

INFLAMMATION MARKERS IN THE PLASMA NMR SPECTRUM
(N-ACETYL METHYL SIGNALS FROM GLYCOSYLATED ACUTE PHASE PROTEINS)

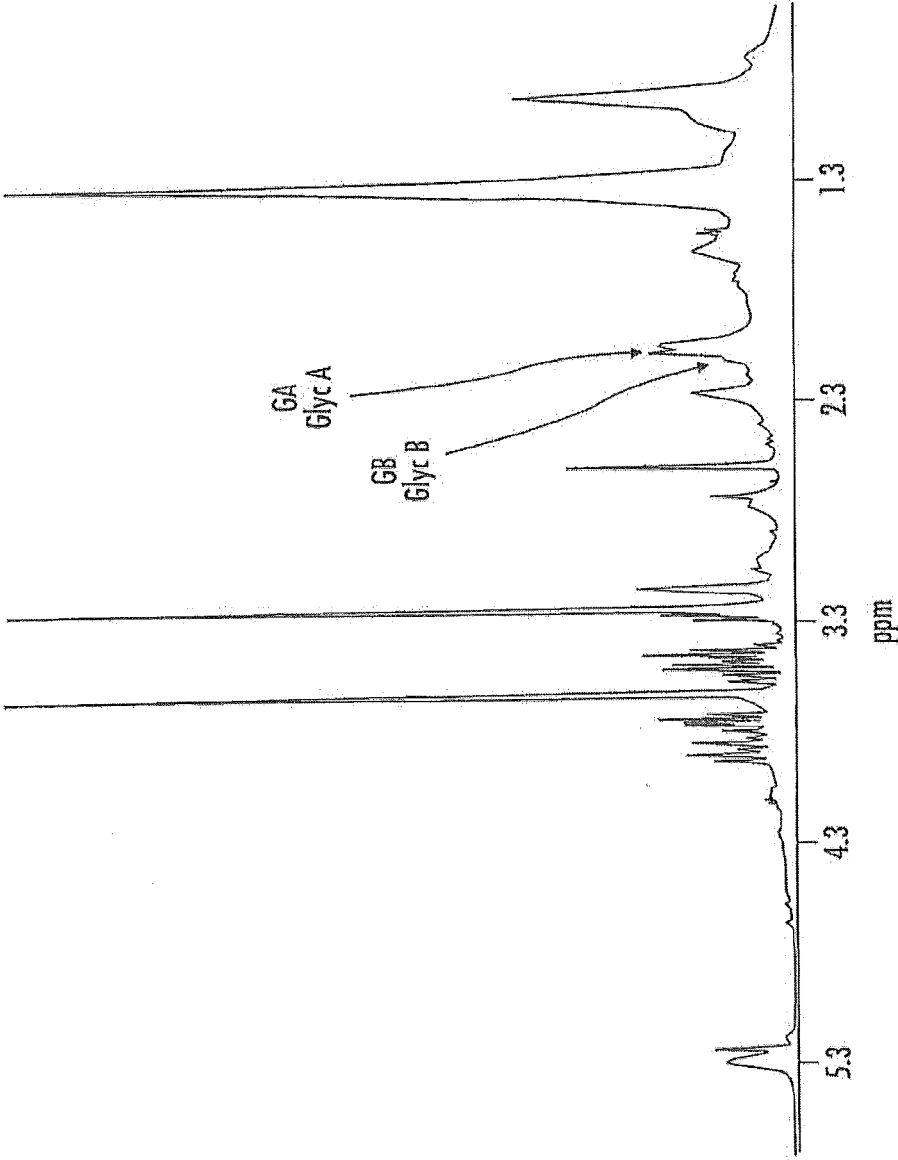


FIG. 1

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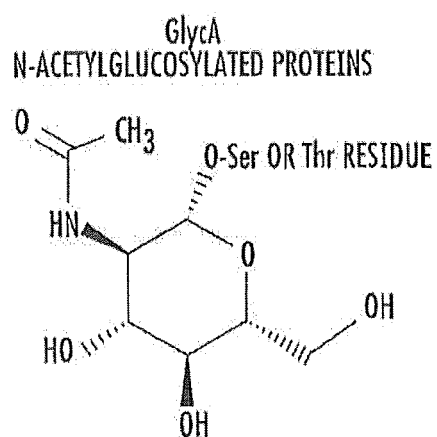


FIG. 2A

GlycA (FROM O- AND N-LINKED GLYCOPROTEINS)

β-D-N-ACETYLGLUCOSAMINE (GlcNAc)	(NHAc)	CH₂OH	GlcNAc
β-D-N-ACETYL GALACTOSAMINE (GalNAc)	(NHAc)	CH₂OH	GalNAc

FIG. 2B

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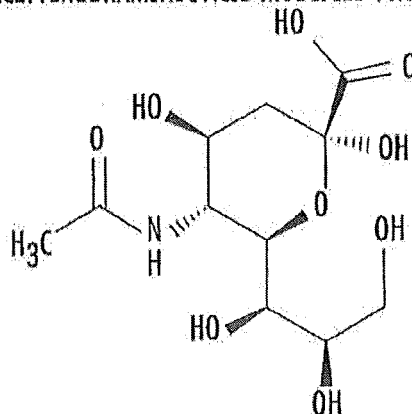
GlycB
N-ACETYLNEURAMINIC ACID MODIFIED PROTEINS

FIG. 3A

GlycB (FROM O- AND N-LINKED GLYCOPROTEINS)

