

containers, the methods and apparatuses disclosed herein can be configured in many ways to deliver therapeutic agents to many locations of the body, such as with implantable devices, syringes coupled to needles and intravenous drug delivery.

[0006a] In a first aspect, the present disclosure provides a flow control device for delivering an ophthalmic formulation, the device comprising: a reservoir, the reservoir comprising the ophthalmic formulation disposed therein, the ophthalmic formulation comprising an ophthalmic agent and a preservative; a nozzle, the nozzle comprising: an outlet, an interior volume comprising a preservative removing device, one or more nozzle apertures fluidically connecting the interior volume with an exterior of the nozzle; a reservoir interface comprising one or more reservoir apertures, wherein upon rotation or translation of the nozzle relative to the reservoir interface, the one or more nozzle apertures are fluidically connected with the one or more reservoir apertures; a bottle cap wherein one or more nozzle apertures are aligned with the one or more reservoir apertures when the bottle cap is removed and wherein one or more nozzle apertures are not aligned with the one or more reservoir apertures when the bottle cap is coupled to the nozzle; and a spring disposed between the nozzle and the reservoir interface, wherein a restoring force of the spring translates the nozzle to an aligned translational position when the bottle cap is removed.

[0006b] In a second aspect, the present disclosure provides a flow control device for delivering an ophthalmic formulation, the device comprising: a reservoir, the reservoir comprising the ophthalmic formulation disposed therein, the ophthalmic formulation comprising an ophthalmic agent and a preservative; a nozzle, the nozzle comprising: an outlet, an interior volume comprising a preservative removing device, and one or more nozzle apertures fluidically connecting the interior volume with an exterior of the nozzle; a reservoir interface positioned between the reservoir and the nozzle, the reservoir interface comprising one or more reservoir apertures fluidically connecting an interior of the reservoir with an exterior of the reservoir, wherein upon rotation or translation of the nozzle relative to the reservoir interface, the one or more nozzle apertures are fluidically connected or disconnected from the one or more reservoir apertures; a spring disposed between the reservoir interface and the nozzle such that the spring provides a restoring force opposing a compressing motion by the nozzle upon rotation or translation of the nozzle relative to the reservoir interface; and a bottle cap, wherein the one or more nozzle apertures are fluidically connected with the one or more reservoir apertures when the bottle cap is removed and wherein the one or more nozzle apertures are fluidically disconnected with the one or more reservoir apertures when the bottle cap is coupled to the nozzle.

[0007] In an example, a flow control device for a compressible bottle is provided. The flow control device may comprise: a reservoir, the reservoir comprising an ophthalmic formulation disposed therein, the ophthalmic formulation comprising an ophthalmic agent and a preservative; a reservoir interface, disposed at a mouth of the reservoir, the reservoir interface comprising one or more apertures, the one or more apertures in the reservoir interface fluidically connecting an interior of the reservoir and an exterior of the reservoir; a nozzle, the nozzle comprising: an outlet and a nozzle cap, the nozzle cap comprising one or more apertures, the one or more apertures in the nozzle cap fluidically connecting the outlet and a reservoir-facing surface of the nozzle; and an axis of rotation, wherein rotation of the nozzle about the axis of rotation relative to the reservoir aligns the one or more apertures in the reservoir interface with the one or more apertures in the nozzle cap.

[0008] In some embodiments, the flow control device further comprises a polymeric matrix disposed in an interior volume of the nozzle, the polymeric matrix comprising absorbed molecules of the preservative from the ophthalmic formulation. In some embodiments, rotation of the reservoir interface prevents flow of the ophthalmic formulation between the interior of the nozzle and the reservoir, thereby stabilizing a concentration of the preservative in the ophthalmic formulation. In some embodiments, the flow control device further comprises a bottle cap, wherein rotation of the bottle cap about the axis of rotation relative to the reservoir rotates the nozzle about the axis of rotation relative to the reservoir. In some embodiments, the nozzle comprises a first one or more ridges on a bottle-cap facing surface, the first one or more ridges receivable by the bottle cap. In some embodiments, the bottle cap comprises one or more alignment channels on an interior surface of the bottle cap, the first one or more ridges on the bottle-cap facing surface of the nozzle cap received within the one or more alignment channels. In some embodiments, the nozzle comprises a second one or more ridges on a reservoir facing surface, the second one or more ridges receivable by the reservoir. In some embodiments, the reservoir comprises one or more rotation guides, the second one or more ridges on a reservoir facing surface received by the one or more rotation guides. In some embodiments, the second one or more ridges on the bottle-facing surface received by the rotation guides limits an angle of rotation of the nozzle relative to the reservoir. In some embodiments, the bottle cap comprises a screw cap.

