Annex A

1. A modified nucleotide molecule comprising a purine or pyrimidine base and a ribose or deoxyribose sugar moiety having a removable 3'-OH blocking group covalently attached thereto, such that the 3' carbon atom has attached a group of the structure

-O-Z

wherein Z is ~~any of -C(R')2-N(R")2'C(R')2-N(H)R", and -C(R')2-N3, wherein each R" is or is part of a removable protecting group; each R' is independently a hydrogen atom, an alkyl, substituted alkyl, arylalkyl, alkenyl, alkynyl, aryl, heteroaryl, heterocyclic, acyl, cyano, alkoxy, aryloxy, heteroaryloxy or amido group, or a detectable label attached through a linking group; or (R')2 represents an alkylidene group of formula =C(R''')2 wherein each R''' may be the same or different and is selected from the group comprising hydrogen and halogen atoms and alkyl groups; and wherein said molecule may be reacted to yield an intermediate in which each R" is exchanged for H, which intermediate dissociates under aqueous conditions to afford a molecule with a free 3'OH~~ an azidomethyl group.

~~2. A molecule according to claim 1 wherein R' is an alkyl or substituted alkyl.~~

~~3. A molecule according to claim 1 or claim 2 wherein - Z is of formula -C(R') N3.~~

~~4. A molecule according to any one of claims 1 to 3 wherein Z is an azidomethyl group.~~

~~5. A molecule according to claim 1 or claim 2 wherein R" is a benzyl or substituted benzyl group.~~

~~6~~2. A molecule according to ~~any preceding~~ claim 1 wherein said base is linked to a detectable label via a cleavable linker or a non-cleavable linker.

~~7~~3. A molecule according to claim ~~6~~2 wherein said linker is cleavable.

~~8~~4. A molecule according to any one of claims 1 ~~to 5~~ wherein a detectable label is linked to the molecule through the blocking group by a cleavable or non-cleavable linker.

~~95~~. A molecule according to any one of claims ~~62~~ to ~~84~~ wherein said detectable label is a fluorophore.

~~106~~. A molecule according to any one of claims ~~62~~ to ~~95~~ wherein said linker is acid labile, photolabile or contains a disulfide linkage.

~~117~~. A modified nucleotide molecule as claimed in any one of claims 1 to ~~106~~ which comprises one or more ^{32}P atoms in its phosphate portion.

~~128~~. A method of controlling the incorporation of a nucleotide as defined in any one of claims ~~62~~ to ~~106~~ and complementary to a second nucleotide in a target single-stranded polynucleotide in a synthesis or sequencing reaction comprising incorporating into the growing complementary polynucleotide said nucleotide, the incorporation of said nucleotide preventing or blocking introduction of subsequent nucleoside or nucleotide molecules into said growing complementary polynucleotide.

~~139~~. The method of claim ~~128~~, wherein the incorporation of said first nucleotide is accomplished by a terminal transferase or polymerase or a reverse transcriptase.

~~1410~~. The method of claim ~~139~~ wherein the polymerase is a *Thermococcus sp*

~~1511~~. The method of claim ~~1410~~ wherein the *Thermococcus sp* is 9°N or a single mutant or double mutant thereof.

~~1612~~. The method of claim ~~1511~~ wherein the double mutant is -Y409V A485L.

~~1713~~. A method for determining the sequence of a target single-stranded polynucleotide, comprising monitoring the sequential incorporation of complementary nucleotides, wherein at least one incorporation is of a nucleotide as defined in any one of claims ~~62~~ to ~~106~~ and wherein the identity of the nucleotide incorporated is determined by detecting the label linked to the base, and the blocking group and said label are removed prior to introduction of the next complementary nucleotide.

~~1814~~. The method according to claim ~~1713~~ wherein the label of the nucleotide and the blocking group are removed in a single chemical treatment step.

~~1915~~. The method according to claim ~~1713~~, comprising:

(a) providing a plurality of different nucleotides wherein said plurality of different nucleotides are either as defined in any one of claims ~~6~~2 to ~~10~~6 and wherein the detectable label linked to each type of nucleotide can be distinguished upon detection from the detectable label used for other types of nucleotides;

(b) incorporating the nucleotide into the complement of the target single-stranded polynucleotide;

(c) detecting the label of the nucleotide of (b), thereby determining the type of nucleotide incorporated;

(d) removing the label of the nucleotide of (b) and the blocking group; and

(e) optionally repeating steps (b)-(d) one or more times;

thereby determining the sequence of a target single-stranded polynucleotide.

~~20~~16. The method according to claim ~~19~~15, wherein each of the nucleotides are brought into contact with the target sequentially, with removal of non-incorporated nucleotides prior to addition of the next nucleotide, and wherein detection and removal of the label and the blocking group is carried out either after addition of each nucleotide, or after addition of all four nucleotides.

~~21~~17. The method according to claim ~~19~~15, wherein each of the nucleotides are brought into contact with the target together simultaneously, and non-incorporated nucleotides are removed prior to detection and subsequent to removal of the label and the blocking group.

~~22~~18. The method according to claim ~~19~~15, comprising a first step and a second step, wherein in the first step, a first composition comprising two of the four nucleotides is brought into contact with the target and non-incorporated nucleotides are removed prior to detection and subsequent to removal of the label, and wherein in the second step, a second composition comprising the two nucleotides not included in the first composition is brought into contact with the target, and non-incorporated nucleotides are removed prior to detection and subsequent tc removal of the label and blocking group, and wherein the first and second steps are optionally repeated one or more times.

~~23~~19. The method according to claim ~~19~~15, comprising a first step and a second step, wherein in the first step, a composition comprising one of the four nucleotides is brought into contact with the target, and non-incorporated nucleotides are removed prior to detection and subsequent tc removal of the label and blocking group and

wherein in the second step, a second composition comprising the three nucleotides not included in the first composition is brought into contact with the target, and non-incorporated nucleotides are removed prior to detection and subsequent to removal of the label and blocking group and wherein the first step and the second step are optionally repeated one or more times.

~~24~~20. The method according to claim ~~19~~15, comprising a first step and a second step, wherein in the first step, a first composition comprising three of the four nucleotides is brought into contact with the target, and non-incorporated nucleotides are removed prior to detection and subsequent to removal of the label and blocking group and wherein in the second step, a composition comprising the nucleotide not included in the first composition is brought into contact with the target, and non-incorporated nucleotides are removed prior to detection and subsequent to removal of the label and blocking group and wherein the first step and the second step are optionally repeated one or more times.

~~25~~21. A kit, comprising:

(a) a plurality of different nucleotides wherein said plurality of different nucleotides are either as defined in any one of claims ~~6~~2 to ~~10~~6; and

(b) packaging materials therefor.

~~26~~22. A kit according to claim ~~25~~21, wherein the detectable label in each nucleotide can be distinguished upon detection from the detectable label used for any of the other three types of nucleotide.

~~27~~23. The kit of claim ~~25~~21 or ~~26~~22, further comprising an enzyme and buffers appropriate for the action of the enzyme.

~~28~~24. Use of a nucleotide as defined in any one of claims 1 to ~~11~~7 in a Sanger or a Sanger-type sequencing method.

~~29~~25. An oligonucleotide comprising a modified nucleotide of claims 1-~~11~~7.

~~30~~26. A nucleotide triphosphate comprising a modified nucleotide of claims 1-~~11~~7.