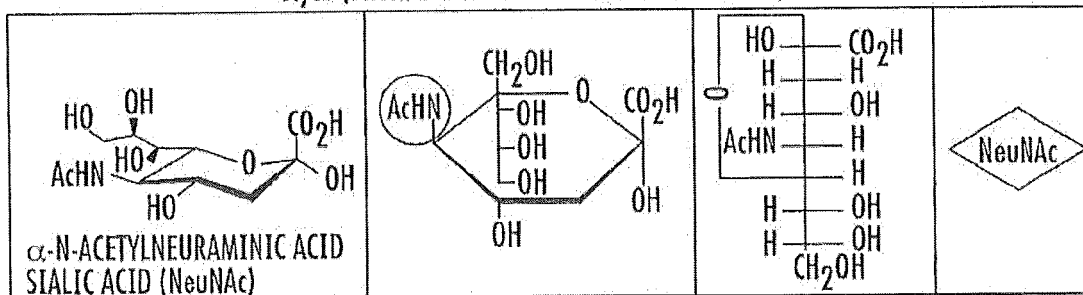


FIG. 3B

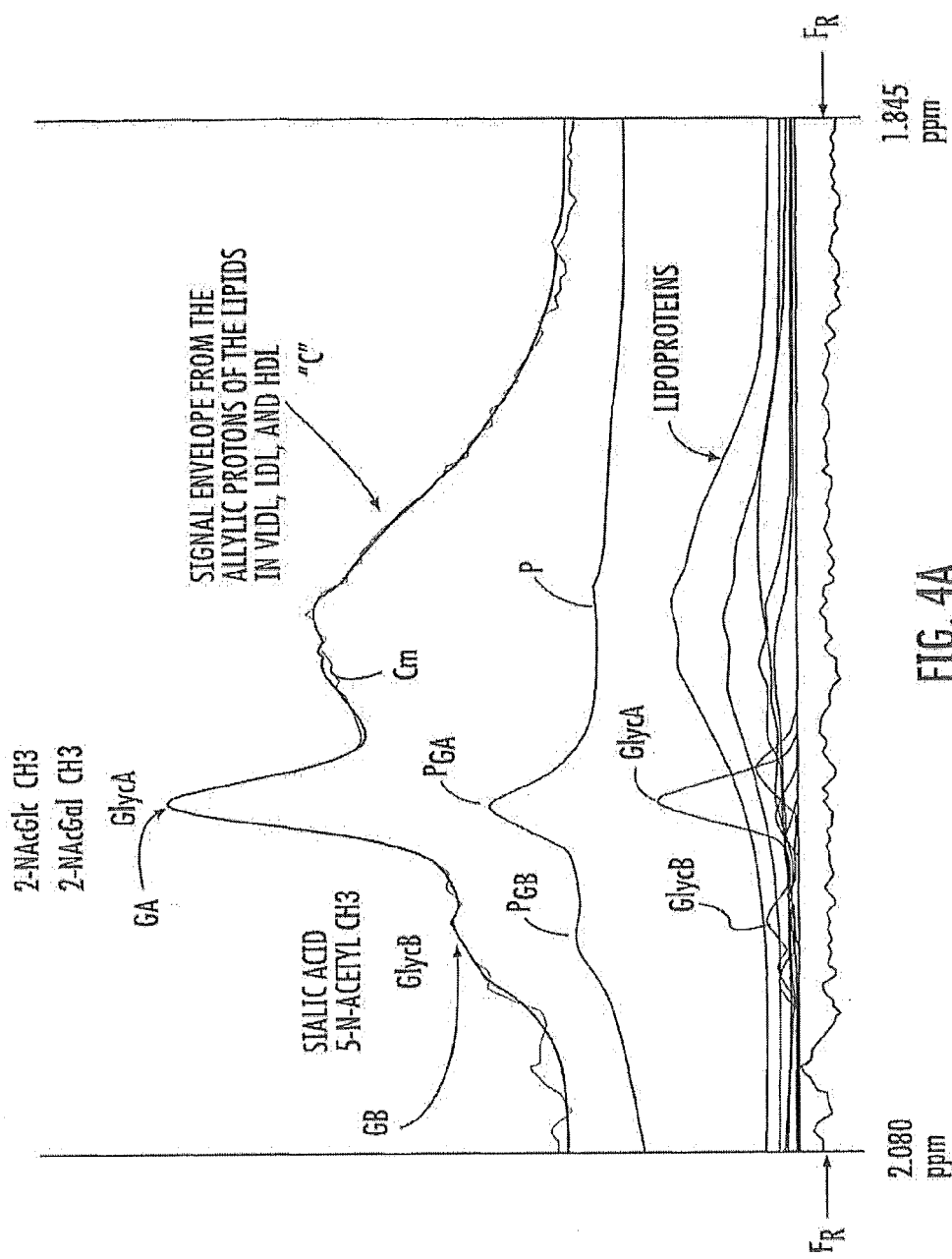
