CLAIMS

1. A process for preparing a purified conjugate in a solution, wherein the conjugate comprises an effector or a reporter molecule linked to a cell binding agent, the process comprising the steps of: (a) contacting the effector or the reporter molecule with a bifunctional linker reagent to covalently attach the linker to the effector or the reporter molecule and thereby prepare an unpurified first mixture comprising the effector or the reporter molecule having linkers bound thereto, (b) conjugating a cell binding agent to the effector or the reporter molecule having linkers bound thereto by reacting the unpurified first mixture with the cell binding agent to prepare a second mixture, and (c) subjecting the second mixture to a tangential flow filtration, dialysis, gel filtration, adsorptive chromatography, selective precipitation or a combination thereof to thereby prepare the purified conjugate.

2. The process of claim 1 in which step (b) is carried out in a solution at a pH from about 4 to about 9.

3. The process of claim 1, wherein the second mixture in step (b) is substantially free of undesired cross-linked, hydrolyzed species formed due to intra-molecular or inter-molecular reactions.

4. The process of claim 1, wherein the effector molecule is a cytotoxic agent.

5. The process of claim 4, wherein the cytotoxic agent is maytansinoids, taxanes, CC1065, or analogs thereof.

6. The process of claim 4, wherein the cytotoxic agent is a maytansinoid.

7. The process of claim 6, wherein the maytansinoid comprises a thiol group.

8. The process of claim 6, wherein the maytansinoid is DM1.

9. The process of claim 6, wherein the maytansinoid is DM4.

10. The process of claim 1, wherein the cell binding agent is interferons, interleukin 2 (IL-2), interleukin 3 (IL-3), interleukin 4 (IL-4), interleukin 6 (IL-6), insulin, EGF, TGF-α, FGF, G-CSF, VEGF, MCSF, GM-CSF, transferrin, or antibodies.

11. The process of claim 10, wherein the cell binding agent is an antibody.

12. The process of claim 11, wherein the antibody is a monoclonal antibody.

13. The process of claim 11, wherein the antibody is a human or a humanized monoclonal antibody.

14. The process of claim 10, wherein the antibody is MY9, anti-B4, EpCAM, CD2, CD3, CD4, CD5, CD6, CD11, CD19, CD20, CD22, CD26, CD30, CD33, CD37, CD38, CD40, CD44, CD56, CD79, CD105, CD138, EphA receptors, EphB receptors, EGFR, EGFRvIII, HER2, HER3, mesothelin, cripto, $alpha_vbeta_3$, $alpha_vbeta_5$, $alpha_vbeta_6$ integrin or C242.

15. The process of claim 13, wherein the human or the humanized antibody is My9-6, B4, C242, N901, DS6, EphA2 receptor, CD38, IGF-IR, CNTO 95, B-B4, trastuzumab, pertuzumab, bivatuzumab, sibrotuzumab, or rituximab.

16. The process of claim 1, wherein the linker is a cleavable or a non cleavable linker.

17. The process of claim 1, wherein the reporter molecule is a radioisotope.

CLAIMS

1. A process for preparing a purified conjugate in a solution, wherein the conjugate comprises a maytansinoid molecule linked to an antibody, the process comprising the steps of:

(a) contacting a maytansinoid molecule comprising a thiol group with a bifunctional linker reagent to covalently attach the linker to the maytansinoid molecule, wherein an excess of maytansinoid molecule relative to the bifunctional linker reagent is used, and thereby prepare an unpurified first mixture comprising the maytansinoid molecule having linkers bound thereto,

(b) conjugating an antibody to the maytansinoid molecule having linkers bound thereto by reacting the unpurified first mixture with the antibody in a solution having a pH from about 4 to about 9 to prepare a second mixture, and

(c) subjecting the second mixture to tangential flow filtration, dialysis, gel filtration, adsorptive chromatography, selective precipitation or a combination thereof to thereby prepare the purified conjugate.

2. The process of claim 1, wherein the second mixture in step (b) is substantially free of undesired cross-linked, hydrolyzed species formed due to intra-molecular or inter-molecular reactions.

3. The process of claim 1, wherein the maytansinoid molecule is DM1.

4. The process of claim 1, wherein the maytansinoid molecule is DM4.

5. The process of claim 1, wherein the antibody is a monoclonal antibody.

6. The process of claim 1, wherein the antibody is a human or a humanized monoclonal antibody.

7. The process of claim 1, wherein the antibody is MY9, anti-B4, C242, or an antibody that binds to an antigen selected from the group consisting of EpCAM, CD2, CD3, CD4, CD5, CD6, CD11, CD19, CD20, CD22, CD26, CD30, CD33, CD37, CD38, CD40, CD44, CD56, CD79, CD105, CD138, EphA receptors, EphB receptors, EGFR, EGFRvIII, HER2, HER3, mesothelin, cripto, $alpha_v beta_3$, $alpha_v beta_5$, and $alpha_v beta_6$ integrin.

8. The process of claim 6, wherein the human or the humanized antibody is huMy9-6, huB4, huC242, huN901, DS6, CNTO 95, B-B4, trastuzumab, pertuzumab, bivatuzumab, sibrotuzumab, rituximab, or a human or humanized antibody that binds to an antigen selected from the group consisting of EphA2 receptor, CD38, and IGF-IR.

9. The process of claim 1, wherein the linker is a cleavable or a non cleavable linker.

10. The process of claim 1, wherein the pH of the solution in step (b) is from about 5 to about 8.7.

11. The process of claim 1, wherein the pH of the solution in step (b) is from about 6.5 to about 8.5.

12. The process of claim 1, wherein the process further comprises the step of quenching the excess maytansinoid in the unpurified first mixture with a quenching reagent between steps (a) and (b).

13. The process of claim 12, wherein the quenching reagent is selected from the group consisting of 4-maleimidobutyric acid, 3-maleimidopropionic acid, N-ethylmaleimide, iodoacetamide, and iodoacetamidopropionic acid.