particles. There is a need for developing particle control strategies that take into consideration the impact of particles on patient safety.

Summary

[0004] Provided herein are methods for making injectable pharmaceutical composition by leveraging information of particles historically detected in injectable compositions (e.g., size and materials composition of particles) and the corresponding toxicology and safety evaluations on patients. In one aspect, the present disclosure refers to a method of making an injectable pharmaceutical composition comprising etanercept, the method comprises: detecting the presence of one or more particles in the composition, analyzing the size of the particles and the materials comprised in the particles, and accepting the injectable pharmaceutical composition if the largest particle of the one or more particles has a length (L) of no more than about 19,200 μm, a width (W) of no more than about 2,939 μm, and a mass (M) of no more than about 97,200 μg, wherein the one or more particles comprise acrylic, aluminum, aliphatic hydrocarbon, charcoal, borosilicate glass, wool and silk, polyester (PET), polyurethane, polyether ether ketone, polytetrafluoroethylene (PTFE), polyoxymethylene (POM), polystyrene, silicon carbide, or stainless steel. In one example, the disclosure as disclosed herein comprises a method of making an injectable pharmaceutical composition comprising etanercept, the method comprises detecting the presence of one or more particles in the composition, analyzing the size of the particles and the materials comprised in the particles, and accepting the injectable pharmaceutical composition if the largest particle of the one or more particles has a size and a mass within certain range disclosed herein. In one example, the invention disclosed herein comprises a method of making an injectable pharmaceutical composition comprising etanercept, the method comprises detecting the presence of one or more particles in the composition, analyzing the size of the particles and the materials comprised in the particles, and accepting the injectable pharmaceutical composition if the largest particle of the one or more particles has a length (L) of no more than about 19,200 μm, a width (W) of no more than about 2,939 μm, and a mass (M) of no more than about 97,200 μg, and wherein the one or more particles comprise acrylic, aluminum, aliphatic hydrocarbon, charcoal, borosilicate glass, wool, silk, polyester (PET), polyurethane, polyether ether, polytetrafluoroethylene (PTFE), polyoxymethylene (POM), polystyrene, silicon carbide, or stainless steel.

The size and mass range of the largest particle that may be found in an injectable entanercept composition comprising each of the materials are also disclosed herein. In one example, the injectable pharmaceutical composition is suitable for subcutaneous administration.

[0005] In another example, the disclosure as disclosed herein comprises a method of making an injectable pharmaceutical composition comprising darbepoetin, the method comprises detecting the presence of one or more particles in the composition, analyzing the size of the particles and the materials comprised in the particles, and accepting the composition if the largest particle of the one or more particles has a L of no more than about 4,530 μm, a W of no more than about 8,890 μm, and a M of no more than about 21,190 μg, and wherein the one or more particles

comprise acrylate, aluminum, cellulose, epoxy resin, keratin, hydrated aluminum silicate, magnesium, magnesium silicate, nitrocellulose, polyurethane, polytetrafluoroethylene (PTFE), stainless steel, zinc, borosilicate glass, iron, iron and nickel rich material with phosphate, polyamide, polyethylene, polyvinyl chloride (PVC), or titanium. The size and mass range of the largest particle that may be found in an injectable darbepoetin composition comprising each of the materials are also disclosed herein. In one example, the injectable pharmaceutical composition comprising darbepoetin is suitable for intravenous or subcutaneous administration.

[0006] In another example, the disclosure as disclosed herein comprises a method of making an injectable pharmaceutical composition comprising pegfilgrastim, the method comprises: detecting the presence of one or more particles in the composition, analyzing the size of the particles and the materials comprised in the particles, and accepting the composition if the largest particle of the one or more particles has a L of no more than about 3,500 μm, a W of no more than about 430 μm, and a M of no more than about 5,100 μg, and wherein the one or more particles comprise aluminum, calcium carbonate, iron, polytetrafluorocarbon, Poly(ethylacrylate), polystyrene, polysulfone, poly(isobutylene)-butyl rubber, rubber, silicate, silicone, or stainless steel. The size and mass range of the largest particle that may be found in an injectable pegfilgrastim composition comprising each of the materials are also disclosed herein. In one example, the injectable pharmaceutical composition comprising pegfilgrastim is suitable for subcutaneous administration.

Brief Description of the Drawings

[0007] Figure 1 shows a particle comprising acrylic in an injectable composition comprising etanercept.