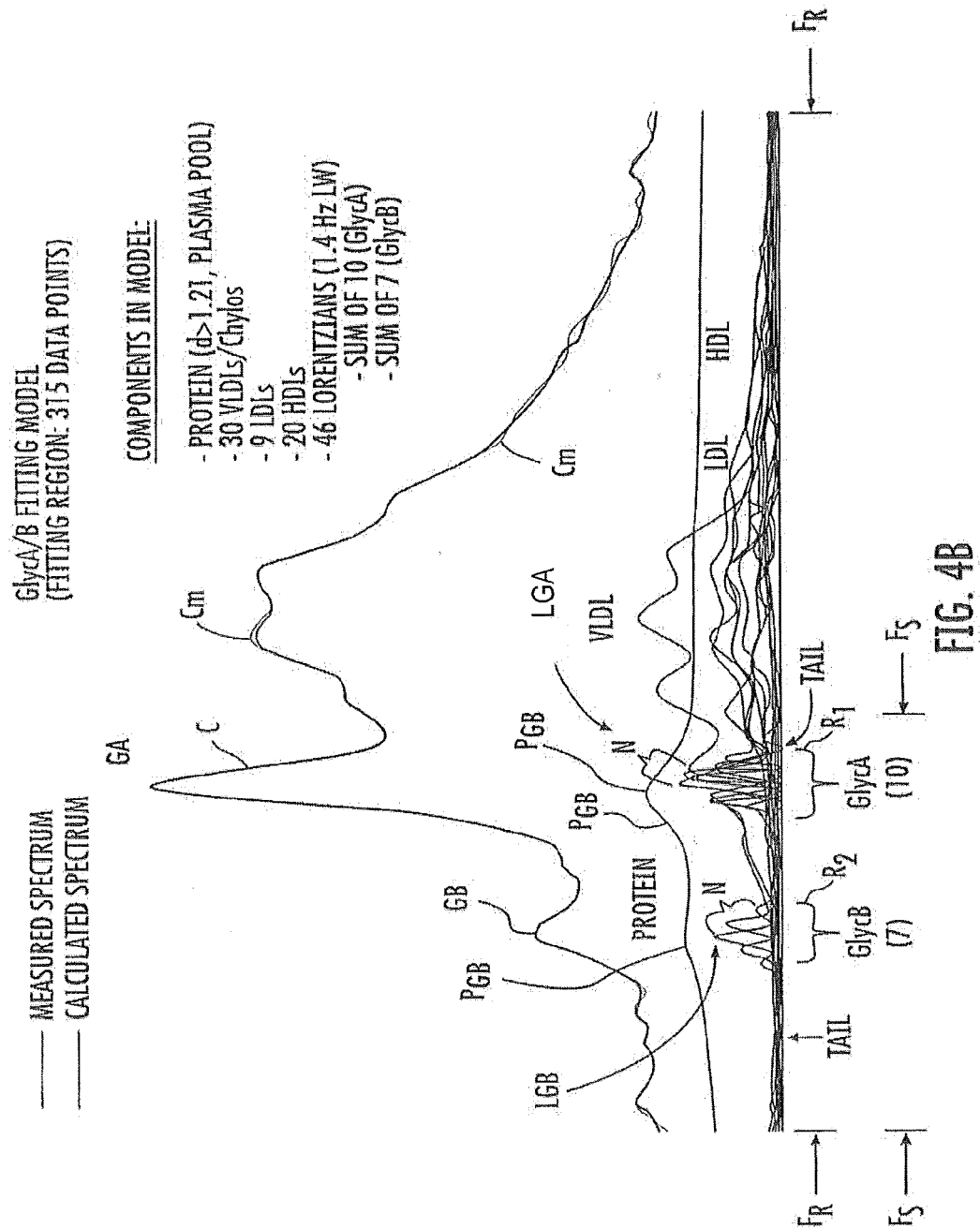
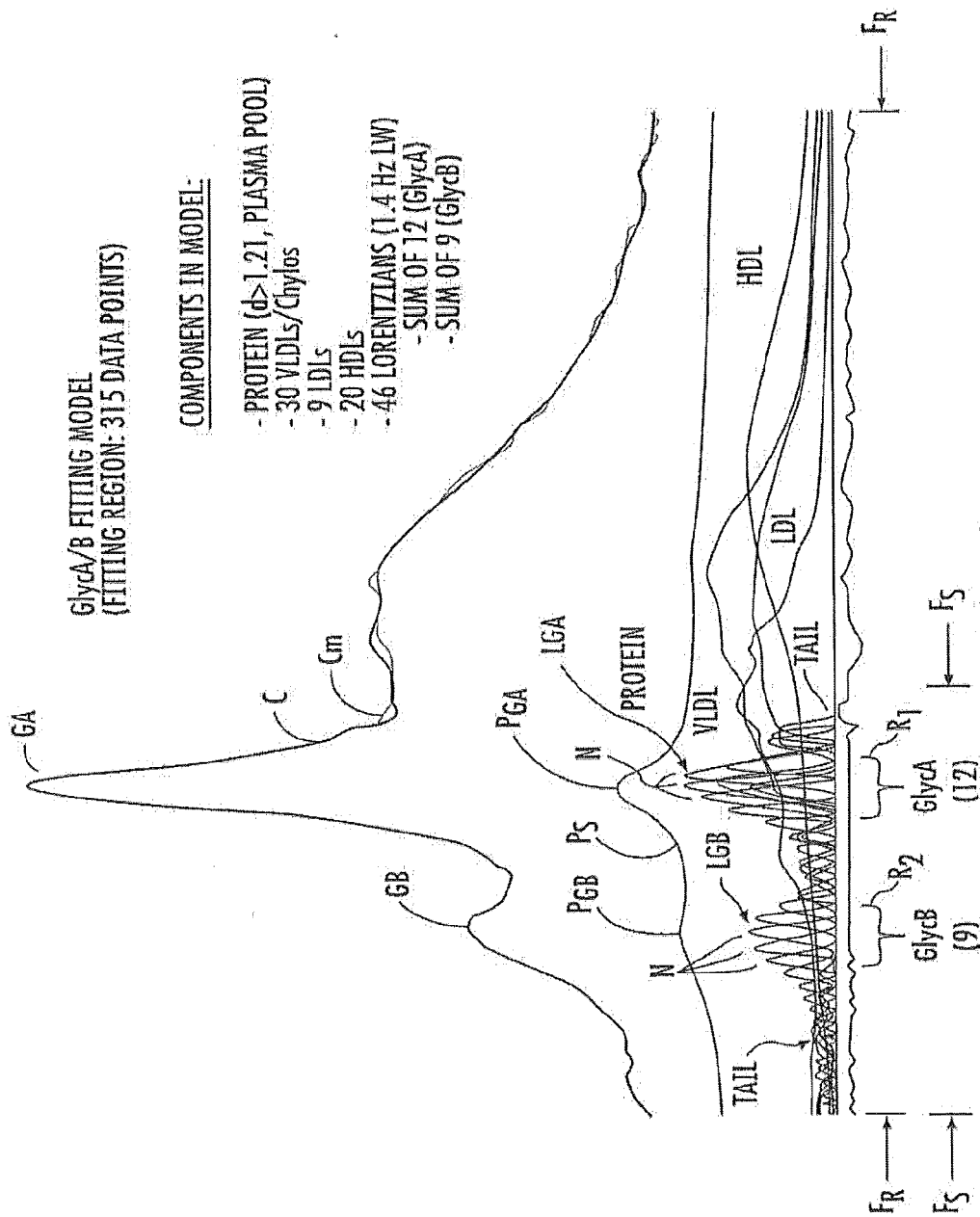


