth of penetration into the skin by one or more of the microneedles in the array. The present inventors recognized the consistency of penetration depth can be controlled by including several features into the design of the article. The inventive design features result in the ability to effectively and consistently insert the needles to a desired depth in the skin. In addition, certain features of the inventive design permit simpler, more robust processes to be used for the manufacture of the articles.

[0007] The present disclosure generally relates to articles comprising microneedles and their use to deliver materials through the surface of skin or remove biological fluids through the surface of skin. In particular, the present disclosure relates to an article comprising an array of a plurality of microneedles that is configured to provide consistent depths of penetration for each microneedle of the plurality of microneedles by facilitating the contact between microneedles and skin and by reducing the possibility of contact between skin and non-microneedle surfaces during the use of the articles.

[0008] Some aspects of the present disclosure provide an article. The article can comprise a first side, a second side opposite the first side, and at least three hollow microneedles. The first side can comprise a central cavity portion and a platform portion that projects from the first side and that is not coplanar with the central cavity portion. The microneedles can extend from the platform portion in a first direction. The platform portion can substantially surround the central cavity portion and can comprise an inner perimeter proximate the central cavity portion and an outer perimeter distal the central cavity portion. Each of the at least three microneedles comprises a body that comprises an outer surface; a base segment having a base and a first shape that is defined by a first section of the outer surface; a tip segment having a tip and a second shape that is defined by a second section of the outer surface, wherein the second shape is distinct from the first shape; a transition plane that delineates the base segment and the tip segment; and a central axis. A first angle, defined by the central axis of each of the at least

three microneedles and a shortest line extending from the outer perimeter of the platform and through the transition plane of the at least one microneedle, is less than about 50°.

[0009] Other aspects of the present disclosure provide an article. The article can comprise a first side, a second side opposite the first side, and at least three hollow microneedles. The first side can comprise a central cavity portion and a platform portion that projects from the first side and that is not coplanar with the central cavity portion. The microneedles can extend from the platform portion in a first direction. The platform portion can substantially surround the central cavity portion and can comprise an inner perimeter proximate the central cavity portion and an outer perimeter distal the central cavity portion. Each of the at least three microneedles comprises a body that comprises an outer surface; a base segment having a base and a first shape that is defined by a first section of the outer surface; a tip segment having a tip and a second shape that is defined by a second section of the outer surface, wherein the second shape is distinct from the first shape; a transition plane that delineates the base segment and the tip segment; and a central axis. Each of the at least three microneedles comprises a height measured from the base to the tip. The tip segment of each of the at least three microneedles can define at least about 30% of the height of the microneedle.

[0010] Other aspects of the present disclosure provide an article. The article can comprise a first side, a second side opposite the first side, and at least three hollow microneedles. The first side can comprise a central cavity portion and a platform portion that projects from the first side and that is not coplanar with the central cavity portion. Each of the at least three microneedles can extend from the platform portion in a first direction. The platform portion can substantially surround the central cavity portion and can comprise an inner perimeter proximate the central cavity portion and an outer perimeter distal the central cavity portion. Each of the at least three microneedles comprises a body that comprises an outer surface; a base segment having a base and a first shape that is defined by a first section of the outer surface; a tip segment having a tip and a second shape that is defined by a second section of the outer surface, wherein the second shape is distinct from the first shape; a transition plane that delineates the base segment and the tip segment; and a central axis. The first side defines a first area and the platform portion defines a second area within the first area. The second area can be less than about 40% of the first area.

[0011] The phrase “injection apparatus” refers to an integrated device capable of delivering or extracting a fluid over a certain period and is not limited to devices intended solely for an infusion. Accordingly, an injection apparatus may be used, for example, for injecting fluid into the dermis or extracting fluid from tissue.

[0012] The term “transdermally” and variations thereof, is generally used to refer to any type of delivery of an active ingredient that crosses any portion of skin. That is, transdermally can

generally include systemic delivery (i.e., where the active ingredient is transported across, or substantially through, the dermis such that the active ingredient is delivered into the bloodstream), as well as intradermal delivery (i.e., where the active ingredient is transported partially through the dermis, e.g., across the outer layer (stratum corneum) of the skin, where the active ingredient is delivered into the skin, e.g., for treating psoriasis or for local anesthetic delivery). That is, transdermal delivery as used herein includes delivery of an active ingredient that is transported across at least a portion of skin (but not necessarily all of the layers of skin), rather than merely being topically applied to an outer layer of the skin.

[0013] The phrase “hollow microneedle” refers to a specific microscopic structure that is designed for piercing the stratum corneum to facilitate the delivery of drugs through the skin. By way of example, microneedles can include needle or needle-like structures, as well as other structures capable of piercing the stratum corneum and delivering liquid drug formulations to skin or tissue layers beneath the stratum corneum.

[0014] The words “preferred” and “preferably” refer to embodiments of the invention that may afford certain benefits, under certain circumstances. However, other embodiments may also be preferred, under the same or other circumstances. Furthermore, the recitation of one or more preferred embodiments does not imply that other embodiments are not useful, and is not intended to exclude other embodiments from the scope of the invention.

[0015] The terms “comprises” and variations thereof do not have a limiting meaning where these terms appear in the description and claims.

[0016] As used herein, “a,” “an,” “the,” “at least one,” and “one or more” are used interchangeably. Thus, for example, a microneedle can be interpreted to mean “one or more” microneedles.

[0017] The term “and/or” means one or all of the listed elements or a combination of any two or more of the listed elements.

[0018] Also herein, the recitations of numerical ranges by endpoints include all numbers subsumed within that range (e.g., 1 to 5 includes 1, 1.5, 2, 2.75, 3, 3.80, 4, 5, etc.).

[0019] The above summary of the present invention is not intended to describe each disclosed embodiment or every implementation of the present invention. The description that follows more particularly exemplifies illustrative embodiments. In several places throughout the application, guidance is provided through lists of examples, which examples can be used in various combinations. In each instance, the recited list serves only as a representative group and should not be interpreted as an exclusive list.

[0020] Additional details of these and other embodiments are set forth in the accompanying drawings and the description below. Other features, objects and advantages will become apparent from the description and drawings, and from the claims.

BRIEF DESCRIPTION OF DRAWINGS

[0021] The present invention will be further explained with reference to the drawing figures listed below, where like structure is referenced by like numerals throughout the several views.

5 [0022] FIG. 1 is a perspective view showing one embodiment of an article comprising a plurality of microneedles according to the present disclosure.

[0023] FIG. 2 is a side view of the article of FIG. 1.

[0024] FIG. 2A is a detail view of a portion of the article of FIG. 2.

[0025] Fig. 3 is a plan view of the first side of the article of FIG. 1.

10 [0026] FIG. 4 is a cross-sectional view, taken along line 4—4, of the article of FIG. 3.

[0027] FIG. 4A is a detailed cross-sectional view of one of the hollow microneedles of FIG. 4.

[0028] FIG. 5A is a schematic side view, partially in section, of a portion of the article of FIG. 1, showing an angle θ_1 formed by the intersection of a central axis of a microneedle with a line passing through a transition plane in the microneedle.

15 [0029] FIG. 5B is a schematic side view, partially in section, of the article of FIG. 5A, showing an angle θ_2 formed by the intersection of a central axis of a microneedle with a line passing through a transition plane in the microneedle.

[0030] FIG. 6 is a schematic side view, partially in section, of a portion of another embodiment of an article comprising a microneedle, showing an angle θ_3 formed by the intersection of a central axis of a microneedle with a line passing through a transition plane in the microneedle.

[0031] FIGS. 7A-7D show a progression of schematic side views of a microneedle of an article according to the present disclosure as the microneedle penetrates a skin surface.

25 [0032] FIG. 8 is a schematic side view of a microneedle of another article as the microneedle penetrates a skin surface.

[0033] FIG. 9 is a schematic side view of an article, comprising an array of microneedles, as the array of microneedles penetrate a skin surface.

[0034] FIG. 10 is a plan view of an article according to the present disclosure; showing areas defined on the first side of the article.

30 [0035] FIG. 11 is a plan view of an applicator coupled to an article comprising a plurality of microneedles according to the present disclosure; showing various dimensions associated with the article and the applicator.

DETAILED DESCRIPTION

[0036] Before any embodiments of the present disclosure are explained in detail, it is to be understood that the invention is not limited in its application to the details of construction and the arrangement of components set forth in the following description or illustrated in the following drawings. The invention is capable of other embodiments and of being practiced or of being carried out in various ways. Also, it is to be understood that the phraseology and terminology used herein is for the purpose of description and should not be regarded as limiting. The use of “including,” “comprising,” or “having” and variations thereof herein is meant to encompass the items listed thereafter and equivalents thereof as well as additional items. Unless specified or limited otherwise, the terms “mounted,” “connected,” “supported,” and “coupled” and variations thereof are used broadly and encompass both direct and indirect mountings, connections, supports, and couplings. It is to be understood that other embodiments may be utilized, and structural or logical changes may be made without departing from the scope of the present disclosure. Furthermore, terms such as “front,” “rear,” “top,” “bottom,” and the like are only used to describe elements as they relate to one another, but are in no way meant to recite specific orientations of the apparatus, to indicate or imply necessary or required orientations of the apparatus, or to specify how the invention described herein will be used, mounted, displayed, or positioned in use.

