CLAIMS:

1. A method for the preparation of an ~~highly purified and heat stable~~ oxygen carrier-containing pharmaceutical composition, the oxygen carrier-containing pharmaceutical composition including hemoglobin, the hemoglobin including cross-linked polymeric hemoglobin, the method comprising:

(a) providing whole blood including at least red blood cells and plasma;

(b) separating the red blood cells from the plasma in the whole blood;

(c) filtering the red blood cells that were separated from the plasma to obtain a filtered red blood cell fraction;

(d) lysing the red blood cells to create a solution comprising a lysate of disrupted red blood cells;

(e) extracting a first hemoglobin solution from the lysate;

(f) performing one or more purification processes ~~to produce a purified~~on the first hemoglobin solution;

(g) cross-linking hemoglobin tetramers in the first hemoglobin solution to create a second hemoglobin solution including cross-linked polymeric hemoglobin, the polymeric hemoglobin including two or more cross-linked hemoglobin tetramers;

(h) heat treating the second hemoglobin solution including the cross-linked polymeric hemoglobin in a deoxygenated environment at a temperature greater than 85°C and less than or equal to approximately 95°C for a period of less than approximately 40 minutes to denature and precipitate any residual ~~non-cross-linked tetrameric~~non-reacted hemoglobin, ~~any dimeric~~ non-stabilized hemoglobin (dimer), and any other impurities ~~such to form a heat stable solution including a cross-linked polymeric hemoglobin~~;

(i) cooling the heat-treated solution to a temperature approximately less than or equal to 25 °C in approximately two minutes or less to prevent formation of met-hemoglobin;

(j) removing precipitate by a centrifugation or a filtration apparatus to form a solution of ~~purified, heat-stable~~ hemoglobin including cross-linked polymeric hemoglobin ~~having an undetectable concentration of dimer~~.

2. The method of claim 1 further comprising adding N-acetyl cysteine immediately following heat treating.

3. The method of claim 1 wherein the cooling is performed in less than one minute.

4. The method of claim 1 wherein the heat treatment occurs at a temperature range of greater than 85 °C and less than 90 °C for a period from about 8 minutes to about 30 minutes.

5. The method of claim 1 wherein the heat treatment occurs at approximately 90 °C for a period from about 45 seconds to about 150 seconds.

6. The method of claim 1 wherein the heat treatment occurs at approximately 95 °C for a period from 30 to about 100 seconds.

7. The method of claim 1 further comprising adding N-acetyl cysteine immediately prior to heat treating.

8. The method of claim 2 further comprising adding N-acetyl cysteine immediately prior to heat treating.

9. The method of claim 1 wherein the performing one or more purification processes ~~to produce a purified hemoglobin solution~~ includes ultrafiltration.

10. The method of claim 1 wherein the performing one or more purification processes ~~to produce a purified hemoglobin solution~~ includes ~~purification by~~ chromatography.

~~11. A highly purified and heat stable oxygen carrier containing pharmaceutical composition including hemoglobin and N-acetyl cysteine, the hemoglobin including cross-linked polymeric hemoglobin, the cross-linked polymeric hemoglobin prepared by:~~

~~(a) providing whole blood including at least red blood cells and plasma;~~

~~(b) separating the red blood cells from the plasma in the whole blood;~~

~~(c) filtering the red blood cells that were separated from the plasma to obtain a filtered red blood cell fraction;~~

~~(d) lysing the red blood cells to create a solution comprising a lysate of disrupted red blood cells;~~

~~(e) extracting a first hemoglobin solution from the lysate;~~

~~(f) performing one or more purification processes on the first hemoglobin solution;~~

(g) cross-linking hemoglobin tetramers in the first hemoglobin solution to create a second hemoglobin solution including cross-linked polymeric hemoglobin, the polymeric hemoglobin including two or more cross-linked hemoglobin tetramers;

(h) heat-treating the second hemoglobin solution including the cross-linked polymeric hemoglobin in a deoxygenated environment at a temperature greater than 85°C and less than or equal to approximately 95°C for a period of less than approximately 40 minutes to denature and precipitate any residual non-reacted hemoglobin, non-stabilized hemoglobin, dimer, and any other impurities such that the resulting hemoglobin solution has an undetectable amount of dimer when measured using high performance liquid chromatography;

(i) cooling the heat-treated solution to a temperature approximately less than or equal to 25 °C in approximately two minutes or less to prevent formation of met-hemoglobin;

(j) adding N-acetyl cysteine either immediately prior to or after heat treating and cooling the second hemoglobin solution;

(k) removing precipitate formed during the heat treating by a centrifugation or a filtration apparatus.

12. A method of oxygenating tissue comprising providing the composition of claim 11 to animal tissue ex vivo.