FIG. 4A

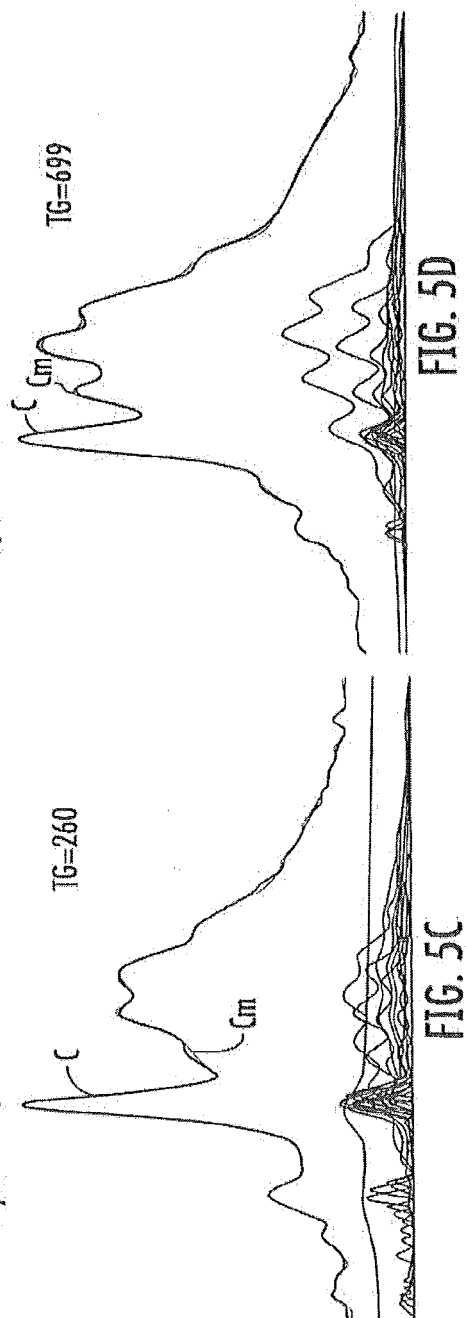
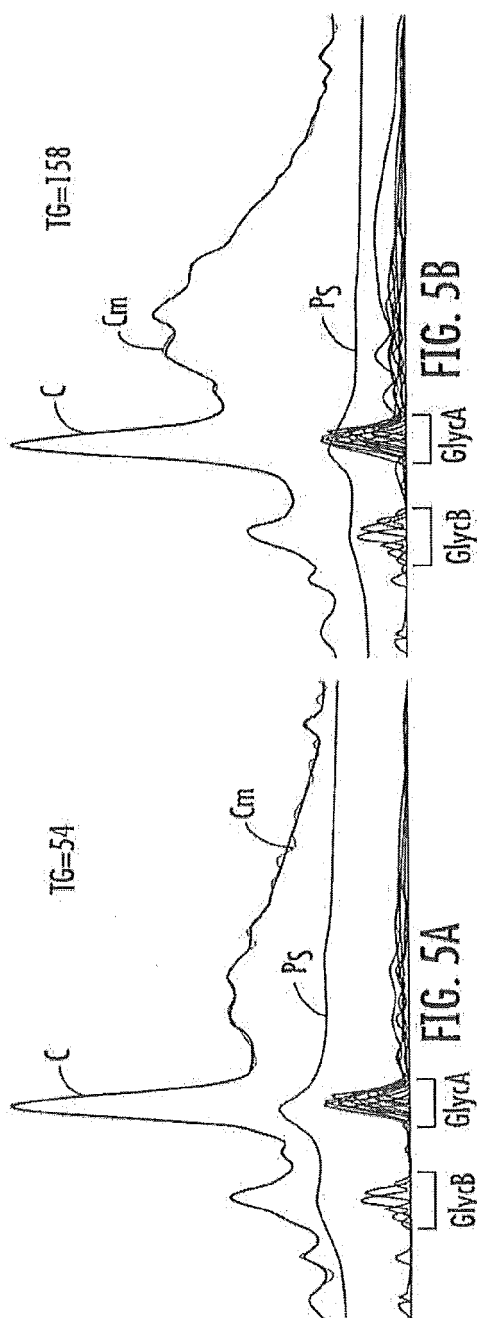
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SPECTRAL OVERLAP FROM LIPOPROTEINS (ESPECIALLY VLDL/CHYLOS)
COMPLICATES ANALYSIS OF SAMPLES WITH HIGH TRIGLYCERIDES (TG)



