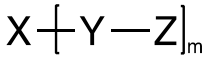
WHAT IS CLAIMED IS

1. A compound of Formula 1:



Formula 1

wherein:

m is an integer from 1 to 10;

X comprises an antigen;

wherein X comprises:

a self-antigen;

a transplant antigen,

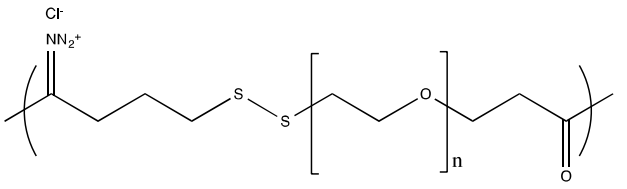
a food antigen, or

a therapeutic agent that is not naturally occurring;

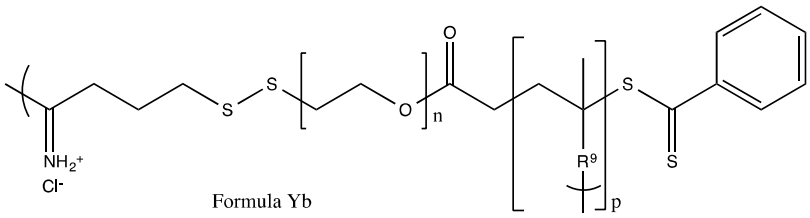
Y is of a linker moiety; and

Z comprises a liver targeting moiety selected from glucose, glucosamine, and N-acetylglucosamine.

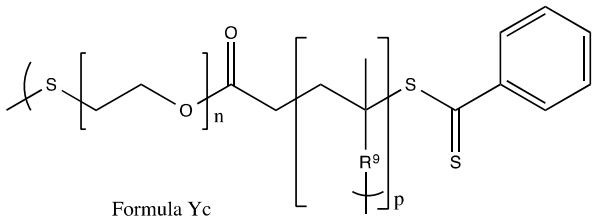
2. The composition of claim 1 where Y comprises a structure represented by one of Formulae Ya to Yp:



