We claim:

1. An improved process of conjugation to obtain novel synthetic oligosaccharide – protein conjugates comprising the steps of:

(a) reacting a synthetic oligosaccharide having at least one terminal amine linker with a reagent having at least one reactive thiol functional group to obtain an activated oligosaccharide;

(b) reacting a carrier protein with at least one aliphatic hetero bifunctional crosslinker to obtain an activated carrier protein having reactive maleimide functional group;

(c) carrying out conjugation reaction of said activated synthetic oligosaccharide of step (a) with said activated carrier protein of step (b) to obtain a synthetic oligosaccharide – protein conjugate (OS-PR) having thioether linkage;

wherein

- said synthetic oligosaccharide of step (a) mimics the chemical composition of the natural polysaccharides of gram negative bacteria such as *Neisseria meningitidis* and *Haemophilus influenzae*,
- said process to obtain said synthetic OS-PR conjugates in purified form takes time ranging from 14 hours to 22 hours.

2. The improved process of conjugation as claimed in claim 1 wherein said synthetic oligosaccharide comprises of:

- at least one in-built terminal amino linker,
- four to eight repeating monomeric units of polysaccharides.

3. The improved process of conjugation as claimed in claim 1 wherein said *Neisseria meningitidis* comprises of serogroups A, C, Y, W135, X and said *Haemophilus influenzae* comprises of type b.

4. The improved process of conjugation as claimed in claim 1 wherein said carrier protein is obtained from gram positive bacteria selected from *Clostridium tetani* (tetanus toxoid), *Corynebacterium diphtheriae* (CRM197) or recombinant versions thereof.

5. The improved process of conjugation as claimed in claim 1 wherein said activated synthetic oligosaccharide is obtained by the steps of:

(a) reacting said synthetic oligosaccharide having at least one terminal amine linker with at least one sulfhydrilating agent to predetermined conditions to obtain a sulfhydrilated oligosaccharide;

(b) subjecting said sulfhydrilated oligosaccharide of step (a) to gel filtration chromatography to remove unreacted said sulfhydrilating agent;

(c) reacting said sulfhydrilated oligosaccharide obtained from step (b) with at least one nucleophile to obtain said activated synthetic oligosaccharide;

wherein

- said predetermined conditions are addition of 2-5X molar excess of said sulfhydrilating agent, preferably 2.5X molar excess of said sulfhydrilating agent at pH of 6.0-8.0, preferably 7.5,
- said sulfhydrilating agent is preferably N-succinimidyl S- acetylthio acetate (SATA).

6. The improved process of conjugation as claimed in claim 5 wherein said sulfhydrilating agent is a chemical sulfhydrilating agent to facilitate conversion of said terminal amine linker to sulfhydryl group.

7. The improved process of conjugation as claimed in claim 5 wherein said nucleophile is selected from a group of reducing agents, preferably

hydroxyl amine hydrochloride to facilitate conversion of sulfhydryl group to reactive thiol group.

8. The improved process of conjugation as claimed in claim 1 wherein said aliphatic heterobifunctional crosslinker is a chemical crosslinker to generate reactive maleimide functional group, said aliphatic heterobifunctional crosslinker is preferably N-(beta-maleimidopropyloxy) succinimide ester (BMPS).

9. The improved process of conjugation as claimed in claim 1 wherein said process yields said activated oligosaccharide in the range of 40% to 90%.

10. The improved process of conjugation as claimed in claim 1 wherein said process yields said synthetic OS-PR conjugates

- in the range of 21% to 48% for Meningococcal conjugates such as MenX, MenC, MenW135, MenY conjugates, preferably in the range of 25% to 30%; and
- in the range of 45% to 65% for Hib conjugates, preferably in the range of 50% to 60%.

11. The improved process of conjugation as claimed in claim 1 wherein said synthetic OS-PR conjugates show high total IgG antibody titres and SBA titres at 1 mcg dose.

12. The improved process of conjugation as claimed in claim 11 wherein

- said total IgG titers are 4 fold to 18 fold higher than the pre-immunization titers for serogroup C oligosaccharide conjugates,
- said SBA titres are at least 4 fold higher than the pre-immunization SBA titers for serogroup C oligosaccharide conjugates,

- said total IgG and SBA titers for MenX oligomer-TT conjugates are 4 fold higher than the negative (vehicle) control and upto 45 fold higher in terms of total IgG and upto 350 fold higher SBA titers than the negative (vehicle) control.

13. The improved process of conjugation as claimed in claim 1 wherein said process is carried out in the absence of nitrogen purging and uses the reagents for which no specific handling skills are required, thereby making the process convenient and cost effective.

14. The process of conjugation as claimed in claim 1 wherein said synthetic OS-PR conjugates elicit specific and homogenous immune response and is capable of being used in the preparation of synthetic conjugate vaccines, either in single or as combination vaccines and also as diagnostic tool.

15. The process of conjugation as claimed in claim 1 wherein said synthetic OS-PR conjugates have OS / PR ratio in the range of 0.17 to 0.5, preferably in the range of 0.2 to 0.4.