CLAIMS

1. A method to sterilize a hydrogel linked with a cross-linker that degrades by beta elimination, which method comprises adjusting the pH of a medium containing said hydrogel so as to minimize degradation of said cross-linker and heating to sufficient temperature and time to effect sterilization, wherein:

(a) the pH of the medium is determined by non-reactive buffering of said medium, wherein said buffer is phosphate or acetate buffer; or

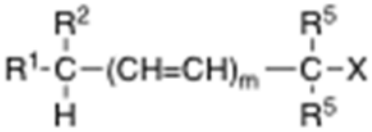
(b) wherein the adjusted pH is 2-5.

2. The method of claim 1, comprising heating said hydrogel at a temperature of up to about 121 ℃ for a time of up to 1 hour.

3. The method of claim 1, wherein the rate of cross-linker degradation by beta elimination is controlled by one or more substituents contained in the cross-linker.

4. The method of claim 3, wherein

(a) the cross-linker is of the formula:



wherein

m is 0 or 1;

X comprises a functional group connecting the crosslinker to a first polymer;

at least one of R^1, R^2, and R^5 comprises a functional group Z connecting the crosslinker to a second polymer;

wherein one and only one of R^1 and R^2 may be H or may be alkyl, arylalkyl or heteroarylalkyl, each optionally substituted;

at least one or both R^1 and R^2 is independently CN; NO_2;

optionally substituted aryl;

optionally substituted heteroaryl;

optionally substituted alkenyl;

optionally substituted alkynyl;

COR^3; SOR^3;or SO_2R^3 wherein

R^3 is H or optionally substituted alkyl;

aryl or arylalkyl, each optionally substituted;

heteroaryl or heteroarylalkyl, each optionally substituted; or

OR^9 or NR^9_2 wherein each R^9 is independently H or optionally substituted alkyl, or both R^9 groups taken together with the nitrogen to which they are attached form a heterocyclic ring;

SR^4 wherein

R^4 is optionally substituted alkyl;

aryl or arylalkyl, each optionally substituted; or

heteroaryl or heteroarylalkyl, each optionally substituted;

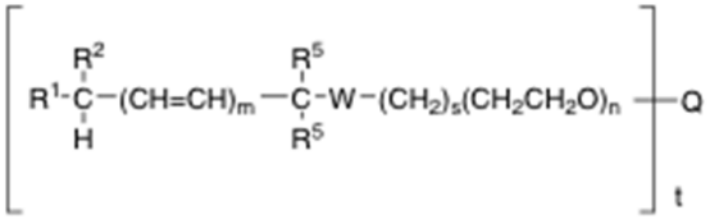
wherein R^1 and R^2 may be joined to form a 3-8 membered ring;

and

each R^5 is independently H or is alkyl, alkenylalkyl, alkynylalkyl, $(OCH_2CH_2)_p$ -O-alkyl wherein p=1-1000, aryl, arylalkyl, heteroaryl or heteroarylalkyl, each optionally substituted;

or

(b) the cross-linker is of the formula:



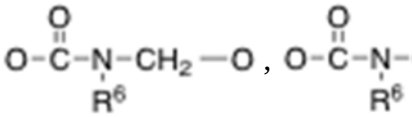
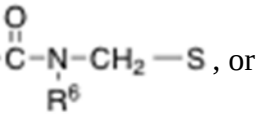
wherein

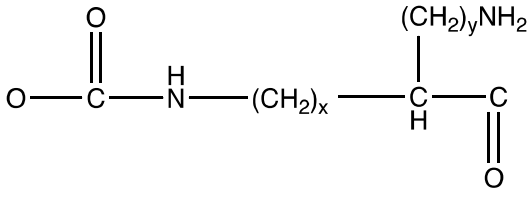
m is 0 or 1;

n is 1-1000;

s is 0-2;

t is 2, 4, 8, 16 or 32;

W is O(C=O)O, O(C=O)NH, O(C=O)S,  ,  , or

 , wherein x and y = 0-4;

Q is a core group having a valency=t;

wherein at least one of R^1, R^2, and R^5 comprises a functional group Z connecting the crosslinker to a second polymer, and

at least one or both R^1 and R^2 is independently CN; NO_2;

optionally substituted aryl;

optionally substituted heteroaryl;

optionally substituted alkenyl;

optionally substituted alkynyl;

COR^3; SOR^3; or SO_2R^3; wherein

R^3 is H or optionally substituted alkyl;

aryl or arylalkyl, each optionally substituted;

heteroaryl or heteroarylalkyl, each optionally substituted; or

OR^9 or NR^9_2 wherein each R^9 is independently H or optionally substituted alkyl, or both R^9 groups taken together with the nitrogen to which they are attached form a heterocyclic ring;

SR^4 wherein

R^4 is optionally substituted alkyl;

aryl or arylalkyl, each optionally substituted; or

heteroaryl or heteroarylalkyl, each optionally substituted; and

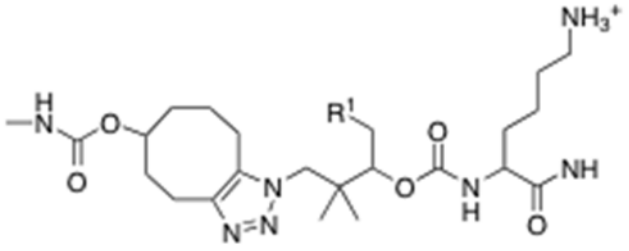
wherein R^1 and R^2 may be joined to form a 3-8 membered ring; and

wherein one and only one of R^1 and R^2 may be H or may be alkyl, arylalkyl or heteroarylalkyl, each optionally substituted; and