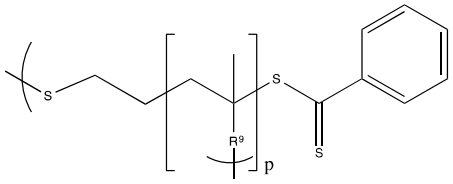
Formula Ya



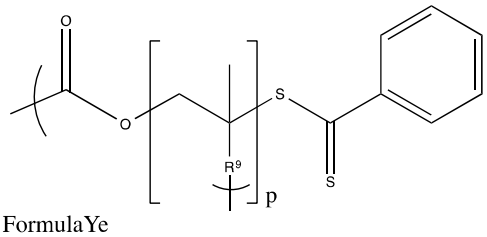
Formula Yb



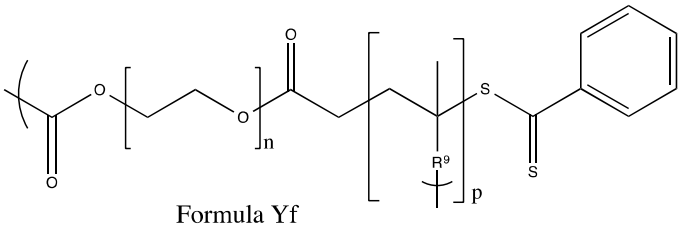
Formula Yc



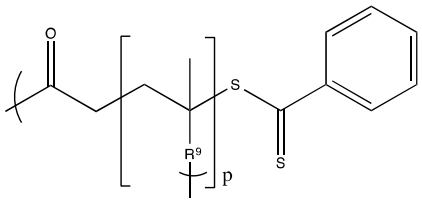
Formula Yd



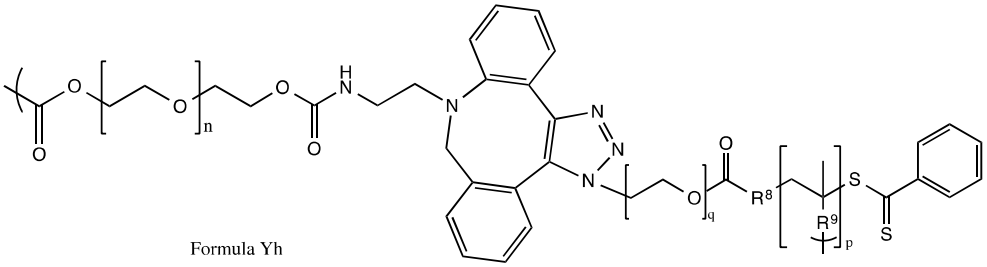
FormulaYe



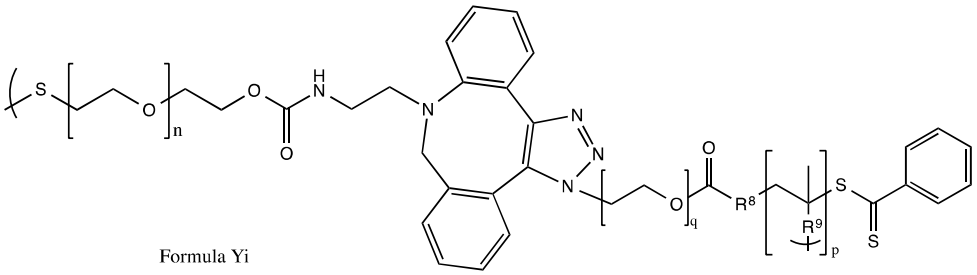
Formula Yf



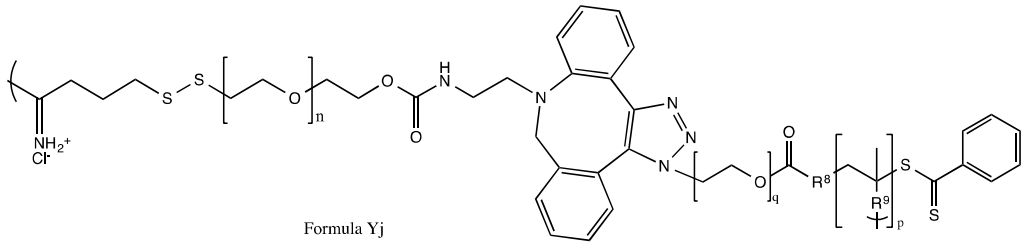
Formula Yg



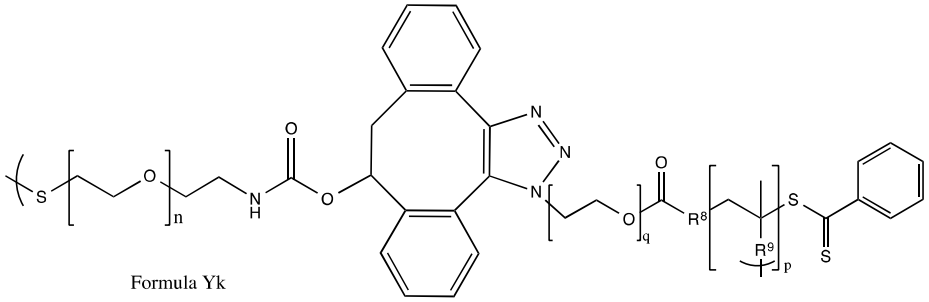
Formula Yh



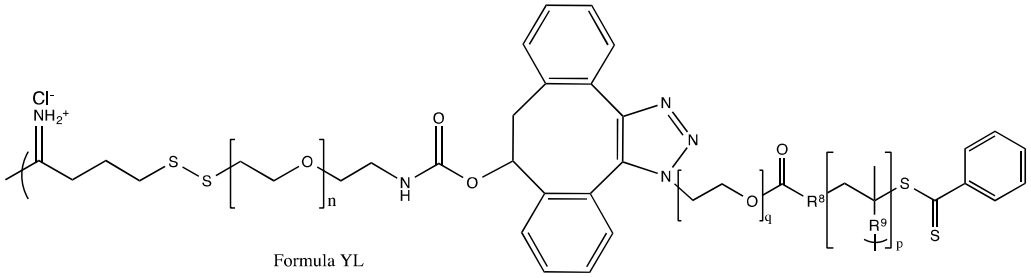
Formula Yi



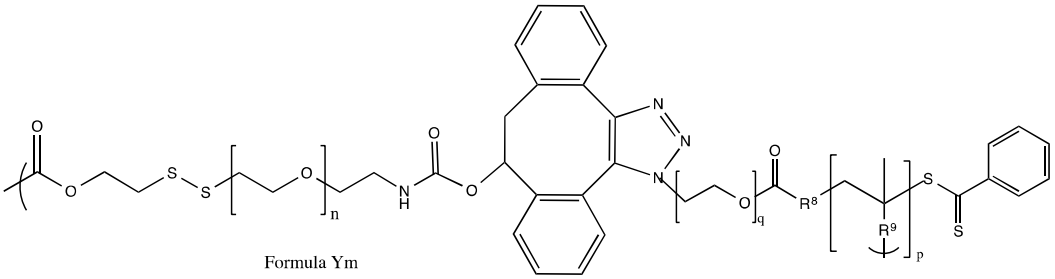
Formula Yj



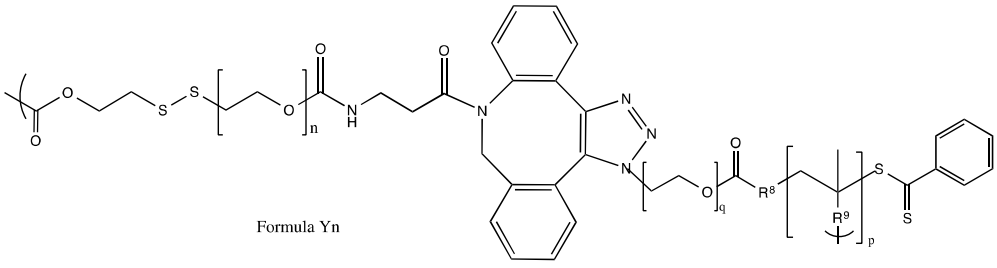
Formula Yk



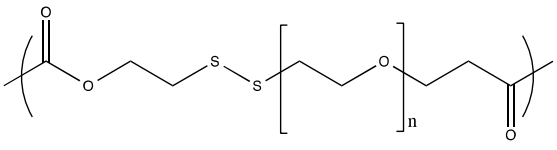
Formula YL



Formula Ym

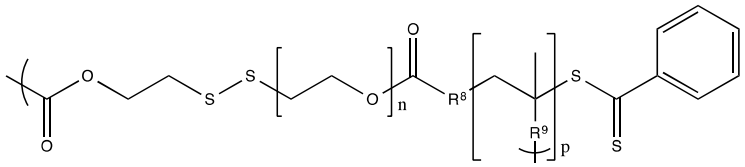


Formula Yn



Formula Yo

and



Formula Yp

where:

the left bracket "(" indicates the bond between X and Y;

the right or bottom bracket and ")" indicates the bond between Y and Z;

n is an integer from 1 to 100;

p is an integer from 2 to 150;

q is an integer from 1 to 44;