[0009] In some embodiments, the reservoir interface further comprises one or more alignment tabs and wherein the mouth of the reservoir comprises one or more alignment channels, wherein

the one or more alignment tabs are received within the one or more alignment channels thereby rotationally fixing an orientation of the reservoir interface relative to the reservoir. In some embodiments, the nozzle cap is rotationally fixed relative to the nozzle. In some embodiments, the flow control device further comprises a filter disposed within the nozzle. In some embodiments, the polymeric matrix comprises poly hydroxyl ethyl methacrylate (pHEMA), poly hydroxyl ethyl methacrylate-co-methacrylic acid, or a combination thereof. In some embodiments, the polymeric matrix comprises at least one monomer selected from the group consisting of hydroxyethyl methacrylate (HEMA), methacrylic acid (MAA), N-vinyl-pyrrolidone (NVP), dimethylacrylamide (DMA), t-butyl methacrylate (TBM), and Methacryloxypropyltris(trimethylsiloxy)silane (TRIS). In some embodiments, the ophthalmic agent comprises at least one of Timolol Maleate, Levofloxacin, Dorzolamide, Brimonidine Tartrate, Bimatoprost, Tetrahydrozolin, or Olopatadine. In some embodiments, the ophthalmic agent comprises Timolol Maleate and Brimonidine Tartrate. In some embodiments, the preservative comprises at least one of benzalkonium chloride, SofZia, or Purite. In some embodiments, the reservoir comprises less than 100 milliliters of an ophthalmic formulation.

[0010] In another example, the present disclosure provides a method of controlling a preservative concentration within an ophthalmic formulation. The method may comprise: receiving the bottle of any aspect or embodiment herein and rotating the nozzle or the bottle cap relative to the reservoir.

[0011] In another aspect, the present disclosure provides a method of fabricating the flow control device of any aspect or embodiment herein. The method may comprise: filling the reservoir with the ophthalmic formulation; placing the reservoir interface on the reservoir; placing the nozzle cap on the nozzle; and placing the nozzle at the mouth of the reservoir. In some embodiments, the method further comprises placing a bottle cap on the nozzle.

[0012] In another aspect a kit comprising the flow control device of any aspect or embodiment herein and a packaging is provided. In some embodiments, the kit further comprises a label, wherein the label comprises an indication of a contents of the ophthalmic formulation disposed within the reservoir.

[0013] In another example, the present disclosure provides a flow control device for delivering an ophthalmic formulation. The device may comprise: a reservoir, the reservoir comprising the ophthalmic formulation disposed therein, the ophthalmic formulation comprising an ophthalmic agent and a preservative; a nozzle, the nozzle comprising: an outlet, an interior volume comprising a preservative removing device, and one or more nozzle apertures fluidically connecting the interior volume with an exterior of the nozzle; and a reservoir interface comprising one or more reservoir apertures, wherein upon rotation or translation of the nozzle

CLAIMS

WHAT IS CLAIMED IS:

1. A flow control device for delivering an ophthalmic formulation, the device comprising:
 - a reservoir, the reservoir comprising the ophthalmic formulation disposed therein, the ophthalmic formulation comprising an ophthalmic agent and a preservative;
 - a nozzle, the nozzle comprising:
 - an outlet,
 - an interior volume comprising a preservative removing device,
 - one or more nozzle apertures fluidically connecting the interior volume with an exterior of the nozzle;
 - a reservoir interface comprising one or more reservoir apertures, wherein upon rotation or translation of the nozzle relative to the reservoir interface, the one or more nozzle apertures are fluidically connected with the one or more reservoir apertures;
 - a bottle cap wherein one or more nozzle apertures are aligned with the one or more reservoir apertures when the bottle cap is removed and wherein one or more nozzle apertures are not aligned with the one or more reservoir apertures when the bottle cap is coupled to the nozzle; and
 - a spring disposed between the nozzle and the reservoir interface, wherein a restoring force of the spring translates the nozzle to an aligned translational position when the bottle cap is removed.
2. The flow control device of claim 1, wherein the preservative removing device comprises a polymeric matrix comprising absorbed molecules of the preservative from the ophthalmic formulation.
3. The flow control device of claim 1, wherein, when the bottle cap is in a closed state, the nozzle is not in the aligned position.
4. The flow control device of claim 3, wherein, when the bottle cap is in a closed state, the spring is at least partially compressed.
5. The flow control device of claim 3, further comprising a translation stop.
6. The flow control device of claim 4, wherein the translation stop comprises a plug configured to seal the one or more nozzle apertures.
7. The flow control device of claim 4, wherein the translation stop comprises a rotation stop for the bottle cap.
8. The flow control device of claim 1, wherein the nozzle comprises a housing configured to contain the preservative removing device, wherein the housing is translated in

relation to an exterior surface of the reservoir interface, optionally wherein a gasket provides a fluidic seal between the reservoir interface and the nozzle, optionally wherein an interference fit provides a fluidic seal between the reservoir interface and the nozzle.