[0037] The present disclosure generally relates to articles comprising microneedles and their use to deliver materials through the surface of skin or remove biological fluids through the surface of skin. In particular, the present disclosure relates to an article comprising an array of a plurality of microneedles that is configured to provide consistent depths of penetration for each microneedle of the plurality of microneedles by facilitating the contact between microneedles and skin and by reducing the possibility of contact between skin and non-microneedle surfaces during the use of the articles.

[0038] Turning to the drawings, FIGS. 1-4 show various views of one embodiment of an article 100 according to the present disclosure. The article 100 comprises a first side 112 and a second side 114 opposite the first side 112. The first side 112 comprises a central cavity portion 120 and a platform portion 130. The platform portion 130 projects from the first side 112 and is not coplanar with the central cavity portion 120. In the illustrated embodiment of FIGS. 1-4, the central cavity portion 120 and platform portion 130 are both formed as portions of a unitary body 110. However, in any embodiment, it is contemplated that the central cavity portion 120 and platform portion 130 may be separate parts (not shown) that are disposed adjacent each other in the article.

[0039] The central cavity portion 120 is not coplanar with the platform portion 130. Although the illustrated embodiment of FIGS. 1-4 depict the central cavity portion 120 having

a curvilinear surface that slopes away from the plane formed by the platform portion 130, it is contemplated that, in any embodiment, the central cavity portion may comprise one or more angular surfaces (not shown) that are not coplanar with the platform portion.

5 [0040] In any embodiment, the central cavity portion 120 may consist of a solid structure, as shown in FIGS. 1-4. Advantageously, if the article is produced as a unitary molded part, as shown in the illustrated embodiment,. Alternatively, in any embodiment, the central cavity portion may comprise, consist essentially of, or consist of an opening (e.g., a through-hole, not shown).

10 [0041] The platform portion 130 substantially surrounds the central cavity portion 120. The platform portion 130 comprises an inner perimeter 132 proximate the central cavity portion 120 and an outer perimeter 134 distal the central cavity portion. In any embodiment, the inner perimeter 132 and/or outer perimeter 134 comprise a substantially rounded edge, as shown in the side view of the outer perimeter in FIG. 2 and as shown in the cross-sectional view of both perimeters of FIG. 4. Alternatively, in any embodiment, the inner perimeter 132 and/or outer
15 perimeter 134 comprise a substantially angular edge (not shown).

[0042] The article 100 further comprises a plurality of hollow microneedles 160 extending from the platform portion 130 in a first direction (see arrow "A", FIG. 2). In any embodiment, the plurality of hollow microneedles 160 can comprise an array. The array can comprise a circular arrangement (i.e., a circinate array), as shown in FIG. 3. It is contemplated that other
20 arrays, having other rectilinear or curvilinear geometric shapes (e.g., a square, a rectangle, an oval, a hexagon; not shown) are also useful in an article according to the present disclosure.

[0043] FIG. 2A shows a detail view of one of the microneedles 160 of the article 100 of FIG. 2. In any embodiment of the article 100, each microneedle 160 of the plurality comprises a body that comprises an outer surface 163, a base segment 166, and a tip segment 168. The
25 base segment 166 comprises a base 162 where the microneedle 160 extends from the platform portion 130. The base segment 166 has a first shape that is defined by the outer surface 163 of the base segment. In the illustrated embodiment of FIG. 2A, the first shape is crateriform (i.e., a generally-conical shape with a radius of curvature) and, thus, the diameter of the microneedle is wider at the base 162 than at the tip. Optionally, the base segment 166 has a concave outer
30 surface.

[0044] The tip segment 168 comprises a tip 164. The tip 164 is the part of the microneedle 160 that is furthest away from the base 162. The tip segment 168 has a second shape that is defined by the outer surface 163 of the microneedle 160. The second shape is distinguishable from the first shape. The respective shapes of the base segment 166 and the tip segment 168
35 become distinguishable at a transition plane 167. "Transition plane", as used herein is the plane where an angle formed by a tangent of the outer surface 163 of the microneedle and the central

axis changes from a first (tip-proximal) angle of $\leq 10^\circ$ to a second (tip-distal) angle of greater than about 10° . In the illustrated embodiment of FIG. 3A, the outer surface 163 of the microneedle 160 is substantially parallel to the central axis (not shown). However, at the transition plane 167, the substantially straight outer surface of the tip segment 168 (i.e. second shape) changes to a flared radius of curvature of the base segment 166 (i.e. first shape) and the angle formed by the intersection of a tangent (not shown) of the outer surface and the central axis (not shown) becomes greater than about 10° . The substantially cylindrically-shaped tip segment 168 of FIG. 2A is truncated by a bevel 165 that forms a tip 164 that is sharp enough to pierce stratum corneum.

[0045] Each microneedle 160 of the plurality further comprises a hollow channel 169. The hollow channel 169 optionally extends all the way through the article from the first surface 112 through the second surface 114, as shown in FIG. 4. In any embodiment, the hollow channel can provide a dead-end reservoir (e.g., a dead-end reservoir in the body of the microneedle, not shown) in which to load an active ingredient for injection/delivery into the skin, for example. In any embodiment, a hollow channel 169 extending through the article 100 can be fluidically connected to a reservoir 108 disposed on the second side of the article and an active ingredient can be infused into a patient from the reservoir 108 of the article 100 and through the hollow channel 169 of the microneedle 160.

[0046] In any embodiment, the first side 112 optionally comprises a microneedle-free peripheral portion 140 extending laterally from at least a part of the outer perimeter 134 of the platform portion 130. In any embodiment, the peripheral portion 140 substantially surrounds the platform portion 130. The peripheral portion 140 is canted away from the platform portion 130 in a second direction (see arrow "B", FIG. 2) opposite the first direction. In the illustrated embodiment of FIGS. 1-4, the central cavity portion 120, the platform portion 130, and the peripheral portion 140 are all formed as portions of a unitary body 110. However, in any embodiment, it is contemplated that the peripheral portion 140 and platform portion 130 may be separate parts (not shown) that are disposed adjacent each other in the article.

[0047] FIG. 4A shows a detail view of one of the sectioned microneedles 160 disposed on the first side 112 of the article the unitary body 110 of FIG. 4. The microneedle 160 comprises a first opening 187 that opens proximate the tip 164 into a hollow channel 169 that extends all the way through the body 110 to a second opening 189 on the second side 112 of the body 110.

[0048] Optionally, in any embodiment, the article 100 further may comprise a tab (e.g., tab 106). The tab 106 may be useful for manufacturing purposes or for alignment purposes during use. In the illustrated embodiment, the tab 106 extends laterally from the peripheral portion 140; however other useful configurations will be apparent to a person having ordinary skill in the art.

[0049] Optionally, the article 100 further comprises a sidewall 150 extending substantially in the direction (i.e., second direction “B” shown in FIG. 2) opposite the plurality of microneedles 160. The side wall 150 of the illustrated embodiment forms a reservoir 108 on the second side 114 of the article 100. The reservoir 108 optionally can be sealed (not shown) and can contain an active agent (e.g., a drug) to be delivered by injection via the plurality of microneedles 160.

[0050] Referring to FIG. 2, the article can comprise at least two height dimensions. The first height dimension H_1 is the height of the canted peripheral portion 140 extending in the second direction B from the platform portion 130. The second height dimension H_2 is the height of each microneedle 160 extending in the first direction A from the platform portion 130.

Referring back to FIG. 2A, each microneedle 160 of the plurality comprises two height components (first height component H_{2A} and second height component H_{2B} , respectively) that contribute to the total height of the microneedle 160. The first height component represents the height of the base segment 166 of the microneedle 160 and the second height component represents the height of the tip segment 168 of the microneedle. In any embodiment, the second height component of each microneedle of the plurality according to the present disclosure is about 300 μm to about 1000 μm . In any embodiment, the second height component of each microneedle of the plurality according to the present disclosure is about 650 μm to about 800 μm . In any embodiment first and second height components in combination. In order to get consistent and effective delivery of an active compound to the proper location in the skin, the inventors have found that the configuration of an article comprising at least three microneedles according to the present disclosure should facilitate penetration of all of the at least three microneedles until at least the tip portion of each microneedle is fully inserted into the skin.

[0051] In one aspect, in any embodiment, there may exist a predefined proportional relationship between first height component and the second height component of each microneedle of the plurality in an article according to the present disclosure. In any embodiment, the tip segment (as measured from the transition plane to the tip of at least one microneedle of the plurality of microneedles) defines at least about 30% of the height of the at least one microneedle. In any embodiment, the tip segment (as measured from the transition plane to the tip of each microneedle of the plurality of microneedles) defines at least about 30% of the height of the microneedles. In any embodiment, the tip segment (as measured from the transition plane to the tip of at least one microneedle of the plurality of microneedles) defines at least about 40% of the height of the at least one microneedle. In any embodiment, the tip segment (as measured from the transition plane to the tip of each microneedle of the plurality of microneedles) defines at least about 40% of the height of the microneedles. In any

embodiment, the tip segment (as measured from the transition plane to the tip of at least one microneedle of the plurality of microneedles) defines at least about 50% of the height of the at least one microneedle. In any embodiment, the tip segment (as measured from the transition plane to the tip of each microneedle of the plurality of microneedles) defines at least about 50% of the height of the microneedles. In any embodiment, the tip segment (as measured from the transition plane to the tip of at least one microneedle of the plurality of microneedles) defines up to about 70% (inclusive) of the height of the at least one microneedle. In any embodiment, the tip segment (as measured from the transition plane to the tip of each microneedle of the plurality of microneedles) defines up to about 70% (inclusive) of the height of the microneedles.