[0008] Figure 2 shows particles comprising charcoal in an injectable composition comprising etanercept.

[0009] Figure 3 shows a particle comprising borosilicate glass in an injectable composition comprising etanercept.

[0010] Figure 4 shows a particle comprising acrylate in an injectable composition comprising darbepoetin.

[0011] Figure 5 shows a particle comprising aluminum in an injectable composition comprising darbepoetin.

[0012] Figure 6 shows a particle comprising calcium carbonate in an injectable composition

Claims

What is claimed is:

1. A method of making an injectable pharmaceutical composition comprising etanercept, the method comprises:
   detecting the presence of one or more particles in the composition,
   analyzing the size of the particles and the materials comprised in the particles, and
   accepting the injectable pharmaceutical composition if the largest particle of the one or more particles has a length (L) of no more than about 19,200 μm, a width (W) of no more than about 2,939 μm, and a mass (M) of no more than about 97,200 μg,
   wherein the one or more particles comprise acrylic, aluminum, aliphatic hydrocarbon, charcoal, borosilicate glass, wool and silk, polyester (PET), polyurethane, polyether ether ketone, polytetrafluoroethylene (PTFE), polyoxymethylene (POM), polystyrene, silicon carbide, or stainless steel.

2. The method of claim 1, wherein the largest particle of the one or more particles has a L of no more than about 257 μm, a W of no more than about 133 μm, and a M of no more than about 5.4 μg, and the one or more particles comprise acrylic.

3. The method of claim 1, wherein the largest particle of the one or more particles has a L of no more than about 420 μm, a W of no more than about 225 μm, and a M of no more than about 0.001 μg, and the one or more particles comprise aluminum.

4. The method of claim 1, wherein the largest particle of the one or more particles has a L of no more than about 131 μm, a W of no more than about 64 μm, and a M of no more than about 0.42 μg, and the one or more particles comprise aliphatic hydrocarbon.

5. The method of claim 1, wherein the largest particle of the one or more particles has a L of no more than about 176 μm, a W of no more than about 110 μm, and a M of no more than about 2.9 μg, and the one or more particles comprise charcoal.

6. The method of claim 1, wherein the largest particle of the one or more particles has a L of no more than about 5,047 μm, a W of no more than about 2,939 μm, and a M of no more than about 97,200 μg, and the one or more particles comprise borosilicate glass.

7. The method of claim 1, wherein the largest particle of the one or more particles has a L of no more than about 19,200 μm, a W of no more than about 50 μm, and a M of no more than about 50 μg wool and no more than about 50 μg silk, and the one or more particles comprise natural protein fiber (wool and silk).

8. The method of claim 1, wherein the largest particle of the one or more particles has a L of no more than about 2,388 μm, a W of no more than about 67 μm, and a M of no more than about 14.7 μg, and the one or more particles comprise polyester.

9. The method of claim 1, wherein the largest particle of the one or more particles has a L of no more than about 359 μm, a W of no more than about 306 μm, and a M of no more than about 21 μg, and the one or more particles comprise polyurethane.

10. The method of claim 1, wherein the largest particle of the one or more particles has a L of no more than about 5,150 μm, a W of no more than about 300 μm, and a M of no more than about 2,330 μg, and the one or more particles comprise polyether ether ketone.

11. The method of claim 1, wherein the largest particle of the one or more particles has a L of no more than about 700 μm, a W of no more than about 250 μm, and a M of no more than about 45.9 μg, and the one or more particles comprise PTFE.

12. The method of claim 1, wherein the largest particle of the one or more particles has a L of no more than of about 1,891 μm, a W of no more than about 596.8 μm, and a M of no more than about 1,010 μg, and the one or more particles comprise POM.

13. The method of claim 1, wherein the largest particle of the one or more particles has a L of no more than of about 6,154 μm, a W of no more than about 2,454 μm, and a M of no more than about 39,300 μg, and the one or more particles comprise polystyrene.

14. The method of claim 1, wherein the largest particle of the one or more particles has a L of no more than of about 359 μm, a W of no more than about 306 μm, and a M of no more than about 48.7 μg, and the one or more particles comprise silicon carbide.

15. The method of claim 1, wherein the largest particle of the one or more particles has a L of no more than of about 450 μm, a W of no more than about 400 μm, and a M of no more than about 72 μg, and the one or more particles comprise stainless steel.

16. The method of claim 1, wherein the injectable pharmaceutical composition is suitable for subcutaneous administration.