

What is claimed is:

1. A method of externally sterilizing a drug delivery device utilizing Nitrogen Dioxide (NO₂), comprising:
placing the drug delivery device in a sterilization chamber;
introducing into the chamber a dose of NO₂ having a concentration of between about 2 and 20 milligrams per Liter by
applying a vacuum level of between about 10 and 600 Torr and holding the vacuum level for a dwell time of between about 2 and 20 minutes;
repeating the step of introducing into the chamber a dose of NO₂ for a number of pulses between about 1 and 24;
purging the sterilization chamber of at least substantially all of the NO₂; and
aerating the sterilization chamber.
2. A method as in claim 1, wherein the drug delivery device is a pre-filled syringe comprising a barrel, a stopper, a plunger rod, and a backstop and wherein the barrel contains a medicament.
3. A method as in any of claims 1-2, wherein the medicament is a VEGF antagonist.
4. A method as in any of claims 1-3, wherein the barrel is a plastic barrel.
5. A method as in any of claims 1-4, wherein the vacuum level is between about 100 and 500 Torr.
6. A method as in any of claims 1-5, wherein the vacuum level is between about 150 and 400 Torr.
7. A method as in any of claims 1-6, wherein the vacuum level is between about 150 and 300.
8. A method as in any of claims 1-7, wherein the concentration of the dose of NO₂ is between about 2 and 10 milligrams per Liter.
9. A method as in any of claims 1-8, wherein the concentration of the dose of NO₂ is between about 2 and 7 milligrams per Liter.
10. A method as in any of claims 1-9, wherein the chamber has a relative humidity is between about 70 and 90 percent.
11. A method as in any of claims 1-10, wherein the dwell time is between about 2 and 12 minutes.
12. A method as in any of claims 1-11, wherein the dwell time is between about 2 and 7 minutes.
13. A method as in any of claims 1-12, wherein the number of pulses is between about 1 and 12.
14. A method as in any of claims 1-13, wherein the number of pulses is between about 1 and 8.
15. A method as in any of claims 1-14, wherein the number of pulses is between about 1 and 4.

16. A method as in any of claims 1-15, wherein the number of pulses is between about 1 and 2.
17. A method as in any of claims 1-16, wherein the step of aerating the sterilization chamber includes aerating the sterilization chamber a number of cycles between about 12 and 70 cycles to at least substantially prevent discoloration of the drug delivery device.
18. A method as in any of claims 1-17, wherein the method of externally sterilizing the drug delivery device achieves at least a 2 logs microbial reduction.
19. A method as in any of claims 1-18, wherein the method of externally sterilizing the drug delivery device achieves at least a 3 logs microbial reduction.
20. A method as in any of claims 1-19, wherein the method of externally sterilizing the drug delivery device achieves at least a 4 logs microbial reduction.
21. A method as in any of claims 1-20, wherein the method of externally sterilizing the drug delivery device achieves at least a 5 logs microbial reduction.
22. A method as in any of claims 1-21, wherein the method of externally sterilizing the drug delivery device achieves at least a 6 logs microbial reduction.
23. A method of externally sterilizing a drug delivery device utilizing Nitrogen Dioxide (NO₂), comprising:
placing the drug delivery device in a sterilization chamber;
introducing into the chamber a dose of NO₂ having a concentration of between about 5 and 20 milligrams per Liter by applying a vacuum level of between about 150 and 500 Torr and holding the vacuum level for a dwell time of between about 5 and 10 minutes;
repeating the step of introducing into the chamber a dose of NO₂ for a number of pulses between about 1 and 8;
purging the sterilization chamber of at least substantially all of the NO₂; and
aerating the sterilization chamber a number of cycles between about 20 and 90.
24. A method of externally sterilizing a pre-filled syringe having a drug container and a medicament contained in the drug container, the method of externally sterilizing comprising the following steps:
placing the drug delivery device in a sterilization chamber;
introducing into the chamber a dose of Nitrogen Dioxide (NO₂) having a predetermined concentration by applying a predetermined vacuum level and holding the vacuum level for a predetermined dwell time;
repeating the step of introducing into the chamber a dose of NO₂ for a predetermined number of pulses;
purging the sterilization chamber of at least substantially all of the NO₂;
aerating the sterilization chamber a predetermined number of cycles;
wherein the method of externally sterilizing the pre-filled syringe achieves at least a log 6 lethality target for the pre-filled syringe while realizing an ingress of NO₂ gas into the drug container of less than 3.0 parts per million, as measured 30 days after externally sterilizing the pre-filled syringe.