USE OF DIFFERENT PROTEIN COMPONENTS IN THE GlycA DECONVOLUTION MODEL GIVES DIFFERENT GlycA CONCENTRATIONS AND DIFFERENT GlycA ASSOCIATIONS WITH CHD EVENTS AND ALL-CAUSE DEATH IN MESA

PROTEIN COMPONENT USED IN FITTING MODEL	GlycA CONCENTRATION $\mu\text{mol/L}$	CHD EVENT PREDICTION		ALL-CAUSE DEATH PREDICTION	
		χ^2	p	χ^2	p
PROTEIN #1	342	13.1	0.0003	23.1	<0.0001
PROTEIN #2	186	12.7	0.0004	11.2	0.0008
PROTEIN #3	162	10.9	0.0003	7.4	0.007

FIG. 6A

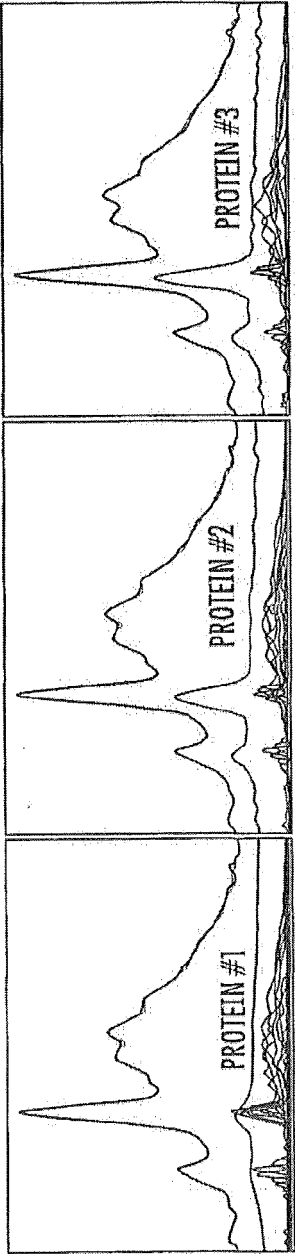


FIG. 6B

FIG. 6C

FIG. 6D

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GlycA CONVERSION FACTOR GIVES
CONCENTRATION OF GLYCOPROTEIN N-ACETYL METHYL GROUPS

