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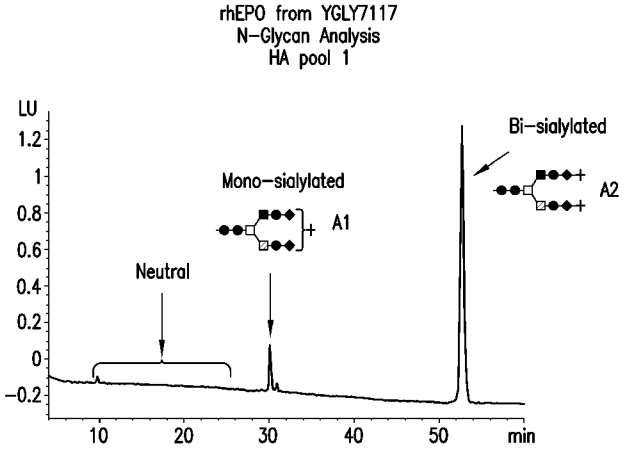
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[Continued on next page]

(54) Title: METHOD FOR PRODUCING PROTEINS IN PICHIA PASTORIS THAT LACK DETECTABLE CROSS BINDING ACTIVITY TO ANTIBODIES AGAINST HOST CELL ANTIGENS



Sample Name	% neutral	%A1	%A2
PK/PD lot (YGLY7117)	1 ($Man_5GlcNAc_2$) (Fungal−type β−mannose glycoforms not detected)	10	89

FIG.40B

(57) Abstract: Methods for producing proteins and glycoproteins in Pichia pastoris that lack detectable cross binding activity to antibodies made against host cell antigens are described. In particular, methods are described wherein recombinant Pichia pastoris strains that do not display a β-mannosyltransferase 2 activity with respect to an N-glycan or O-glycan and do not display at least one activity selected from a β-mannosyltransferase 1, 3, and 4 activity to produce recombinant proteins and glycoproteins. These recombinant Pichia pastoris strains can produce proteins and glycoproteins that lack detectable α-mannosidase resistant β-mannose residues thereon and thus, lack cross binding activity to antibodies against host cell antigens. Further described are methods for producing bi-sialylated human erythropoietin in Pichia pastoris that lack detectable cross binding activity to antibodies against host cell antigens.

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