[0052] In any embodiment, each microneedle 160 of the plurality of microneedles in an article of the present disclosure comprises a central axis 180 as shown in FIGS. 5A, 5B, and 6. The central axis 180 also represents a longitudinal axis of the microneedle 160 extending through the microneedle from the base 162 toward the tip 164. In one aspect, each microneedle 160 of the plurality may have a spatial relationship between a structural feature (i.e., the microneedle transition plane 167) of the microneedle 160 and one or more of the perimeters (i.e., inner perimeter 132 and outer perimeter 134) of the platform portion 130, as illustrated in FIGS. 5A-B.

[0053] In another aspect, in any embodiment, there may exist a spatial relationship between each microneedle of the plurality and the outer perimeter of the platform on which the microneedle projects in an article according to the present disclosure. FIG. 5A shows a schematic view of a section of an article comprising a plurality of microneedles according to the present disclosure. The article comprises a first side 112 having a central cavity portion 120, a platform portion 130, a canted peripheral portion 140, and an outer perimeter 134 disposed between the platform portion 130 and the peripheral portion 140, as described above. Extending from the platform portion 130 is a microneedle 160. The microneedle 160 comprises a base segment 166 with a first shape and a tip segment 168 with a second shape, the segments being separated by a transition line 167. Also shown in FIG. 5A is the central axis 180 of the microneedle 160 and a shortest line 184 extending from the outer perimeter 134, through the closest point 185 of the transition plane 167 to the outer perimeter 134, to the central axis 180. The intersection of the shortest line 184 with the central axis 180 forms an angle θ_1 . In any embodiment of the article of the present disclosure the angle θ_1 is less than about 50°. In any embodiment, the angle θ_1 is less than about 45°. In any embodiment, the angle θ_1 is less than about 40°. In any embodiment, the angle θ_1 is less than about 35°. In any embodiment, the angle θ_1 is less than about 30°. In any embodiment, the angle θ_1 is less than about 25°. In any embodiment, the angle θ_1 is at least about 10°. A person having ordinary

skill in the art will appreciate that, as the angle θ_1 decreases, the amount of potential area of platform portion between the microneedle and the outer perimeter also decreases. The significance of this relationship is discussed below.

[0054] Alternatively, or additionally, there may exist a spatial relationship between the each
5 microneedle of the plurality and the inner perimeter of the platform on which the microneedle projects. FIG. 5B shows a similar schematic view of the section of the article shown in FIG. 5A. The article comprises a first side 112 having a central cavity portion 120, a platform portion 130, a canted peripheral portion 140, and an inner perimeter 132 disposed between the platform portion 130 and the peripheral portion 140, as described above. Extending from the
10 platform portion 130 is a microneedle 160. The microneedle 160 comprises a base segment 166 with a first shape and a tip segment 168 with a second shape, the segments being separated by a transition line 167. Also shown in FIG. 5B is the central axis 180 of the microneedle 160 and a shortest line 182 extending from the inner perimeter 132, through the closest point 183 of the transition plane 167 to the inner perimeter 132, to the central axis 180. The intersection of
15 the shortest line 182 with the central axis 180 forms an angle θ_2 . In any embodiment of the article of the present disclosure the angle θ_2 is less than about 50° . In any embodiment, the angle θ_2 is less than about 45° . In any embodiment, the angle θ_2 is less than about 40° . In any embodiment, the angle θ_2 is less than about 35° . In any embodiment, the angle θ_2 is less than about 30° . In any embodiment, the angle θ_2 is less than about 25° . In any embodiment, the
20 angle θ_1 is at least about 10° . A person having ordinary skill in the art will appreciate that, as the angle θ_2 decreases, the amount of potential area of platform portion between the microneedle and the inner perimeter also decreases. The significance of this relationship is discussed below.

[0055] The spatial relationships discussed above may apply regardless of the first and
25 second shapes defined by the base segment and the tip segment of each microneedle of the plurality. FIG. 6 shows a schematic view of a section of an article comprising a plurality of microneedles similar to that shown in FIG. 5A except the base segment 166 has a first shape that defines a truncated pyramid or truncated cone shape, rather than a crateriform shape. The article comprises a first side 112 having a central cavity portion 120, a platform portion 130, a
30 canted peripheral portion 140, and an outer perimeter 134 disposed between the platform portion 130 and the peripheral portion 140, as described above. Extending from the platform portion 130 is a microneedle 160. The microneedle 160 comprises a base segment 166 with a first shape and a tip segment 168 with a second shape, the segments being separated by a transition line 167. Also shown in FIG. 6 is the central axis 180 of the microneedle 160 and a
35 shortest line 184 extending from the outer perimeter 134, through the closest point 185 of the transition plane 167 to the outer perimeter 134, to the central axis 180. The intersection of the

shortest line 184 with the central axis 180 forms an angle θ_3 . In any embodiment of the article of the present disclosure the angle θ_3 is less than about 50° . In any embodiment, the angle θ_3 is less than about 45° . In any embodiment, the angle θ_3 is less than about 40° . In any embodiment, the angle θ_1 is less than about 35° . In any embodiment, the angle θ_3 is less than about 30° . In any embodiment, the angle θ_3 is less than about 25° . A person having ordinary skill in the art will appreciate that, as the angle θ_3 decreases, the amount of potential area of platform portion between the microneedle and the outer perimeter also decreases. The significance of this relationship is discussed below.

[0056] In any embodiment of an article according to the present disclosure, the transition plane of at least one microneedle of the plurality is disposed about $500\text{ }\mu\text{m}$ to about $1000\text{ }\mu\text{m}$ away from the platform portion when measured along the central axis. In any embodiment of an article according to the present disclosure, the transition plane of at least one microneedle of the plurality is disposed about $500\text{ }\mu\text{m}$ to about $800\text{ }\mu\text{m}$ away from the platform portion when measured along the central axis.

[0057] In any embodiment of an article according to the present disclosure, the height of at least one microneedle (measured from the base to the tip) of the plurality is about $600\text{ }\mu\text{m}$ to about $2000\text{ }\mu\text{m}$. In any embodiment of an article according to the present disclosure, the height of at least one microneedle (measured from the base to the tip) of the plurality is about $800\text{ }\mu\text{m}$ to about $1800\text{ }\mu\text{m}$. In any embodiment of an article according to the present disclosure, the height of at least one microneedle (measured from the base to the tip) of the plurality is about $1200\text{ }\mu\text{m}$ to about $1600\text{ }\mu\text{m}$.

[0058] Arrays of microneedles according to the present disclosure comprise a plurality of spaced-apart microneedles extending from a plane (i.e., the platform portion 130, as shown in FIGS. 1-4). FIGS. 7-9 show the interaction of microneedles, skin and the surface of the article from which the microneedle extends. These interactions illustrate at least one advancement that the articles of the present disclosure provide over other configurations.

[0059] FIG. 7A-D show schematic views of a portion of an article 100 comprising a plurality of microneedles 160 as the article is urged against the surface 202 of skin. The article comprises a unitary body 110 comprising a first side 112 that comprises a central cavity portion 120, a platform portion 130 with a microneedle 160 extending therefrom, and a peripheral portion 140 according to the present disclosure. The platform portion 130 is defined by an inner perimeter 132 proximate the central cavity portion 120 and an outer perimeter 134 distal the central cavity portion. The microneedle 160 comprises a base segment 166, a tip segment 168 with a tip 164, and a transition plane 167 disposed between the base segment and the tip segment.

[0060] FIG. 7B shows the article 100 contacting the surface 202 of the skin. As the article is urged in the direction of arrow F, the tip of the needle begins to pierce the surface 202 of the skin. As the article 100 is urged further against the surface 202 of the skin, as shown in FIG. 7C, the tip 164 of the microneedle 160 passes through the surface 202 of the skin into the deeper layers of the skin (not shown). The resistance of the tissue to the penetration of the microneedle 160 causes “tenting” 190 of the skin surface 202 proximate the microneedle 160. As more force is applied to the article 100, the tenting 190 becomes more pronounced, as shown in FIG. 7D. However, because of the dimensions of the microneedle 160 with respect to the platform portion 130; and because of the non-coplanar spatial relationships between the central cavity portion 120, the platform portion 130, and the peripheral portion 140; the tented skin surface 202 does not contact the first side 112 of the article 100 in a manner that substantially interferes with the penetration of the microneedle 160 into the skin.

[0061] FIG. 8 shows a schematic view of a portion of an article 100' comprising a plurality of microneedles 160 as the article is urged against the surface 202 of skin. The article comprises a unitary body 110 comprising a first side 112 that comprises a central cavity portion 120, a platform portion 130 with a microneedle 160 extending therefrom, and a peripheral portion 140. The platform portion 130 is defined by an inner perimeter 132 proximate the central cavity portion 120 and an outer perimeter 134 distal the central cavity portion. In contrast to the article 100 of FIGS. 7A-D, the inner perimeter 132 and outer perimeter 134 are located further away from the microneedles 160. Similar to the article 100 shown in FIGS. 7A-D, the microneedle 160 comprises a base segment 166, a tip segment 168 with a tip 164, and a transition plane 167 disposed between the base segment and the tip segment. It is evident that the skin tenting 190 that occurs as the tip 164 penetrates the skin surface 202 causes the skin surface 202 to contact the platform portion 130. In the illustrated comparative embodiment of FIG. 8, this contact hinders penetration of the microneedle 160 to a preferred depth.