$$1 \text{ GlycA/B UNIT} = 17.8 \text{ } \mu\text{mol/L}$$

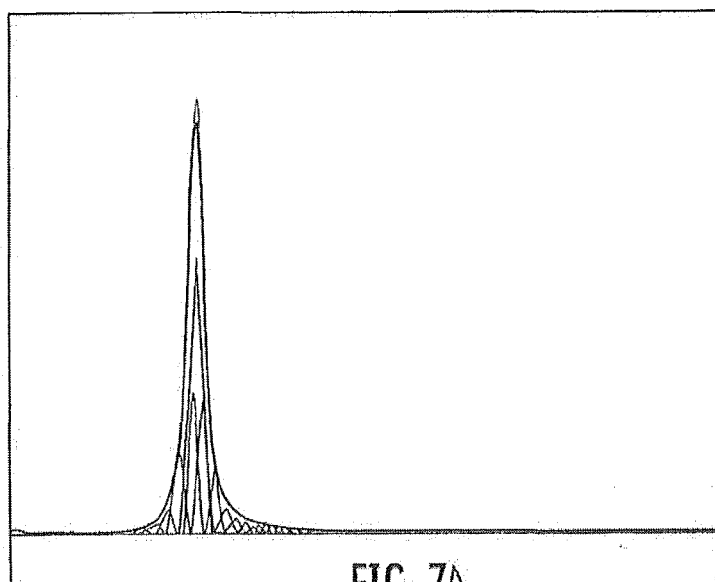


FIG. 7A

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Fig. 7B

Component ID	Component Class	Chemical Shift (ppm)	Component ID	Component Class	Chemical Shift (ppm)	Component ID	Component Class	Chemical Shift (ppm)
AA1	Metabolite A	1.875040	VLDL7	VLDL	1.966840	GLYC21		2.019880
AA2	Metabolite A	1.876400	VLDL8	VLDL	1.968200	GLYC22		2.021240
AA3	Metabolite A	1.876400	VLDL9	VLDL	1.969560	GLYC23		2.022600
AA4	Metabolite A	1.876400	VLDL10	VLDL	1.970920	GLYC24		2.023960
AA5	Metabolite A	1.877760	VLDL11	VLDL	1.971600	GLYC25		2.025320
AA6	Metabolite A	1.879120	VLDL12	VLDL	1.973640	GLYC26		2.026680
AA7	Metabolite A	1.880480	VLDL13	VLDL	1.975000	GLYC27		2.028040
HDL1	HDL	1.915840	VLDL14	VLDL	1.976360	GLYC28		2.029400
HDL2	HDL	1.918560	VLDL15	VLDL	1.975680	GLYC29		2.030760
HDL3	HDL	1.919240	VLDL16	VLDL	1.977040	GLYC30		2.032120
HDL4	HDL	1.919920	CHY1	CHYLOS	1.978400	GLYC31		2.034840
HDL5	HDL	1.920600	CHY2	CHYLOS	1.979080	GLYC32		2.037560
HDL6	HDL	1.921280	CHY3	CHYLOS	1.979760	GLYC33		2.040280
HDL7	HDL	1.925360	CHY4	CHYLOS	1.980440	GLYC34		2.043000
HDL8	HDL	1.928760	CHY5	CHYLOS	1.981120	GLYC35		2.045720
HDL9	HDL	1.930800	CHY6	CHYLOS	1.981800	GLYC36		2.048440
HDL10	HDL	1.933520	CHY7	CHYLOS	1.982480	GLYC37		2.051160
HDL11	HDL	1.934880	CHY8	CHYLOS	1.983160	GLYC38		2.053880
HDL12	HDL	1.936240	CHY9	CHYLOS	1.983840	GLYC39		2.056600
HDL13	HDL	1.936920	CHY10	CHYLOS	1.984520	GLYC40		2.059320
HDL14	HDL	1.937600	CHY11	CHYLOS	1.985200	GLYC41		2.062040
HDL15	HDL	1.938280	CHY12	CHYLOS	1.985880	GLYC42		2.064760
HDL16	HDL	1.938960	GLYC1		1.992680	GLYC43		2.067480
HDL17	HDL	1.939640	GLYC2		1.994040	GLYC44		2.070200
HDL18	HDL	1.941000	GLYC3		1.995400	GLYC45		2.072920
HDL19	HDL	1.941680	GLYC4		1.996760	GLYC46		2.075640
HDL20	HDL	1.943040	GLYC5		1.998120	Protein		
LDL1	LDL	1.947800	GLYC6		1.999480			
LDL2	LDL	1.948480	GLYC7		2.000840			
LDL3	LDL	1.949160	GLYC8		2.002200			
LDL4	LDL	1.949840	GLYC9		2.003560			
LDL5	LDL	1.950520	GLYC10		2.004920			
LDL6	LDL	1.951200	GLYC11		2.006280			
LDL7	LDL	1.952560	GLYC12		2.007640			
LDL8	LDL	1.953920	GLYC13		2.009000			
LDL9	LDL	1.955280	GLYC14		2.010360			
VLDL1	VLDL	1.960040	GLYC15		2.011720			
VLDL2	VLDL	1.961400	GLYC16		2.013080			
VLDL3	VLDL	1.962760	GLYC17		2.014440			
VLDL4	VLDL	1.964120	GLYC18		2.015800			
VLDL5	VLDL	1.965480	GLYC19		2.017160			
VLDL6	VLDL	1.966840	GLYC20		2.018520			

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Fig. 7C

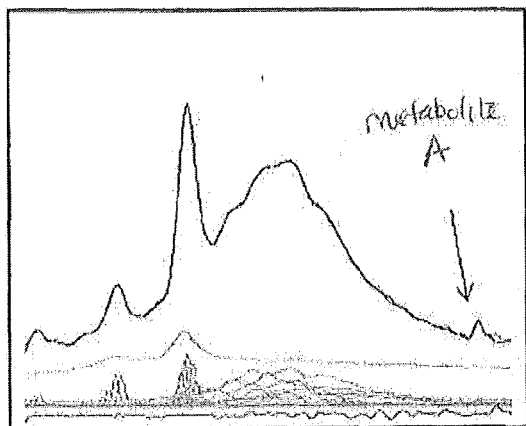
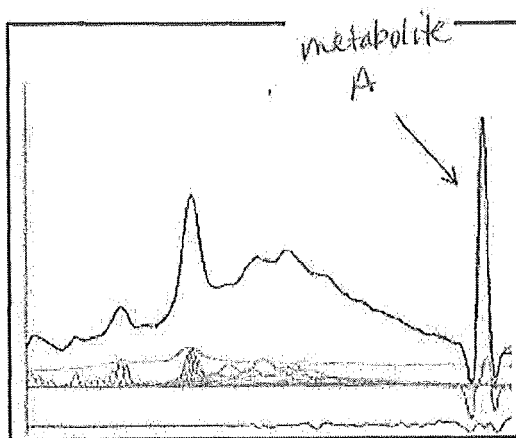