R^8 is $–CH_2–$ or $–CH_2\text{-}CH_2\text{-}C(CH_3)(CN)–$; and

R^9 is a direct bond or $–C(O)\text{-}NH–CH_2\text{-}CH_2–$.

3. The compound of Claim 1, wherein:

n is 40 to 80;

q is 3 to 20;

R^8 is $–CH_2\text{-}CH_2\text{-}C(CH_3)(CN)–$;

when R^9 is $–CH_2\text{-}CH_2–NH–C(O)–$; and

when W is a copolymer, R^{10} is 2-hydroxypropyl.

4. The compound of Claim 2 or 3, wherein Y comprises Formula Yc.

5. The composition of any one of Claims 2 to 4, wherein Y comprises Formula Ya, Formula Yb, Formula Ym or Formula Yn.

6. A compound for inducing tolerance to an antigen to which a subject develops an unwanted immune response, the compound comprising a compound of Formula 1:

$$X\left[Y—Z\right]_m$$

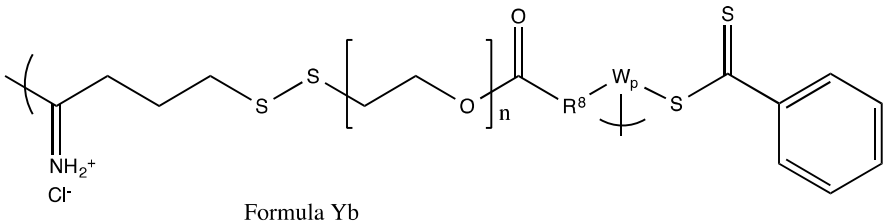
Formula 1

wherein:

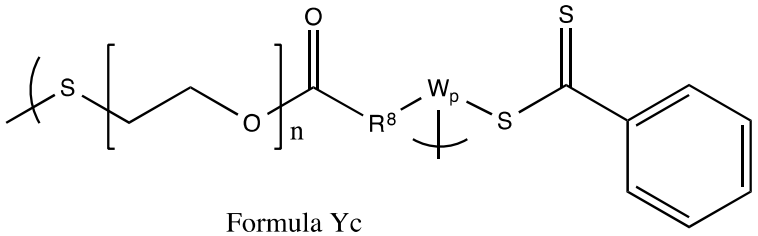
m is an integer from 1 to 10;

X comprises an antigen, wherein the antigen is a food antigen, a therapeutic agent, a transplant antigen, or a self-antigen;

