albumin remains in the supernatant. Taken together, these advantages result in a significant increase in the overall recovery of these important commercial products.

[0018] As shown in the Examples, the use of a low pH, high alcohol precipitation step (Fraction I-IV-1 precipitation) as an initial step in the purification of IgG from cryo-poor plasma, allows for the production of pharmaceutical grade IgG compositions with unprecedented yields of 4.3-4.7 g IgG/L source plasma. These yields represent an approximate 20% to 25% increase in yield as compared to state-of-the-art manufacturing processes, such as those used to manufacture GAMMAGARD LIQUID® (Baxter International; Deerfield, IL) from the same plasma type.

[0018a] In one aspect, the present invention relates to a method for manufacturing an enriched immunoglobulin composition from a Cohn pool, the method comprising the steps of: (a) co-precipitating immunoglobulins and alpha-1-antitrypsin (A1PI) from a Cohn pool, in a first precipitation step by the addition of ethanol to the Cohn pool at a final concentration of from 20% to 30% (v/v) at a pH of from 5.0 to 6.0, to form a first precipitate and a first supernatant; (b) solubilizing immunoglobulins in the first precipitate, to form a first suspension having a soluble portion comprising immunoglobulins and an insoluble portion comprising A1PI;(c) separating the soluble portion of the first suspension from the insoluble portion of the first suspension; and (d) recovering the soluble fraction of the first suspension, thereby forming an enriched immunoglobulin composition.

[0018b] In another aspect, there is provided an enriched immunoglobulin composition prepared by a method disclosed herein.

[0018c] In another aspect, there is provided the use of an enriched immunoglobulin composition as disclosed herein in the preparation of a medicament for treating an immune deficiency, an inflammatory disease, an autoimmune disease, or an acute infection in an individual in need thereof, the medicament being suitable for administration to the subject.

[0019] Accordingly, among other aspects, the present invention provides a new plasma fractionation process which separates plasma or cryo-poor plasma in an initial step into a Fraction I-IV-1 precipitate and a Fraction I-IV-1 supernatant. The Fraction I-IV-1 precipitate contains nearly all immunoglobulins (*e.g.*, IgG, IgA, and IgM) and alpha 1 elastase inhibitor (A1PI), while the supernatant contains mainly albumin.

[0020] In one ~~aspect~~embodiment, the present ~~invention~~ disclosure provides a method for preparing an enriched immunoglobulin composition from a Cohn pool, the method comprising the steps of: (a) co-precipitating immunoglobulins and alpha-1-antitrypsin (A1PI) from cryo-poor plasma, in a first precipitation step, to form a first precipitate and a first supernatant; (b) solubilizing immunoglobulins in the first precipitate, to form a first suspension having a soluble portion comprising immunoglobulins and an insoluble portion comprising A1PI; (c) separating the soluble portion of the first suspension from the insoluble portion of the first suspension; and (d) recovering the soluble fraction of the first suspension, thereby forming an enriched immunoglobulin composition.

[0021] In one embodiment of the methods described above, the first precipitation step is an alcohol precipitation step.

[0022] In one embodiment of the methods described above, the alcohol precipitation step comprises adding ethanol to the cryo-poor plasma to achieve a final concentration of from 20% to 30% ethanol (v/v) at a pH of from 5 to 6.

[0055] In one embodiment of the methods described above, the final enriched IgG composition comprises at least 99% IgG.

[0056] In one embodiment of the methods described above, the method yields at least 4 g of IgG per L of cryo-poor plasma used in step (a).

[0057] In one embodiment of the methods described above, the method yields at least 4.25 g of IgG per L of cryo-poor plasma used in step (a).

[0058] In one embodiment of the methods described above, the method yields at least 4.5 g of IgG per L of cryo-poor plasma used in step (a).

[0059] In one embodiment of the methods described above, alpha-1-antitrypsin (A1PI) is further purified from an insoluble fraction of the first suspension.

[0060] In one embodiment of the methods described above, fibrinogen is further purified from an insoluble fraction of the first suspension

[0061] In one embodiment of the methods described above, Factor H is further purified from an insoluble fraction of the first suspension.

[0062] In one embodiment of the methods described above, an Inter-alpha-Trypsin Inhibitor protein (IαIp) is further purified from an insoluble fraction of the first suspension.

[0063] In one embodiment of the methods described above, the insoluble fraction of the first suspension is treated with finely divided silicon dioxide (SiO_2).

[0064] In one embodiment of the methods described above, albumin is further purified from the first supernatant.

[0065] In one ~~aspect~~embodiment, the present ~~invention~~ disclosure provides an enriched immunoglobulin composition prepared by a method according to any one of claims 1 to 63.

[0066] In one ~~aspect~~embodiment, the present ~~invention~~ disclosure provides a method for treating an immune deficiency, an inflammatory disease, an autoimmune disease, or an acute infection in an individual in need thereof, the method comprising administering an enriched immunoglobulin composition of claim 64 to the subject.

61. Use of an enriched immunoglobulin composition of claim 60 in the preparation of a medicament ~~A method~~ for treating an immune deficiency, an inflammatory disease, an autoimmune disease, or an acute infection in an individual in need thereof, the ~~method comprising~~ medicament being suitable for administration~~ering an enriched immunoglobulin composition of claim 60~~ to the subject.