Fig. 7D



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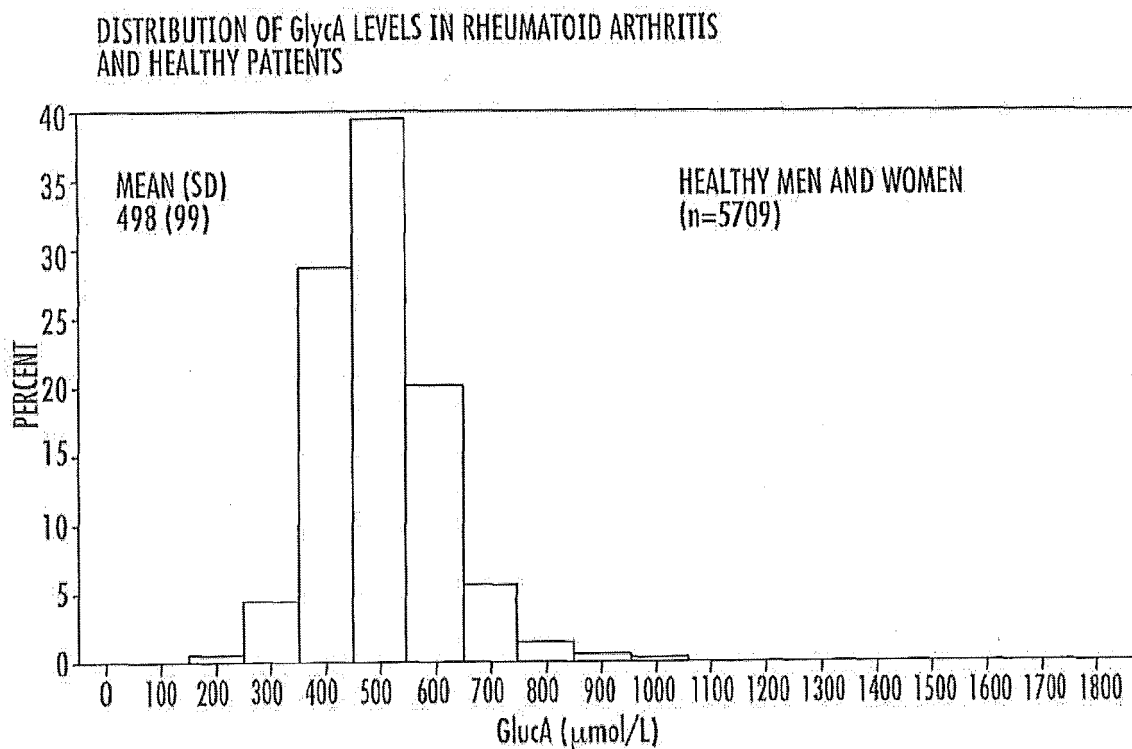


FIG. 8A

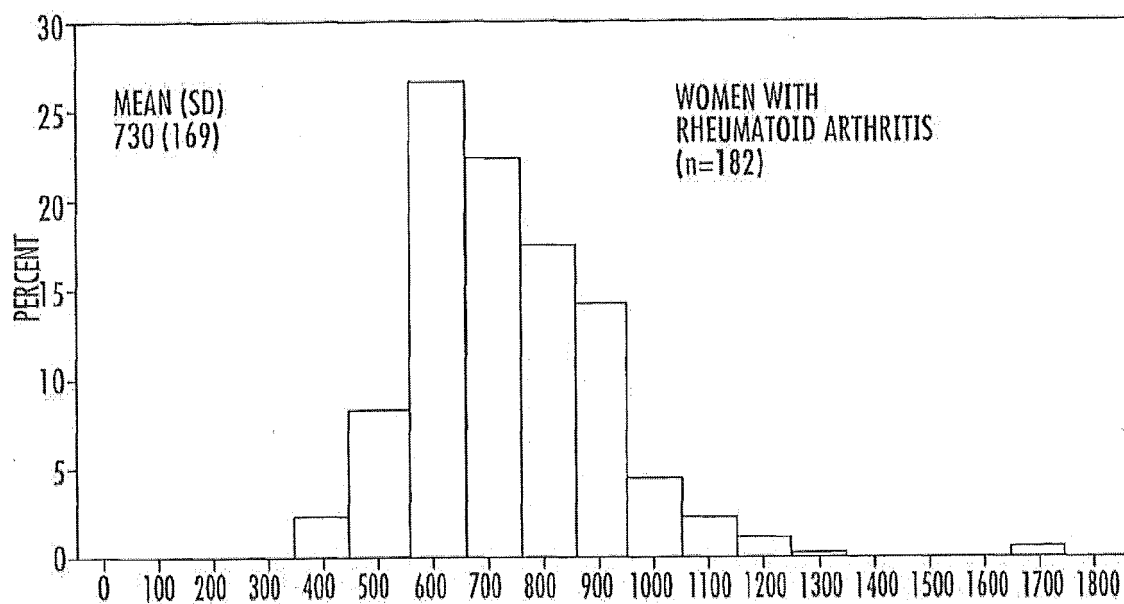


FIG. 8B

PROSPECTIVE ASSOCIATIONS OF NMR-MEASURED GlycA AND VALINE LEVELS AND HS-CRP WITH SELECTED DISEASE OUTCOMES IN MESA (n=5680)

	GlycA		hs-CRP		VALINE		GlycA+VALINE
	χ^2	p	χ^2	p	χ^2	p	
CHD EVENTS (N=289)	7.0	0.007	3.1	ns	0.3	ns	7.8
ALL-CAUSE DEATH (N=346)	24.8	<0.0001	13.9	0.0003	14.4	0.0002	36.7
CONGESTIVE HEART FAILURE (N=149)	2.5	ns	2.9	ns	12.3	0.0006	14.1
STROKE (N=117)	1.3	ns	0	ns	0	ns	1.4
CHRONIC KIDNEY DISEASE (N=181)	29.3	<0.0001	3.4	0.05	2.9	ns	31.0
COPD (N=120)	20.5	<0.0001	3.6	0.03	6.7	0.01	26.3
CANCER (N=440)	8.0	0.004	3.0	ns	3.8	0.05	11.3
ASTHMA (N=154)	3.5	0.06	1.6	ns	2.0	ns	6.2
DEMENTIA (N=71)	5.8	0.01	0	ns	3.9	0.05	10.0
DIABETES (N=493)	10.3	0.001	4.7	0.04	29.0	<0.0001	40.3