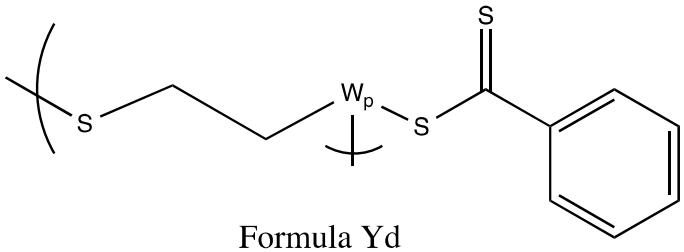
Y is selected from the group consisting of:



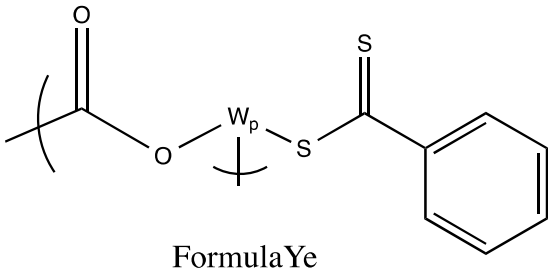
Formula Yb



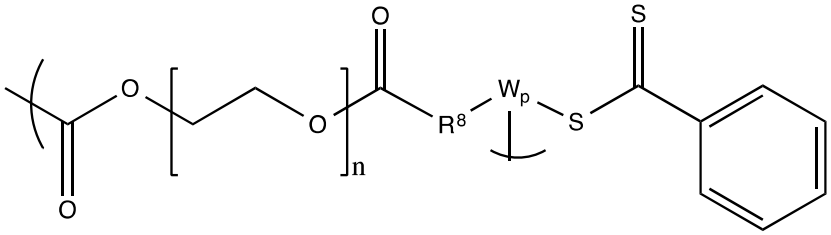
Formula Yc



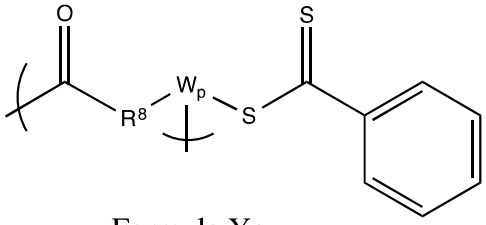
Formula Yd



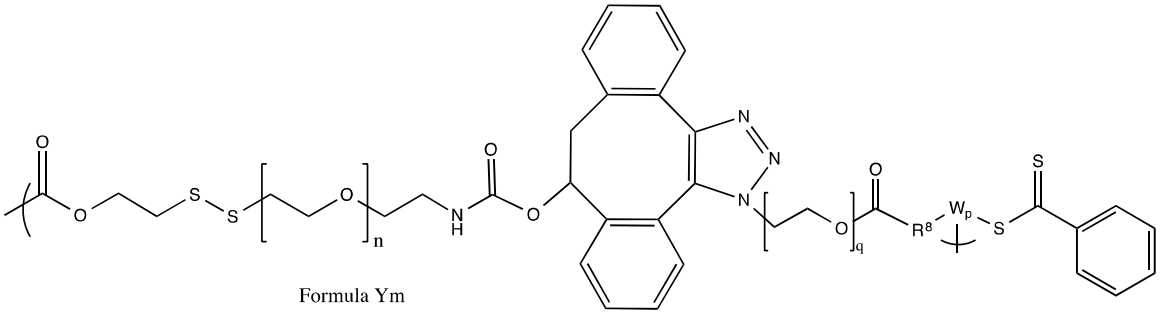
FormulaYe



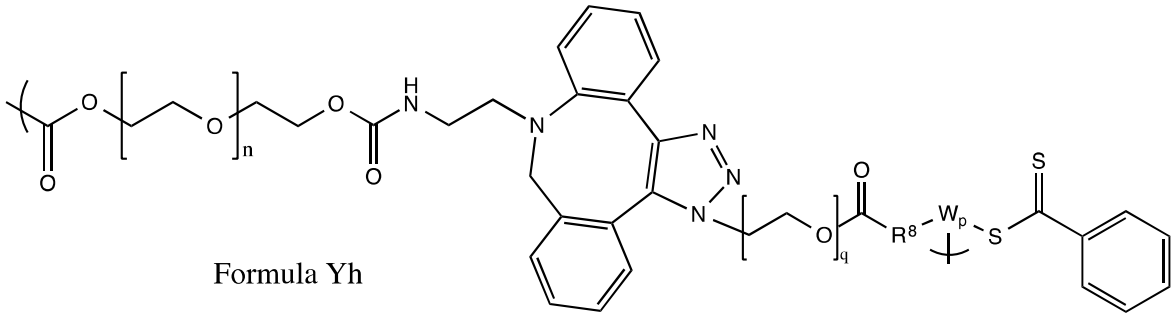
Formula Yf



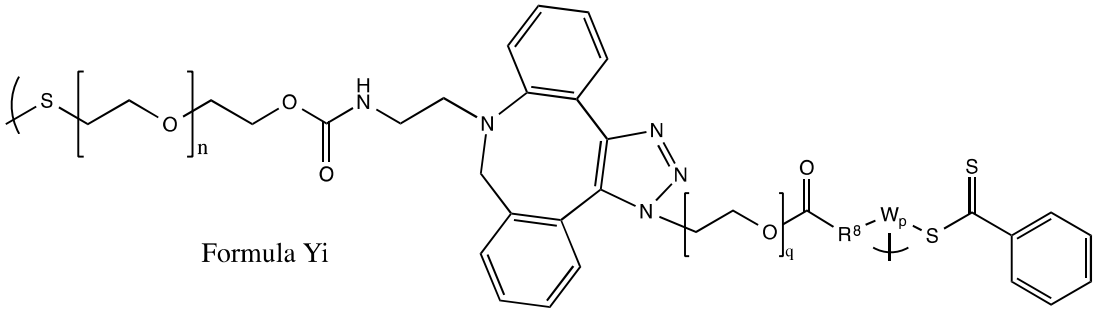
Formula Yg



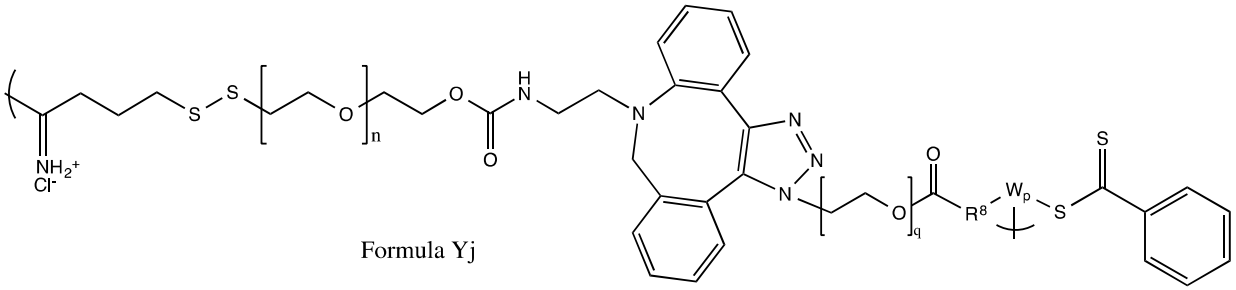
Formula Ym



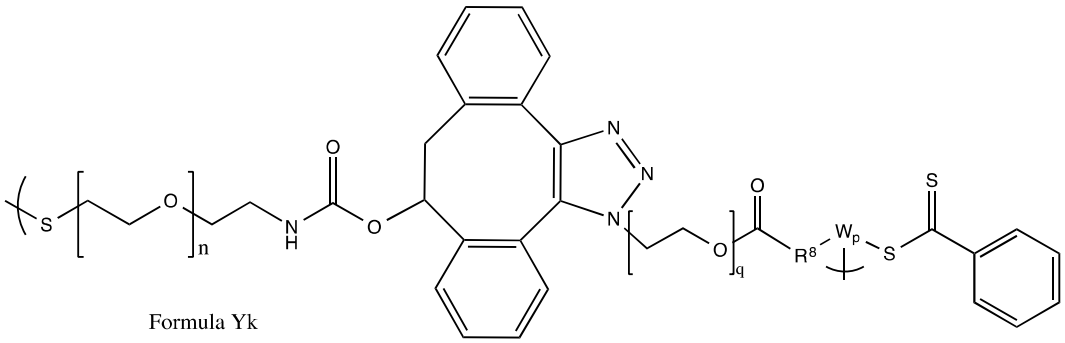
Formula Yh



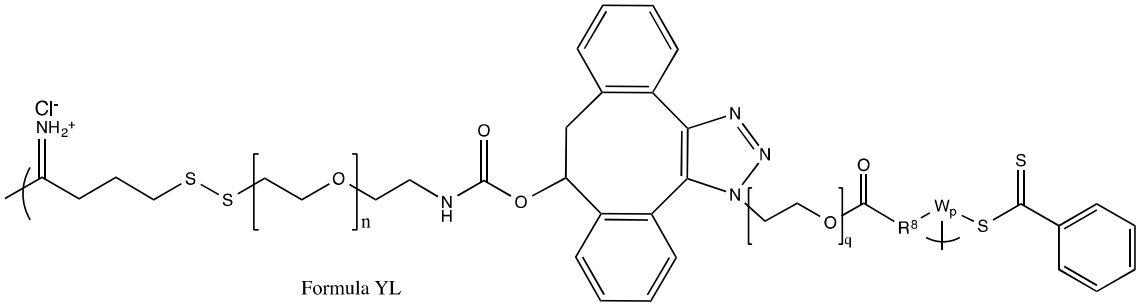