[0062] Without being bound by theory, it is believed that the contact between the skin surface 202 and the platform portion 130 absorbs a portion of the force that is used to urge the skin and the microneedles together, thereby lessening the amount of force available to facilitate deeper penetration of the microneedle tip 164. Although this contact may not obviate the ability of the microneedle to deliver an active ingredient, for example, through the skin; it may result in less consistency of the delivery of the active ingredient by one or more microneedles (e.g., the peripheral microneedles) in an article comprising an array of microneedles.

[0063] The effect shown in FIG. 8 is mitigated along an axis of the article that comprises at least one more microneedle, as shown in FIG. 9. FIG. 9 shows a schematic view of a portion of the article 100 of FIG. 7A comprising an array of at least two microneedles (microneedles 160a and 160b, respectively) as the article is urged against the surface 202 of skin. The article

comprises a unitary body 110 comprising a first side 112 that comprises a platform portion 130 with a microneedle 160 extending therefrom, and a peripheral portion 140. The platform portion 130 is defined in part by the outer perimeter 134. The central cavity portion and inner perimeter are not visible in this view. Similar to the article 100 shown in FIGS. 7A-D, each microneedle comprises a base segment 166, a tip segment 168 with a tip 164, and a transition plane 167 disposed between the base segment and the tip segment.

[0064] Although the distance between the microneedles 160 in FIG. 9 is larger than the distance between the microneedle 160 and the platform perimeters (132 and 134, respectively, of FIG. 7A-D), the skin surface 202 is prevented from contacting the platform portion 130 between one microneedle (e.g., microneedle 160a) because of contact between the skin surface 202 and a nearest-neighbor microneedle (e.g., microneedle 160b) along the longitudinal dimension of the array. Thus, along the longitudinal dimension of the array of microneedles, consistent penetration depth (e.g., penetration beyond the transition plane 167 of the microneedle 160) of the microneedle tips is achieved.

[0065] In another aspect, in any embodiment, there may exist a spatial relationship between a first projected area defined by the first side of the article and a second area defined by the platform portion of the article according to the present disclosure. The term “projected area”, as used herein, refers to an area of the article that is projected one side of the article and, thus, is capable of coming into contact with a surface (e.g., a skin surface) as that side of the article is urged toward the surface. FIG. 10 shows a top view (i.e., showing the first side 112) of an article 100 comprising a plurality of microneedles 160 according to the present disclosure. In the illustrated embodiment of FIG. 10, the article 100 comprises a plurality of microneedles 160 that form an array having a circular (circinate) shape. The first side 112 comprises a central cavity portion 120; a platform portion 130, from which the plurality of microneedles 160 extend, surrounding the central cavity portion; and a peripheral portion 140 surrounding the platform portion 130. The first side 112 defines a first area A_1 (i.e., a projected area) that includes the central cavity portion 120 and peripheral portion 140 (both shown with a first shading type), the area defined by the base of the microneedles 160 (not shaded), and the platform portion 130 (shown with a second shading type). The platform portion 130 defines a second area A_2 within the first area A_1 . The second area includes the shaded platform area and the area defined by the base of the microneedles. In any embodiment, the second area A_2 is less than about 40% of the first area A_1 . In any embodiment, the second area A_2 is less than about 35% of the first area A_1 . In any embodiment, the second area A_2 is less than about 30% of the first area A_1 . In any embodiment, the second area A_2 is about 25% to about 40% of the first area A_1 .

[0066] Microneedle articles (e.g., including articles comprising hollow microneedles) that are made according to the present disclosure can have a variety of configurations and features, such as those described in the following patents and patent applications, the disclosures of which are incorporated herein by reference in their entirety. One embodiment for microneedle array articles includes the structures disclosed in U.S. Patent Application Publication No. 2005/0261631 (Clarke et al.), which describes microneedles having a truncated tapered shape and a controlled aspect ratio. Another embodiment for the microneedle articles includes the structures disclosed in U.S. Patent No. 6,091,975 (Daddona et al.), which describes blade-like microprotrusions for piercing the skin. Still another embodiment for the microneedle articles includes the structures disclosed in U.S. Patent No. 6,312,612 (Sherman et al.), which describes tapered structures having a hollow central channel. Yet still another embodiment for the microneedle array articles includes the structures disclosed in U.S. Patent No. 6,379,324 (Gartstein et al.), which describes hollow microneedles having at least one longitudinal blade at the top surface of the tip of the microneedle. A further embodiment for the microneedle array articles includes the structures disclosed in U.S. Patent Application Publication Nos. US2012/0123387 (Gonzalez et al.) and US2011/0213335 (Burton et al.), which both describe hollow microneedles. A still further embodiment for the microneedle array articles includes the structures disclosed in U.S. Patent Nos. 6,558,361 (Yeshurun) and 7,648,484 (Yeshurun et al.), which both describe hollow microneedle arrays and methods of manufacturing thereof.

[0067] Various embodiments of features of microneedles that can be employed in the microneedle articles of the present disclosure are described in PCT Publication No. WO 2012/074576 (Duan et al.), which describes liquid crystalline polymer (LCP) microneedles; and PCT Publication No. WO 2012/122162 (Zhang et al.), which describes a variety of different types and compositions of microneedles that can be employed in the microneedles of the present disclosure.

[0068] Articles comprising microneedles having features according to the present disclosure can be made, for example, by injection molding processes that are known in the art. In some embodiments, the microneedle material can be (or include) a metal or a polymeric material, preferably a medical grade polymeric material. Exemplary types of medical grade polymeric materials include polycarbonate, liquid crystalline polymer (LCP), polyether ether ketone (PEEK), cyclic olefin copolymer (COC), polybutylene terephthalate (PBT). Preferred types of medical grade polymeric materials include polycarbonate and LCP.

[0069] The microneedle articles of the present disclosure can be manufactured in any suitable way such as by injection molding, compression molding, metal injection molding, stamping, or extrusion. In any embodiment, hollow microneedle arrays can be made by injection molding of a polymer such as medical grade polycarbonate or LCP, followed by laser

drilling to form the channels of the microneedles. Nonlimiting examples of molding processes for molding polymeric materials into the solid microneedle articles of the present disclosure can be found in U.S. Patent No. 8,088,321 (Ferguson et al.) and U.S. Patent Application Publication Nos. 2012/0258284 (Rendon) and 2012/0041337 (Ferguson et al.), each of which is incorporated herein by reference in its entirety. A non-limiting example of a publication that discloses the formation of articles comprising hollow microneedles is U.S. Provisional Patent Application No. 61/746,198, which is incorporated herein by reference in its entirety

[0070] In some embodiments, the microneedle material can be (or include) a biodegradable polymeric material, preferably a medical grade biodegradable polymeric material. Exemplary types of medical grade biodegradable materials include polylactic acid (PLA), polyglycolic acid (PGA), PGA and PLA copolymer, polyester-amide polymer (PEA).

[0071] In some embodiments, the microneedles can be prepared from a dissolvable, degradable, or disintegratable material referred to herein as “dissolvable microneedles”. A dissolvable, degradable, or disintegratable material is any solid material that dissolves, degrades, or disintegrates during use. In particular, a “dissolvable microneedle” dissolves, degrades, or disintegrates sufficiently in the tissue underlying the stratum corneum to allow a therapeutic agent to be released into the tissue. The therapeutic agent may be coated on or incorporated into a dissolvable microneedle. In some embodiments, the dissolvable material is selected from a carbohydrate or a sugar. In some embodiments, the dissolvable material is polyvinyl pyrrolidone (PVP). In some embodiments, the dissolvable material is selected from the group consisting of hyaluronic acid, carboxymethylcellulose, hydroxypropylmethylcellulose, methylcellulose, polyvinyl alcohol, sucrose, glucose, dextran, trehalose, maltodextrin, and a combination thereof.

[0072] In any embodiment, the microneedles can be made from (or include) a combination of two or more of any of the above mentioned materials. For example, the tip of a microneedle may be a dissolvable material, while the remainder of the microneedle is a medical grade polymeric material.

[0073] A microneedle or the plurality of microneedles in a microneedle-containing article of the present disclosure can have a variety of shapes that are capable of piercing the stratum corneum. In some of the embodiments, one or more of the plurality of microneedles can have a segment (e.g., a base segment, a tip segment, or a combination thereof) having a square pyramidal shape, triangular pyramidal shape, stepped pyramidal shape, conical shape, microblade shape, or the shape of a hypodermic needle. In any embodiment, a segment (e.g., a base segment, a tip segment, or a combination thereof) of one or more of the plurality of microneedles can have a square pyramidal shape. In any embodiment, a segment (e.g., a base segment, a tip segment, or a combination thereof) of one or more of the plurality of

microneedles can have a triangular pyramidal shape. In any embodiment, a segment (e.g., a base segment, a tip segment, or a combination thereof) of one or more of the plurality of microneedles can have a stepped pyramidal shape. In any embodiment, a segment (e.g., a base segment, a tip segment, or a combination thereof) of one or more of the plurality of microneedles can have a conical shape. In any embodiment, a segment (e.g., a base segment, a tip segment, or a combination thereof) of one or more of the plurality of microneedles can have a microblade shape. In any embodiment, a segment (e.g., a base segment, a tip segment, or a combination thereof) of one or more of the plurality of microneedles can have the shape of a hypodermic needle. In any embodiment, a microneedle array article may comprise an array of microneedles having a combination of any two or more of the foregoing microneedle shapes. The shape of any microneedle in the microneedle array article can be symmetric or asymmetric. The shape of any microneedle in the microneedle array article can be truncated (for example, the plurality of microneedles can have a truncated pyramid shape or truncated cone shape). In a preferred embodiment, each microneedle of the plurality of microneedles in a microneedle array article has a square pyramidal shape.