9. A flow control device for delivering an ophthalmic formulation, the device comprising:

a reservoir, the reservoir comprising the ophthalmic formulation disposed therein, the ophthalmic formulation comprising an ophthalmic agent and a preservative;

a nozzle, the nozzle comprising:

an outlet,

an interior volume comprising a preservative removing device, and

one or more nozzle apertures fluidically connecting the interior volume with an exterior of the nozzle;

a reservoir interface positioned between the reservoir and the nozzle, the reservoir interface comprising one or more reservoir apertures fluidically connecting an interior of the reservoir with an exterior of the reservoir, wherein upon rotation or translation of the nozzle relative to the reservoir interface, the one or more nozzle apertures are fluidically connected or disconnected from the one or more reservoir apertures;

a spring disposed between the reservoir interface and the nozzle such that the spring provides a restoring force opposing a compressing motion by the nozzle upon rotation or translation of the nozzle relative to the reservoir interface; and

a bottle cap, wherein the one or more nozzle apertures are fluidically connected with the one or more reservoir apertures when the bottle cap is removed and wherein the one or more nozzle apertures are fluidically disconnected with the one or more reservoir apertures when the bottle cap is coupled to the nozzle.

10. The flow control device of claim 9, wherein the preservative removing device comprises a polymeric matrix comprising absorbed molecules of the preservative from the ophthalmic formulation.

11. The flow control device of claim 10, wherein upon rotation or translation of the nozzle, the one or more nozzle apertures are fluidically connected or disconnected from the one or more reservoir apertures, thereby allowing or preventing flow of the ophthalmic formulation between the interior volume of the nozzle and the reservoir and stabilizing a concentration of the preservative in the ophthalmic formulation disposed within the reservoir.

12. The flow control device of claim 9, wherein, when the bottle cap is removed, the nozzle is in an aligned rotational position.

13. The flow control device of claim 12, wherein rotation of the bottle cap about an axis of rotation relative to the reservoir rotates the nozzle about the axis of rotation relative to the reservoir.

14. The flow control device of claim 9, wherein, when the bottle cap is removed, the nozzle is in an aligned translational position.

15. The flow control device of claim 14, wherein the restoring force of the spring translates the nozzle to the aligned translational position when the bottle cap is removed.

16. The flow control device of claim 15, wherein, when the bottle cap is in a closed state, the nozzle is not in the aligned position.

17. The flow control device of claim 16, wherein, when the bottle cap is in a closed state, the spring is at least partially compressed.

18. The flow control device of claim 16, further comprising a translation stop.

19. The flow control device of claim 18, wherein the translation stop comprises a plug configured to seal the one or more nozzle apertures.

20. The flow control device of claim 18, wherein the translation stop comprises a rotation stop for the bottle cap.

21. The flow control device of claim 9, wherein the nozzle comprises a housing configured to contain the preservative removing device, wherein the housing is translated in relation to an exterior surface of the reservoir interface.

22. The flow control device of claim 10, wherein the polymeric matrix comprises at least one monomer selected from the group consisting of hydroxyethyl methacrylate (HEMA), methacrylic acid (MAA), N-vinyl-pyrrolidone (NVP), dimethylacrylamide (DMA), t-butyl methacrylate (TBM), 2-sulfoethyl methacrylate (SEM), acrylamide (AM), and Methacryloxypropyltris(trimethylsiloxy)silane (TRIS).

23. The flow control device of claim 9, wherein the ophthalmic agent comprises at least one of Timolol Maleate, Levofloxacin, Dorzolamide, Brimonidine Tartrate, Bimatoprost, Tetrahydrozolin, Latanoprost, or Olopatadine.

24. The flow control device of claim 9, wherein the preservative comprises at least one of benzalkonium chloride, solutions of borate, sorbitol, propylene glycol, cetrimonium chloride, cetrimonium bromide, or stabilized oxychloro complexes.