Formula Yi



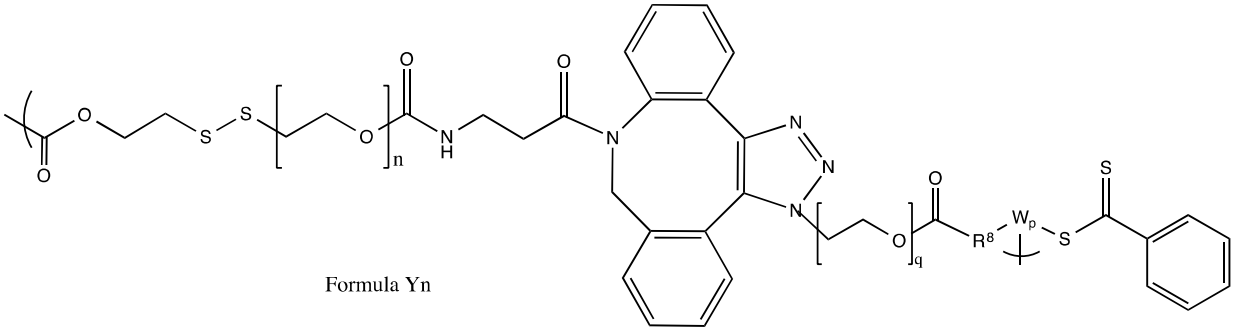
Formula Yj



Formula Yk

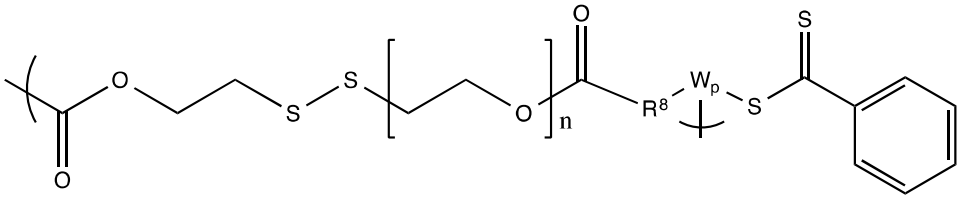


Formula YL



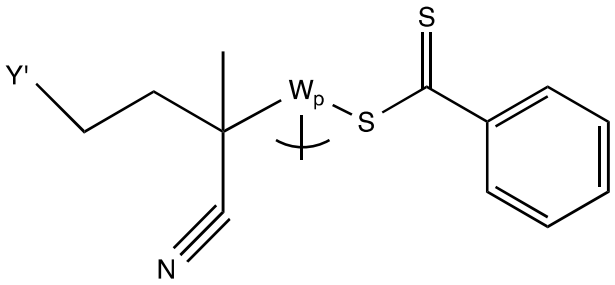
Formula Yn

and



Formula Yp

or Y has a portion represented by Formula Y'-CMP:



Formula Y'-CMP

where:

the left bracket "(" indicates the bond between X and Y;

the right or bottom bracket and ")" indicates the bond between Y and Z;

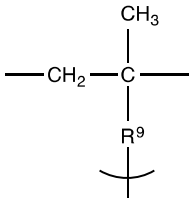
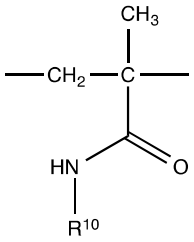
n is an integer from 1 to 100;

q is an integer from 1 to 44;

R^8 is $–CH_2–$ or $–CH_2-CH_2-C(CH_3)(CN)–$;

Y' represents the remaining portion of Y; and

W is a copolymer or a random copolymer of the same or different W^1 and W^2 groups, where:

W^1 =  and W^2 = 

where:

p is an integer from 2 to 150;

R^9 is a direct bond, $–CH_2-CH_2-–NH–C(O)–$, or $-CH_2-CH_2-(O-CH_2-CH_2)_t-NH-C(O)-$;

t is an integer from 1 to 5; and

R^{10} is an aliphatic group, an alcohol or an aliphatic alcohol; and

Z comprises a liver targeting moiety, wherein the liver targeting moiety comprises one or more of a glucosylating moiety and a galactosylating moiety.