[0074] In any embodiment, each microneedle of the plurality of microneedles in a microneedle article is solid microneedles (that is, the microneedles do not comprise a through-hole). In any embodiment, each microneedle of the plurality of solid microneedles in a solid microneedle array article can have a segment (e.g., a base segment, a tip segment, or a combination thereof) with a square pyramidal shape, triangular pyramidal shape, stepped pyramidal shape, conical shape, or microblade shape. In a preferred embodiment, each microneedle of the plurality of solid microneedles in a solid microneedle array article has a segment (e.g., a base segment, a tip segment, or a combination thereof) with a square pyramidal shape or a conical shape with a radius of curvature.

[0075] In some embodiments, each microneedle of the plurality of microneedles in a microneedle array is a hollow microneedle (that is, the microneedle contains a hollow bore through the microneedle). The hollow bore can be from the base of the microneedle to the tip of the microneedle or the bore can be from the base of the microneedle to a position offset from the tip of the microneedle. In any embodiment, one or more of the plurality of hollow microneedles in a hollow microneedle array can have a conical shape, cylindrical shape, square pyramidal shape, triangular pyramidal shape, or the shape of a hypodermic needle.

[0076] In any embodiment, one or more microneedle of the plurality of hollow microneedles in a hollow microneedle array article can have a conical shape; optionally, with a radius of curvature. In any embodiment, one or more microneedle of the plurality of hollow microneedles in a hollow microneedle array article can have a cylindrical shape. In any embodiment, one or more microneedle of the plurality of hollow microneedles in a hollow

microneedle array article can have a segment (e.g., a base segment, a tip segment, or a combination thereof) having a square pyramidal shape. In any embodiment, one or more microneedle of the plurality of hollow microneedles in a hollow microneedle array article can have a segment (e.g., a base segment, a tip segment, or a combination thereof) having a triangular pyramidal shape. In any embodiment, one or more microneedle of the plurality of hollow microneedles in a hollow microneedle array article can have a segment (e.g., a base segment, a tip segment, or a combination thereof) having the shape of a hypodermic needle. In a preferred embodiment, each microneedle of the plurality of hollow microneedles in a hollow microneedle array article has a segment (e.g., a base segment, a tip segment, or a combination thereof) with the shape of a conventional hypodermic needle.

[0077] In any embodiment, an article comprising a hollow microneedle according to the present disclosure may comprise a plurality of the microneedles. The plurality of the microneedles optionally may form an array. In any embodiment, the article can comprise an array of about 3 to about 30, inclusive, of the hollow microneedles of the present disclosure. In a preferred embodiment, the article can comprise an array of about 8 to about 20, inclusive, of the hollow microneedles of the present disclosure. In a more-preferred embodiment, the article can comprise an array of 12, 16, or 18 of the hollow microneedles of the present disclosure.

[0078] In any embodiment of an article comprising a plurality of hollow microneedles according to the present disclosure, the overall height of each microneedle is about 400 μm to about 3000 μm . In any embodiment of an article comprising a plurality of hollow microneedles according to the present disclosure, the overall height of each microneedle is about 400 μm to about 2000 μm . In any embodiment of an article comprising a plurality of hollow microneedles according to the present disclosure, the overall height of each microneedle is about 750 μm to about 1600 μm .

[0079] In any embodiment of an article comprising a plurality of hollow microneedles according to the present disclosure, a hollow channel extending through each of the microneedles has a diameter, proximate the tip of the microneedle, of about 10 μm to about 200 μm . In any embodiment of an article comprising a plurality of hollow microneedles according to the present disclosure, a hollow channel extending through each of the microneedles has a diameter, proximate the tip of the microneedle, of about 10 μm to about 120 μm . In any embodiment of an article comprising a plurality of hollow microneedles according to the present disclosure, a hollow channel extending through each of the microneedles has a diameter, proximate the tip of the microneedle, of about 25 μm to about 75 μm .

[0080] In any embodiment of an article comprising a plurality of hollow microneedles according to the present disclosure, a hollow channel extending through each of the

microneedles has a cross-sectional area of about $75\ \mu\text{m}^2$ to about $32,000\ \mu\text{m}^2$. In any embodiment of an article comprising a plurality of hollow microneedles according to the present disclosure, a hollow channel extending through each of the microneedles has a cross-sectional area of about $75\ \mu\text{m}^2$ to about $18,000\ \mu\text{m}^2$. In any embodiment of an article comprising a plurality of hollow microneedles according to the present disclosure, a hollow channel extending through each of the microneedles has a cross-sectional area of about $700\ \mu\text{m}^2$ to about $3,000\ \mu\text{m}^2$.

[0081] The microneedle array articles of the present disclosure can be manufactured by injection molding of a polymer such as medical grade polycarbonate or LCP. Typically, these processes use molds to form the substrate with the microneedles extending therefrom.

[0082] In any embodiment, at least one hollow microneedle in an article according to the present disclosure can have a tip segment that has any shape or structure that facilitates, or does not interfere with, the ability of the microneedle to penetrate the surface of skin. In addition, the tip segment may comprise an opening (e.g., either a depression, dead-end cavity, or a through-hole that extends all the way through the microneedle) that facilitates the delivery of (and, optionally, storage therein) an active compound. In any embodiment, at least one hollow microneedle of the plurality of microneedles comprises a base, an elongated body having a central axis and a body diameter, and a tip segment with two bevel faces. The tip segment comprises a tip, a first bevel face oriented diagonally with respect to the central axis and extending through at least 75% of the body diameter, a second bevel face oriented substantially perpendicular to the central axis and intersecting the first bevel face, a bevel opening defined by a first edge of the first bevel face and a second edge of the second bevel face. A microneedle tip with two bevel faces is described in US Provisional Patent Application No. 61/846,934, filed on July 16, 2013 and incorporated herein by reference in its entirety.

[0083] In any embodiment, at least one hollow microneedle in an article according to the present disclosure can have a tip segment that comprises an opening that is formed by two channels that merge to form the opening. Thus, in these embodiments, the at least one microneedle comprises a base, an elongated body having a central axis, a tip segment with a beveled surface and a bevel opening in the bevel surface, a first channel that extends axially from the bevel opening through at least a portion of the elongated body, and a second channel that extends radially from the first channel to the bevel opening.. The first channel has a first wall that is substantially aligned with the central axis. The second channel has a second wall that is oriented substantially orthogonal to the central axis. The first channel and second channel merge to form the bevel opening. A microneedle tip that comprises an opening that is formed by two channels that merge to form the opening, is described in US Provisional Patent

Application No. 61/846,945, filed on July 16, 2013 and incorporated herein by reference in its entirety.

[0084] In any embodiment, articles of the present disclosure can be used with an applicator (e.g., a single-use applicator or a reusable applicator) that is configured to urge the plurality of microneedles of the article against a skin surface. In any embodiment, actuation of the applicator can occur through single actuation or through dual actuation. A non-limiting example of a single-actuation applicator is disclosed in US Patent Application Publication No. 2012/0123387 (Gonzalez et al.), which is incorporated herein by reference in its entirety. The use of microneedle articles with a dual-actuation or dual automatic actuation is described, for example, in US Provisional Patent Application No. 61/740,941, which is incorporated herein by reference in its entirety.

[0085] In any embodiment, an article of the present disclosure can be used with an applicator comprising an adhesive assembly such as, for example, the applicator comprising the adhesive assembly described in US Provisional Patent Application No. 61/740,941. In any embodiment, the adhesive assembly can comprise a skin-contact adhesive layer such as, for example, the applicator comprising the skin-contact adhesive layer described in US Provisional Patent Application No. 61/740,941. In any embodiment, the skin-contact adhesive layer can comprise an annular configuration that, in use, surrounds the microneedle article of the present disclosure and, optionally, secures the article to a skin surface while an active compound (e.g., an active compound that is part of a pharmaceutical composition) is delivered from (or through) the microneedle into a patient.

[0086] FIG. 11 shows a plan view of a portion of the skin-facing surface of one embodiment of an applicator configured for use with an article comprising a plurality of hollow microneedles according to the present disclosure. The applicator 400 comprises a skin-contact adhesive layer 490 that substantially surrounds the article 100. The article comprises a first side 112 that comprises a central cavity portion 120 surrounded by a platform portion 130 that is not coplanar with the central cavity portion 120 (i.e., the platform is raised above the central cavity). A circinate array of spaced-apart microneedles 160 extend from the first side of the platform portion 130. The first side 112 further comprises an optional peripheral portion 140 that surrounds the platform portion 130 and that is not coplanar with the platform portion (i.e., the platform is raised above the peripheral portion). The article 100 is attached (e.g., detachably attached) to the applicator 400 using various attachment means (e.g., an adhesive, a clamp, friction fit, and the like, not shown).

[0087] Also shown in FIG. 11 are various spatial dimensions associated with the article 100 and the applicator. In the illustrated embodiment, the platform portion 130 is a ring-shaped (i.e., circinate) platform that surrounds the central cavity portion. Dimension D1 represents the

diameter of the central cavity portion 120, as defined by the inner perimeter 132 of the platform portion 130. Dimension D2 represents the outer diameter of the platform portion 130, as defined by the outer perimeter 134 of the platform portion. Dimension D3 represents the outer diameter of the ring-shaped peripheral portion 140 that surrounds the platform portion 130.

