

Appendix II-A: Example of amendments to description page (Addition of paragraphs)

13

CONJUGATES HAVING A DEGRADABLE LINKAGE AND POLYMERIC REAGENTS
USEFUL IN PREPARING SUCH CONJUGATES

BACKGROUND OF THE INVENTION

**Numbering of additional
paragraphs**

[0001] The present invention relates generally to polymeric reagents useful in providing a conjugate having a degradable linkage between a polymer and another moiety. In addition, the invention relates to, among other things, conjugates of the polymeric reagents, methods for synthesizing the polymeric reagents and methods for conjugating the polymeric reagents to active agents and other moieties.

[0001a] Scientists and clinicians face a number of challenges in their attempts to develop active agents into forms suited for delivery to a patient. Active agents that are polypeptides, for example, are often delivered via injection rather than orally. In this way, the polypeptide is introduced into the systemic circulation without exposure to the proteolytic environment of the stomach. Injection of polypeptides, however, has several drawbacks.

[0001b] For example, many polypeptides have a relatively short half-life, thereby necessitating repeated injections, which are often inconvenient and painful. Moreover, some polypeptides can elicit one or more immune responses with the consequence that the patient's immune system attempts to destroy or otherwise neutralize the immunogenic polypeptide. Of course, once the polypeptide has been destroyed or otherwise neutralized, the polypeptide cannot exert its intended pharmacodynamic activity. Thus, delivery of active agents such as polypeptides is often problematic even when these agents are administered by injection. Some success has been achieved in addressing the problems of delivering active agents via injection.

[0002] Some success has been achieved in addressing the problems of delivering active agents via injection. For example, conjugating the active agent to a water-soluble polymer has resulted in polymer-active agent conjugates having reduced immunogenicity and antigenicity. In addition, these polymer-active agent conjugates often have greatly increased half-lives compared to their unconjugated counterparts as a result of decreased clearance through the kidney and/or decreased enzymatic degradation in the systemic circulation. As a result of having a greater half-life, the polymer-active agent conjugate requires less frequent dosing, which in turn reduces the overall number of painful injections and inconvenient visits with a health care professional.