7. The compound of any one of claims 1 to 6, wherein Z is the beta anomer.

8. The compound of any one of claims 1 to 7, wherein Z is conjugated at its C1, C2 or C6 to Y.

9. The compound of any one of claims 1 to 8, wherein Y is prepared using a linker precursor selected from N-hydroxysuccinamidyl-based linkers, malaemide-based linkers, vinylsulfone-based linkers, pyridyl di-thiol-poly(ethylene glycol) -based linkers, pyridyl di-thiol-based linkers, n-nitrophenyl carbonate-based linkers, NHS-ester-based linkers, and nitrophenoxy poly(ethylene glycol)ester-based linkers.

10. The compound of any one of claims 1 to 9, wherein X comprises a food antigen, wherein the food antigen is selected from the group consisting of conarachin (Ara h 1), allergen II (Ara h 2), arachis agglutinin, conglutin (Ara h 6), 31 kda major allergen/disease resistance protein homolog (Mal d 2), lipid transfer protein precursor (Mal d 3), major allergen Mal d 1.03D (Mal d 1), a-lactalbumin (ALA), lactotransferrin, actinidin (Act c 1, Act d 1), phytocystatin, thaumatin-like protein (Act d 2), kiwellin (Act d 5), ovomucoid, ovalbumin, ovotransferrin, and lysozyme, livetin, apovitillin, vosvetin, 2S albumin (Sin a 1), 1 IS globulin (Sin a 2), lipid transfer protein (Sin a 3), profilin (Sin a 4), profilin (Api g 4), high molecular weight glycoprotein (Api g 5), Pen a 1 allergen (Pen a 1), allergen Pen m 2 (Pen m 2), tropomyosin fast isoform, high molecular weight glutenin, low molecular weight glutenin, alpha-

, gamma- and omega-gliadin, hordein, secalin, avenin, major strawberry allergy Fra a 1-E (Fra a 1), and profilin (Mus xp 1).

11. The compound of claim 10, wherein the food antigen is selected from the group consisting of high molecular weight glutenin, low molecular weight glutenin, alpha-, gamma- and omega-gliadin, hordein, secalin, and avenin.

12. The compound of any one of claims 1 to 9, wherein X comprises a self-antigen, wherein the self-antigen is selected from insulin, proinsulin, preproinsulin, glutamic acid decarboxylase-65 (GAD-65), GAD-67, insulinomaassociated protein 2 (IA-2), and insulinoma-associated protein 2β (IA-2β), ICA69, ICA12 (SOX-13), carboxypeptidase H, Imogen 38, GLIMA 38, chromogranin- A, HSP-60, caboxypeptidase E, peripherin, glucose transporter 2, hepatocarcinoma-intestinepancreas/pancreatic associated protein, S100β, glial fibrillary acidic protein, regenerating gene II, pancreatic duodenal homeobox 1, dystrophia myotonica kinase, islet-specific glucose-6- phosphatase catalytic subunit-related protein, and SST G-protein coupled receptors 1-5.

13. The compound of claim 12, wherein X comprises a self-antigen, wherein the self-antigen is selected from myelin basic protein, myelin oligodendrocyte glycoprotein, and proteolipid protein antigens.

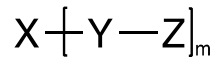
14. The compound of any one of claims 1 to 9, wherein X comprises a therapeutic agent, wherein the therapeutic agent is selected from Abciximab, Adalimumab, Agalsidase alfa, Agalsidase beta, Aldeslukin, Alglucosidase alfa, Factor VIII, Factor IX, Infliximab, L-asparaginase, Laronidase, Natalizumab, Octreotide, Phenylalanine ammonia-lyase (PAL), and Rasburicase (uricase).

15. The compound of any one of claims 1 to 9, wherein X comprises a human allograft transplant antigen, wherein the transplant antigen is selected from the group consisting of subunits of the MHC class I and MHC class II haplotype proteins, and minor blood group antigens RhCE, Kell, Kidd, Duffy and Ss.

16. A composition comprising the compound of any one of claims 1 to 15.

17. The use of the compound or composition of any one of claims 1 to 16, for the manufacture of a medicament for the treatment of a patient.