5 Dimension D4 represents the width of the platform portion, as measured along a radius (not shown) extending from the center of the circular-shaped article. In addition, D5 represents the shortest distance, as measured along a radius (not shown) extending from the center of the circular-shaped article, between the tip of a microneedle 160 and the skin-contact adhesive 490 of the applicator 400. In a preferred embodiment, the shape of the skin-contact

10 adhesive layer is shaped and dimensioned so that the shortest distance between each microneedle tip in the array is and the skin-contact adhesive layer 490 approximately equal (e.g., less than about 10% variability).

EXEMPLARY EMBODIMENTS

15 **[0088]** Embodiment A is an article, comprising:

- a first side comprising a central cavity portion and a platform portion that projects from the first side and that is not coplanar with the central cavity portion;
- a second side opposite the first side; and
- at least three hollow microneedles extending from the platform portion in a

20 first direction;

- wherein the platform portion substantially surrounds the central cavity portion;
- wherein the platform portion comprises an inner perimeter proximate the central cavity portion and an outer perimeter distal the central cavity portion;
- wherein the at least three hollow microneedles each comprise a body that

25 comprises:

- an outer surface;
- a base segment having a base and a first shape that is defined by a first section of the outer surface;
- a tip segment having a tip and a second shape that is defined by a

30 second section of the outer surface, wherein the second shape is distinct from the first shape;

- a transition plane that delineates the base segment and the tip segment;
- and
- a central axis;

wherein a first angle, defined by the central axis of each of the at least three hollow microneedles and a shortest line extending from the outer perimeter of the platform and through the transition plane of the microneedle, is less than about 50°.

[0089] Embodiment B is the article of Embodiment A, wherein a second angle, defined by the central axis and a shortest line extending from the inner perimeter and through the transition plane, is less than about 50°.

[0090] Embodiment C is the article of Embodiment A or Embodiment B, wherein the first angle is less than about 45° and/or wherein the second angle is less than about 45°.

[0091] Embodiment D is the article of any one of the preceding Embodiments, wherein the transition plane is disposed about 500 μm to about 800 μm away from the platform portion when measured along the central axis.

[0092] Embodiment E is an article, comprising:

a first side comprising a central cavity portion and a platform portion that projects from the first side and that is not coplanar with the central cavity portion;

a second side opposite the first side; and

at least three hollow microneedles extending from the platform portion in a first direction;

wherein the platform portion substantially surrounds the central cavity portion;

wherein the platform portion comprises an inner perimeter proximate the central cavity portion and an outer perimeter distal the central cavity portion;

wherein each of the at least three hollow microneedles comprises a body that comprises:

an outer surface;

a base segment having a base and a first shape that is defined by a first section of the outer surface;

a tip segment having a tip and a second shape that is defined by a second section of the outer surface, wherein the second shape is distinct from the first shape;

a transition plane that delineates the base segment and the tip segment;

and

a central axis;

wherein each of the at least three hollow microneedles comprises a height measured from the base to the tip;

wherein the tip segment of each of the at least three hollow microneedle defines at least about 30% of the height of the microneedle.

[0093] Embodiment F is the article of Embodiment E, wherein the base segment is conical-shaped and the tip segment is substantially cylindrical-shaped.

[0094] Embodiment G is the article of Embodiment E or Embodiment F, wherein the height comprises a first height component associated with the base segment and a second height component associated with the tip segment; wherein the second height component is about 300 μm to about 825 μm .

[0095] Embodiment H is the article of Embodiment G, wherein the height comprises a first height component associated with the base segment and a second height component associated with the tip segment; wherein the second height component is about 650 μm to about 800 μm .

[0096] Embodiment I is an article, comprising:

- a first side comprising a central cavity portion and a platform portion that projects from the first side and that is not coplanar with the central cavity portion;

- a second side opposite the first side; and

- at least three hollow microneedles extending from the platform portion in a first direction;

- wherein the platform portion substantially surrounds the central cavity portion;

- wherein the platform portion comprises an inner perimeter proximate the central cavity portion and an outer perimeter distal the central cavity portion;

- wherein each of the at least three hollow microneedles comprises a body that comprises:

- an outer surface;

- a base segment having a base and a first shape that is defined by a first section of the outer surface;

- a tip segment having a tip and a second shape that is defined by a second section of the outer surface, wherein the second shape is distinct from the first shape;

- a transition plane that delineates the base segment and the tip segment; and

- a central axis;

- wherein the first side defines a first area;

- wherein the platform portion defines a second area within the first area;

- wherein the second area is less than about 40% of the first area.

[0097] Embodiment J is the article of any one of the preceding Embodiments, wherein the at least three microneedles forms a two-dimensional array.

[0098] Embodiment K is the article of Embodiment J, wherein the array of microneedles is distributed all the way around the platform portion.

[0099] Embodiment L is the article of Embodiment K, wherein a tip-to-tip distance between each pair of adjacent microneedles in the array is approximately equal.

[00100] Embodiment M is the article of any one of the preceding Embodiments, wherein the first side further comprises a microneedle-free peripheral portion extending laterally from at least a part of the outer perimeter of the platform portion, wherein the peripheral portion is canted away from the platform portion in a second direction opposite the first direction.

5 [00101] Embodiment N is the article of any one of the preceding Embodiments; wherein the article further comprises a side wall portion that extends from the platform portion or, if present, the peripheral portion; wherein the sidewall portion extends substantially opposite the first direction.

10 [00102] Embodiment O is the article of any one of the preceding Embodiments, wherein the central cavity is a closed cavity.

[00103] Embodiment P is the article of any one of Embodiments A through N, wherein the central cavity is a through-hole extending from the first side through the second side.

[00104] Embodiment Q is the article of any one of the preceding Embodiments, wherein the platform is circinate.

15 [00105] Embodiment R is the article of any one of the preceding Embodiments, wherein the array of microneedles is circinate.

[00106] Embodiment S is the article of any one of the preceding Embodiments, wherein a unitary body comprises the platform portion, the peripheral portion, and the central cavity portion.

20 [00107] Embodiment T is the article of any one of the preceding Embodiments, wherein at least one microneedle of the plurality comprises:

a base;

an elongated body having a central axis and a body diameter;

25 a tip portion comprising a tip, a first bevel face oriented diagonally with respect to the central axis and extending through at least 75% of the body diameter, a second bevel face oriented substantially perpendicular to the central axis and intersecting the first bevel face, a bevel opening defined by a first edge of the first bevel face and a second edge of the second bevel face; and

a hollow channel that extends axially into the body from the bevel opening.

30 [00108] Embodiment U is the article of any one of Embodiments A through S, wherein at least one microneedle of the plurality comprises:

a base;

an elongated body having a central axis;

35 a tip portion comprising a tip, a beveled surface, and a bevel opening in the beveled surface;

a first channel that extends axially from the bevel opening through at least a portion of the elongated body, wherein the first channel has a first wall that is substantially aligned with the central axis; and

5 a second channel that extends radially from the first channel to the bevel opening, wherein the second channel has a second wall that is oriented substantially orthogonal to the central axis;

wherein the first channel and second channel merge to form the bevel opening.

[00109] Embodiment V is the article of any one of the preceding Embodiments, wherein each of the at least three microneedles comprises a hollow channel extending through the article
10 from a first opening proximate the tip to a second opening in the second side of the article.

[00110] Embodiment W is the article of Embodiment V, further comprising a reservoir that is in fluidic communication with each of the hollow channels.

[00111] Embodiment X is the use of the article of any one of the preceding Embodiments, for injecting fluid into a body.

15 [00112] Embodiment Y is the article of any one of Embodiments A through W, for extracting fluid from a body.

[00113] Embodiment Z is the use of the article as according to Embodiment X or Embodiment Y, wherein the article is operatively coupled to an actuator.

[00114] Embodiment AA is the use of the article according to Embodiment Z, wherein the
20 actuator comprises an adhesive assembly, wherein the adhesive assembly comprises a skin-contact adhesive layer that, when the actuator is actuated, is urged against a skin surface.

[00115] Embodiment BB is the use of the article according to Embodiment AA; wherein the article comprises an array of the at least three hollow microneedles, each microneedle having a tip and a shortest distance from the tip to the skin-contact adhesive layer; wherein all of the
25 shortest distances of the at least three microneedles are approximately equal.

EXAMPLES

[00116] **Example 1. Fabrication of microneedle articles.**

[00117] The microneedle articles were prepared from polymeric material using standard
30 injection molding procedures. The molded microneedle articles were prepared using a mold assembly prepared from three mold sections with each section machined from steel. The first mold section contained projections that defined the beveled shape of the needle tip in the molded array. Each projection in the first mold section had a further cylindrical extension that defined features of the tip segment of the microneedles tip, including the opening on a bevel
35 proximate the tip of the microneedle and a portion of the hollow channel extending through the body of each microneedle. The second mold section served as a template to define the pattern

of the microneedles in the molded article, the external shape and size of the microneedles in the molded article, and the first side of the article (including the central cavity portion, platform portion, and peripheral portion, as described above). The third mold section contained cylindrical projections emerging from a planar surface with each projection defining a second (base-proximal) part of the microneedle hollow channel and the opening located at the base of each microneedle in the molded article. The planar surface from which the projections emerged served to define the second major surface of the base segment of the molded article. The first and second mold sections were assembled to form a tight fit by inserting the projections of the first mold section into the corresponding openings in the second mold section. The assembled first and second mold sections formed the first mold half. The third mold section was used as the second mold half.