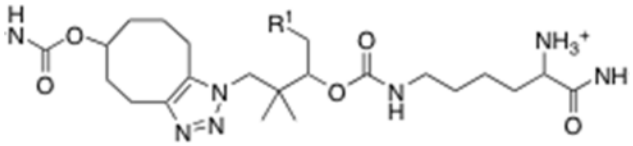
each R^5 is independently H or is alkyl, alkenylalkyl, alkynylalkyl, $(OCH_2CH_2)_p$ -O-alkyl wherein p=1-1000, aryl, arylalkyl, heteroaryl or heteroarylalkyl, each optionally substituted.

5. The method of Claim 4, wherein X is a carbamate and Z is a triazole, carboxamide, or carbamate.

6. The method of Claim 1, wherein the cross-linker is of the formula:



or



, wherein

(a) R^1 is CN; NO_2;

optionally substituted aryl;

optionally substituted heteroaryl;

optionally substituted alkenyl;

optionally substituted alkynyl;

COR^3; SOR^3; or SO_2R^3 wherein:

R^3 is H or optionally substituted alkyl;

aryl or arylalkyl, each optionally substituted;

heteroaryl or heteroarylalkyl, each optionally substituted; or

OR^9 or NR^9_2 wherein each R^9 is independently H or optionally substituted alkyl, or both R^9 groups taken together with the nitrogen to which they are attached form a heterocyclic ring; and

SR^4 wherein

R^4 is optionally substituted alkyl;

aryl or arylalkyl, each optionally substituted; or

heteroaryl or heteroarylalkyl, each optionally substituted;

or

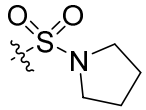
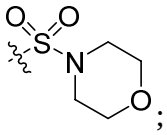
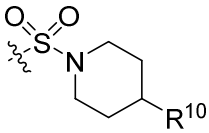
(b) wherein R^1 is CN or SO_2R^3 wherein

R^3 is H or optionally substituted alkyl;

aryl or arylalkyl, each optionally substituted;

heteroaryl or heteroarylalkyl, each optionally substituted; or

OR^9 or NR^9_2 wherein each R^9 is independently H or optionally substituted alkyl, or both R^9 groups taken together with the nitrogen to which they are attached form a heterocyclic ring.

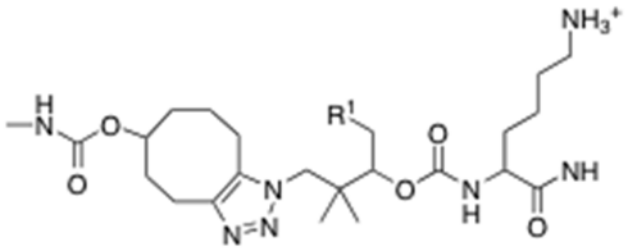
7. The method of Claim 6, wherein R^1 is CN; SO_2Me; SO_2NMe_2; ; ; ; or $SO_2(Ph\text{-}R^{10})$, wherein R^{10} is H, alkyl, alkoxy, NO_2, or halogen.

8. The method of Claim 1, wherein sterilization is achieved by heating to 121 ^oC with a hold time of 20 minutes.

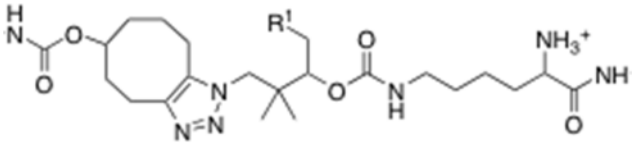
9. The method of any one of claims 1-8, wherein step (b) comprises adjusting the pH of the medium containing said hydrogel to between 3 and 4.

10. The method of any one of claims 1-9, wherein the hydrogel comprises [Gln^{28}]exenatide.

11. A hydrogel comprising a cross-linker degradable by a beta-elimination mechanism that has been sterilized by adjusting to pH 2-5, and heating at a temperature of up to about 121 °C, wherein the hydrogel comprises a cross-linker of the formula:



or



, wherein

R^1 is H; CN; NO_2; optionally substituted aryl; optionally substituted heteroaryl; optionally substituted alkenyl; optionally substituted alkynyl; COR^3; SOR^3; SO_2R^3; or SR^4; wherein

R^3 is H or optionally substituted alkyl; aryl or arylalkyl, each optionally substituted; heteroaryl or heteroarylalkyl, each optionally substituted; or OR^9 or $NR^9{}_2$ wherein each R^9 is independently H or optionally substituted alkyl, or both R^9 groups taken together with the nitrogen to which they are attached form a heterocyclic ring; and

R^4 is optionally substituted alkyl; aryl or arylalkyl, each optionally substituted; or heteroaryl or heteroarylalkyl, each optionally substituted.