18. A compound for inducing tolerance to an antigen to which a subject develops an unwanted immune response, the compound comprising a compound of Formula 1:



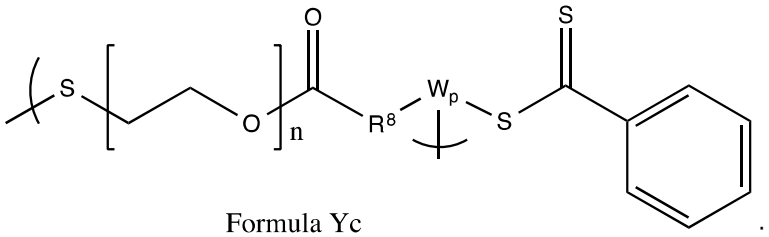
Formula 1

where:

m is an integer from 1 to 10;

X comprises an antigen to which patients develop an unwanted immune response, wherein the antigen is a food antigen, a therapeutic agent, or a self-antigen;

Y is :



Formula Yc ;

wherein:

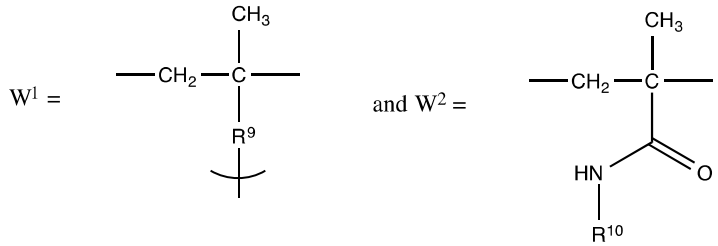
the left bracket "(" indicates a bond to X;

the bottom bracket and ")" indicates the bond between Y and Z;

n is an integer from 1 to 100;

where present R^8 $–CH_2\text{-}CH_2\text{-}C(CH_3)(CN)–$;

W represents a copolymer or a random copolymer of the same or different W^1 and W^2 groups, where:



where:

p is an integer from 2 to 150;

where present R^9 is a direct bond, $–CH_2\text{-}CH_2–NH–C(O)–$, or $\text{-}CH_2\text{-}CH_2\text{-}(O\text{-}CH_2\text{-}CH_2)_t\text{-}NH\text{-}C(O)\text{-}$ -;

t is an integer from 1 to 5; and

R^{10} is an aliphatic group, an alcohol, or an aliphatic alcohol; and

Z is a liver targeting moiety, wherein the liver targeting moiety comprises one or more of a glucosylating moiety and a galactosylating moiety.

19. The compound of claim 18, wherein Z comprises one or more of galactose, galactosamine,

N-acetylgalactosamine, glucose, glucosamine, or N-acetyl glucosamine.

20. The compound of claim 19, wherein Z is the beta anomer.

21. The compound of any one of claims 19 or 20, where Z conjugated at its C1, C2 or C6 to Y.

22. The compound of any one of claims 18 to 21, wherein X comprises:

a foreign transplant antigen against which transplant recipients develop an unwanted immune response;

a foreign food, animal, plant or environmental antigen against which patients develop an unwanted immune response;

a foreign therapeutic agent against which patients develop an unwanted immune response; or

a synthetic self-antigen against the endogenous version of which patients develop an unwanted immune response.

23. The compound of any one of claims 18 to 21, wherein X is a self-antigen and the unwanted immune response is an autoimmune response.

24. The compound of any one of claims 18 to 21, wherein X is selected from the group consisting of myelin oligodendrocyte glycoprotein, myelin proteolipid protein, and myelin basic protein and wherein the unwanted immune response is associated with multiple sclerosis.

25. The compound of any one of claims 18 to 21, wherein X is a is a food antigen selected from the group consisting of: conarachin (Ara h 1), allergen II (Ara h 2), arachis agglutinin, conglutin (Ara h 6), a-lactalbumin (ALA), lactotransferrin, Pen a 1 allergen (Pen a 1), allergen Pen m 2 (Pen m 2), tropomyosin fast isoform, high molecular weight glutenin, low molecular weight glutenin, alpha- gliadin, gamma-gliadin, omega-gliadin, hordein, secalin, and avenin.

26. The compound of any one of claims 18 to 21, wherein X is a therapeutic agent selected from Abciximab, Adalimumab, Agalsidase alfa, Agalsidase beta, Aldeslukin, Alglucosidase alfa, Factor VIII, Factor IX, Infliximab, L-asparaginase, Laronidase, Natalizumab, Octreotide, Phenylalanine ammonia-lyase (PAL), and Rasburicase (uricase).

27. The compound of any one of claims 18 to 21, wherein X is selected from the group consisting of insulin, proinsulin, and preproinsulin and wherein the unwanted immune response is associated with type 1 diabetes

mellitus.