[00118] The first and second mold halves were installed in a mold base in a 60-ton injection molding press (Sodick Plustech LA 60, Sodick Plustech Co., Yokohama, Japan). As is common in the art, the parting line of the mold assembly had both primary and secondary vents for general air evacuation during injection of the polymeric material. Vectra MT1300 liquid crystal polymer (LCP) pellets (Ticona Engineering Polymers, Florence, KY) were loaded into a reciprocating screw and heated until molten. The first mold half and second mold half were heated to a temperature (hereafter referred to as the "mold temperature at injection") of 200 °F (93.3 °C). The molding cycle was initiated by closing the first mold half with the second mold half. The molds were clamped together with approximately 20 to 60 tons of force. In the clamped position, the surfaces at the tips of the projections in the second mold half were aligned with and in contact with the surfaces at the tips of the projections in the first mold half. A first portion (approx. 50-95% of the part size volume) of the total amount of material from the reciprocating screw was injected into the mold chamber at a fixed velocity (hereafter referred to as the "injection velocity") of about 7 inches/second (17.8 cm/second). After injecting the first portion of material, the process was switched from an injection-driven to a pressure-driven mode by applying a fixed pressure (hereafter referred to as the "pack pressure") of about 13,500 psi (93,079 kilopascal) to force the remainder of the molten material into the negative mold insert. The pack pressure was applied for a fixed time (hereafter referred to as the "hold time") of 5 seconds. The pack pressure was subsequently released and the mold chamber was cooled to an ejection temperature set below the softening temperature of LCP. The mold chamber was opened and the microneedle article was ejected.

[00119] Example 2. Injection apparatus used to test the microneedle articles.

[00120] Fully assembled microneedle article injection apparatuses similar to apparatuses described in U.S. Patent Application Publication No. US2012/0123387 (FIGS. 1-13) and U.S. Provisional Patent Application No. 61/740,941 (FIGS. 2, 14 and 15) were used. The drug

cartridge in each apparatus contained a 1 mL solution of 0.005% methylene blue in five percent aqueous dextrose. The injection apparatus from Example 1 of U.S. Provisional Patent Application No. 61/740,941 was used with the following exceptions. First, the section of the apparatus joined to the adhesive assembly was not milled to remove material. Second, the construction of the adhesive assembly was different. Instead of using the four layer adhesive of U.S. Provisional Patent Application No. 61/740,941, the adhesive assembly used was a laminate composed of only two layers. The first layer was a 0.10 mm thick sheet of 3M 1510 double sided tape (available from the 3M Company). The second layer was a 0.07 mm sheet of 3M 1524 transfer adhesive. The two layer adhesive assembly was positioned to cover the first major surface of base member of the lower housing at the rounded end section of the device. The adhesive assembly laminate was laser cut so that the size and shape of the adhesive assembly was matched to that of the device. The two layers of the adhesive assembly each contained cut-out regions that were aligned to each other and exactly matched the opening in the device housing. The device and adhesive assembly were oriented so that the first layer of the adhesive assembly was adhered to the lower housing of the device. The adhesive assembly was aligned with the device so that the opening in the first layer of the adhesive assembly was coincident with the opening in the device. A release liner was used during storage of the device to protect the exposed adhesive of the second layer of the adhesive assembly.

[00121] The hollow microneedle article used in the microneedle article injection apparatus (as shown in FIG. 1) was molded (as described in Example 1) from Vectra MT1300 liquid crystal polymer (LCP) in the shape of a circle approximately 1.25 cm in diameter (dimension D3 of FIG. 11). The circular platform portion projected about 1.0 mm from the outside edge of the article (Height H₁ of FIG. 2) and the peripheral portion canted away from the platform portion with a 36.9 degree cant, relative to the plane of the platform portion. The closed circular cavity of the article was centered on the article with a diameter of about 6.8 mm (diameter measurement D1 (FIG. 11) defined by the circular region formed by the inner perimeter of the platform), a depth of about 500 microns at the center of the cavity, and a radius of curvature of about 11 mm. The diameter of the circular region formed by the outer perimeter of the platform was about 10.3 mm (dimension D2 in FIG. 11). The width of the platform was about 1.75 mm (dimension D4 in FIG. 11). The article featured an array of 12 hollow microneedles extending from the circular platform portion of the article. The microneedles were evenly spaced with the distance between neighboring microneedles being about 2.2 mm (as measured from tip to tip). Each microneedle was oriented so that the opening at the tip was facing toward the outer perimeter of the article along a radial vector. The external diameter of each microneedle at the base was about 1.5 mm. The flared base segment of each microneedle had a radius of curvature of about 1 mm. The tip segment of each microneedle was in the shape of a

conventional hypodermic needle with a 33.6 degree bevel and a chamfered tip that had an included angle of 70 degrees. The opening near the tip was obround in shape (as shown in FIG. 2A) with dimensions of 303 microns by 80 microns. Each microneedle had a total height of about 1500 microns as measured from the base of the microneedle at the platform surface to the tip of the microneedle. The length of the tip segment (as measured from the tip to the transition plane that delineated the flared base segment from the substantially cylindrical tip segment, FIG. 2A) was about 564 microns with the external diameter at the midpoint of this region being about 254 microns (i.e. at a distance about 282 microns below the microneedle tip the external diameter of each microneedle was about 254 microns). The distance from the tip of each microneedle to the center of the opening near the tip was about 382 microns. The average diameter of the hollow channel through the tip segment of each microneedle was about 80 microns. The angle theta (θ_1 , as shown in FIG. 5A) was 48.5 degrees.

[00122] Example 3. Injection apparatus.

[00123] The same microneedle injection apparatus as described in Example 2 was used with the exception that the wire diameter of the U-shaped leaf-like insertion spring (i.e. first stored energy device as described in U.S. Patent Application Publication No. US2012/0123387 (FIGS. 1-13) and U.S. Provisional Patent Application No. 61/740,941 (FIGS. 2, 14 and 15)) was 1.50 mm instead of 1.59 mm.

[00124] Example 4. Alternative injection apparatus.

[00125] The same microneedle injection apparatus as described in Example 2 was used with the exception that the wire diameter of the U-shaped leaf-like insertion spring (i.e. first stored energy device as described in U.S. Patent Application Publication No. US2012/0123387 (FIGS. 1-13) and U.S. Provisional Patent Application No. 61/740,941 (FIGS. 2, 14 and 15)) was 1.40 mm instead of 1.59 mm.

[00126] Example 5. Use of microneedle article to inject a substance.

[00127] The study was conducted using Yorkshire cross domestic pigs (Midwest Research Swine, Gibbon, MN) *in vivo*. A soft region of the belly having minimal muscle content was selected as the application site for microneedle insertion. The application site was first trimmed with an electric clipper and then shaved using a razor and shaving cream. The shaved area was scrubbed using soapy water and a BUF-PUF exfoliation sponge (3M Company, St. Paul, MN) and then rinsed with deionized water. The animal was placed in a lateral recumbent position on a heated table (38 °C). The animal was anesthetized with isofluorene gas and maintained under anesthesia throughout the experiment. The application site was then wiped with a 70% isopropanol in water solution.

[00128] The injection apparatus of Example 4 was used. The release liner was removed from the adhesive assembly and the apparatus was adhered to the skin of the pig. During attachment

of the device to the pig, the skin at the application site was gently stretched to provide a slight tension to the skin. The skin was then allowed to relax and the push-button was depressed to cause release of the applicator element and insertion of the microneedle article into the skin of the pig. Removal of the tapered pin from the housing released the coiled spring which initiated the injection of the methylene blue solution into the pig. After completion of the injection, the apparatus was maintained on the skin for one additional minute. The apparatus was removed from the skin and the skin surface was examined to determine if there was any methylene blue solution on the surface of the skin. The presence of methylene blue solution on the skin was an indication that not all of the methylene blue was injected into the animal. The injection site was wiped with a pre-tared absorbent wipe and the wipe was then weighed to determine the amount of methylene blue that was not successfully delivered.

[00129] A total of three replicates were conducted. The injection times ranged from 29 to 111 seconds with the average injection time being 63 seconds. Two of the apparatuses successfully delivered the methylene blue solution without any "leakage" (i.e. no methylene blue solution was observed on the skin surface). The third apparatus successfully delivered 97% of the methylene blue solution.

[00130] Example 6. Use of microneedle article.

[00131] A study was conducted to determine the depth of penetration (DOP) of the microneedles of the article when applied to the skin surface of a Yorkshire cross domestic pigs (Midwest Research Swine), *in vivo*. The hollow microneedle article described in Example 2 was used.

[00132] The microneedles on the article were coated using a three step process. The first two steps involved applying primer coatings to the microneedles and the third step involved applying a thin coating of Rhodamine B to the microneedles. In Step 1, the articles were flood coated with a 35 microliter solution containing 0.5 mg/mL polyvinyl alcohol (80% hydrolyzed) (Sigma-Aldrich, Inc., St. Louis, MO) and 35 µg/ml of TWEEN® 80 (Sigma-Aldrich) in 90% (w/v) ethanol. The coated articles were then dried at 35 °C for 20 minutes. In Step 2, the articles from Step 1 were flood coated with 35 microliters of an aqueous solution of 33.3 mg/ml aluminum potassium sulfate (Penta Manufacturing, Livingston, NJ). The coated articles were then dried at 35 °C for 30 minutes. In Step 3, the primed articles from Step 2 were flood coated with 40 microliters of an aqueous solution of 0.08% (w/v) Rhodamine B (Sigma-Aldrich). The coated articles were dried at 35 °C for 30 minutes. The three step process provided articles in which the microneedles were completely covered with a thin, opaque coating of Rhodamine B.

[00133] The ham region was selected as the application site for microneedle insertion. The application site was first trimmed with an electric clipper and then shaved using a razor and shaving cream. The shaved area was scrubbed using soapy water and a BUF-PUF exfoliation

sponge (3M Company) and then rinsed with deionized water. The animal was placed in a lateral recumbent position on a heated table (38 °C). The animal was anesthetized with isofluorene gas and maintained under anesthesia throughout the experiment. The application site was then wiped with a 70% isopropanol in water solution.

5 **[00134]** The injection apparatus described in Example 2 with a Rhodamine B coated article was used. The release liner was removed from the adhesive assembly and the apparatus was adhered to the skin of the pig. The push-button was depressed to cause release of the applicator element and insertion of the microneedles of the microneedle article into the skin of the pig. The injection apparatus was maintained on the skin for an additional 5 minutes.

10 **[00135]** The injection apparatus was removed from the animal. The depth of penetration (DOP) of the microneedles into the pig skin was determined indirectly by measuring the distance from the tip of the microneedle to where the Rhodamine B coating was wiped or dissolved from the microneedle after application into the skin. The measurement was conducted using a Nikon LV-100 microscope at 100X magnification (Nikon Instruments, Melville, NY)
15 with Image Pro® Plus digital image analysis software (Media Cybernetics, Bethesda, MD). A total of two replicates were conducted. The mean microneedle DOP was determined by sampling all of the microneedles from each article (n=24). The results are presented in Table 1.

[00136] Table 1: Depth of Penetration (DOP) when Microneedle Article was Applied to the Ham Area (Example 6)

Minimum DOP	729 microns
Maximum DOP	901 microns
Mean DOP	827 microns
Standard Deviation	48 microns
% RSD	6%

20 **[00137]** **Example 7. Use of microneedle article.**

[00138] The procedure as described in Example 6 was used with the exception that the injection apparatus of Example 3 was used instead of the injection apparatus of Example 2. The results are presented in Table 2.

[00139] Table 2: Depth of Penetration (DOP) when Microneedle Article was Applied to the Ham Area (Example 7)

Minimum DOP	558 microns
Maximum DOP	849 microns
Mean DOP	751 microns
Standard Deviation	74 microns
% RSD	10%

[00140] Example 8. Use of microneedle article.

[00141] The procedure as described in Example 6 was used with the exception that the injection apparatus of Example 4 was used instead of the injection apparatus of Example 2.

5 The results are presented in Table 3.

[00142] Table 3: Depth of Penetration (DOP) when Microneedle Article was Applied to the Ham Area (Example 8)

Minimum DOP	709 microns
Maximum DOP	863 microns
Mean DOP	787 microns
Standard Deviation	45 microns
% RSD	6%

[00143] The complete disclosure of all patents, patent applications, and publications, and electronically available material cited herein are incorporated by reference. In the event that any inconsistency exists between the disclosure of the present application and the disclosure(s) of any document incorporated herein by reference, the disclosure of the present application shall govern. The foregoing detailed description and examples have been given for clarity of understanding only. No unnecessary limitations are to be understood therefrom. The invention is not limited to the exact details shown and described, for variations obvious to one skilled in the art will be included within the invention defined by the claims.

[00144] All headings are for the convenience of the reader and should not be used to limit the meaning of the text that follows the heading, unless so specified.

[00145] Various modifications may be made without departing from the spirit and scope of the invention. These and other embodiments are within the scope of the following claims.

CLAIMS:

1. An article, comprising:
- 5 a first side comprising a central cavity portion and a platform portion that projects from the first side and that is not coplanar with the central cavity portion;
- a second side opposite the first side; and
- at least three hollow microneedles extending from the platform portion in a first direction;
- wherein the platform portion substantially surrounds the central cavity portion;
- 10 wherein the platform portion comprises an inner perimeter proximate the central cavity portion and an outer perimeter distal the central cavity portion;
- wherein the at least three hollow microneedles each comprise a body that comprises:
- an outer surface;
- 15 a base segment having a base and a first shape that is defined by a first section of the outer surface;
- a tip segment having a tip and a second shape that is defined by a second section of the outer surface, wherein the second shape is distinct from the first shape;
- 20 a transition plane that delineates the base segment and the tip segment;
- and
- a central axis;
- wherein a first angle, defined by the central axis of each of the at least three hollow microneedles and a shortest line extending from the outer perimeter of the platform and
- 25 through the transition plane of the microneedle, is less than about 50°.
2. The article of claim 1, wherein a second angle, defined by the central axis and a shortest line extending from the inner perimeter and through the transition plane, is less than about 50°.
- 30 3. The article of any one of the preceding claims, wherein the transition plane is disposed about 500 μm to about 800 μm away from the platform portion when measured along the central axis.

4. An article, comprising:
a first side comprising a central cavity portion and a platform portion that projects from the first side and that is not coplanar with the central cavity portion;
a second side opposite the first side; and
5 at least three hollow microneedles extending from the platform portion in a first direction;
wherein the platform portion substantially surrounds the central cavity portion;
wherein the platform portion comprises an inner perimeter proximate the central cavity portion and an outer perimeter distal the central cavity portion;
10 wherein each of the at least three hollow microneedles comprises a body that comprises:
an outer surface;
a base segment having a base and a first shape that is defined by a first section of the outer surface;
15 a tip segment having a tip and a second shape that is defined by a second section of the outer surface, wherein the second shape is distinct from the first shape;
a transition plane that delineates the base segment and the tip segment;
and
20 a central axis;
wherein each of the at least three hollow microneedles comprises a height measured from the base to the tip;
wherein the tip segment of each of the at least three hollow microneedle defines at least about 30% of the height of the microneedle.

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5. The article of claim 4, wherein the base segment is conical-shaped and the tip segment is substantially cylindrical-shaped.

6. The article of claim 4 or claim 5, wherein the height comprises a first height component associated with the base segment and a second height component associated with the tip segment; wherein the second height component is about 300 μm to about 825 μm .

7. An article, comprising:
a first side comprising a central cavity portion and a platform portion that projects from the first side and that is not coplanar with the central cavity portion;
35 a second side opposite the first side; and

at least three hollow microneedles extending from the platform portion in a first direction;

wherein the platform portion substantially surrounds the central cavity portion;

5 wherein the platform portion comprises an inner perimeter proximate the central cavity portion and an outer perimeter distal the central cavity portion;

wherein each of the at least three hollow microneedles comprises a body that comprises:

an outer surface;

10 a base segment having a base and a first shape that is defined by a first section of the outer surface;

a tip segment having a tip and a second shape that is defined by a second section of the outer surface, wherein the second shape is distinct from the first shape;

15 a transition plane that delineates the base segment and the tip segment; and

a central axis;

wherein the first side defines a first area;

wherein the platform portion defines a second area within the first area;

20 wherein the second area is less than about 40% of the first area.

8. The article of any one of the preceding claims, wherein the first side further comprises a microneedle-free peripheral portion extending laterally from at least a part of the outer perimeter of the platform portion, wherein the peripheral portion is canted away from the platform portion in a second direction opposite the first direction.

25 9. The article of any one of the preceding claims; wherein the article further comprises a side wall portion that extends from the platform portion or, if present, the peripheral portion; wherein the sidewall portion extends substantially opposite the first direction.

30 10. The article of any one of the preceding claims, wherein the central cavity is a closed cavity.

35 11. The article of any one of claims 1 through 9, wherein the central cavity is a through-hole extending from the first side through the second side.

12. The article of any one of the preceding claims, wherein the platform is circinate.

5 13. The article of any one of the preceding claims, wherein the array of microneedles is circinate.

14. The article of any one of the preceding claims, wherein a unitary body comprises the platform portion, the peripheral portion, and the central cavity portion.

10 15. The article of any one of the preceding claims, wherein at least one microneedle of the plurality comprises:
a base;
an elongated body having a central axis and a body diameter;
a tip portion comprising a tip, a first bevel face oriented diagonally with respect to the
15 central axis and extending through at least 75% of the body diameter, a second bevel face oriented substantially perpendicular to the central axis and intersecting the first bevel face, a bevel opening defined by a first edge of the first bevel face and a second edge of the second bevel face; and
a hollow channel that extends axially into the body from the bevel opening.

20 16. The article of any one of the preceding claims, wherein at least one microneedle of the plurality comprises:

a base;
an elongated body having a central axis;
25 a tip portion comprising a tip, a beveled surface, and a bevel opening in the beveled surface;
a first channel that extends axially from the bevel opening through at least a portion of the elongated body, wherein the first channel has a first wall that is substantially aligned with the central axis; and
30 a second channel that extends radially from the first channel to the bevel opening, wherein the second channel has a second wall that is oriented substantially orthogonal to the central axis;
wherein the first channel and second channel merge to form the bevel opening.

17. The article of any one of the preceding claims, wherein the at least one microneedle comprises a hollow channel extending through the article from a first opening proximate the tip to a second opening in the second side of the article.

5 18. The use of the article, as claimed in any one of claims 1 through 17, for injecting fluid into a body.

19. The article, as claimed in any one of claims 1 through 17, for extracting fluid from a body.

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20. The use of the article as according to claim 18 or claim 19, wherein the article is operatively coupled to an actuator.