FIG. 9

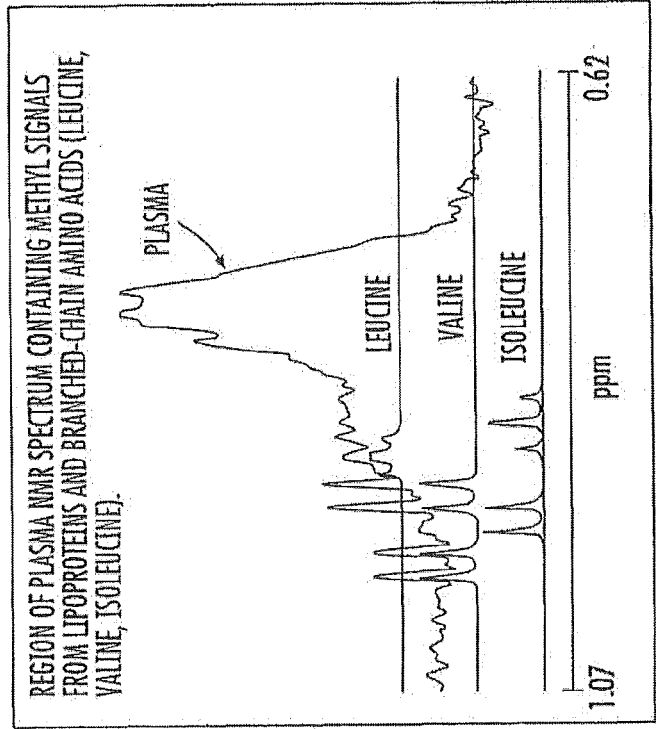


FIG. 10A

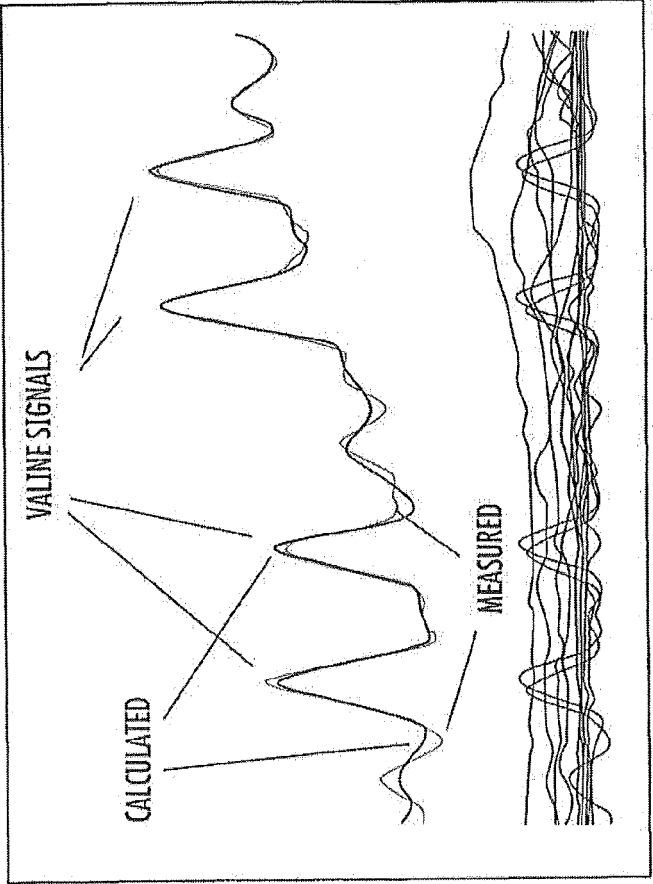


FIG. 10B

CHARACTERISTICS OF MESA SUBJECTS BY GlycA QUARTILE

	GlycA QUARTILE			
	1	2	3	4
GlycA	21.6	25.8	29.3	35.3
hsCRP (mg/L)	1.3	2.2	3.8	7.6
SMOKING (%)	9	11	13	17
HYPERTENSION (%)	34	41	47	55
DIABETES (%)	8.1	10.8	12.8	18.8
MetSyn (%)	20	31	39	55
LP-IR SCORE	35	44	46	52

FIG. 11

INDEPENDENT ASSOCIATIONS OF INFLAMMATION MARKERS
WITH CHD EVENTS IN MESA

N=5607 289 CHD EVENTS	χ^2 MODEL	HR per 1SD	c2 PARAM	P
BASE MODEL	235.4	---	---	---
hsCRP	239.1	1.07	1.8	ns
FIBRINOGEN	238.5	1.15	5.4	0.02
GlycA	244.9	1.21	10.4	0.001

COX MODELS ADJUSTED FOR AGE, SEX, ETHNICITY, SMOKING, SBP, HYPERTENSION MEDICATION, BMI, DIABETES, LDL-P, AND HDL-P

FIG. 12

ASSOCIATIONS WITH ALL-CAUSE DEATH IN MESA

N=5607 345 DEATHS	χ^2 MODEL	HR per 1SD	c2 PARAM	P
BASE MODEL	338.0	---	---	---
TC, LDL-C, LDL-P				ns
HDL-C	342.9	0.90	2.6	ns
CRP	352.8	1.15	19.2	<0.0001
FIBRINOGEN	350.7	1.21	13.8	0.0002
HDL-P	356.1	0.76	17.5	<0.0001
GlycA	363.8	1.30	30.2	<0.0001
HDL-P/GlycA	378.7	0.68	38.6	<0.0001

COX MODELS ADJUSTED FOR AGE, SEX, ETHNICITY, SMOKING, SBP, HYPERTENSION MEDICATION, BMI, AND DIABETES

FIG 13

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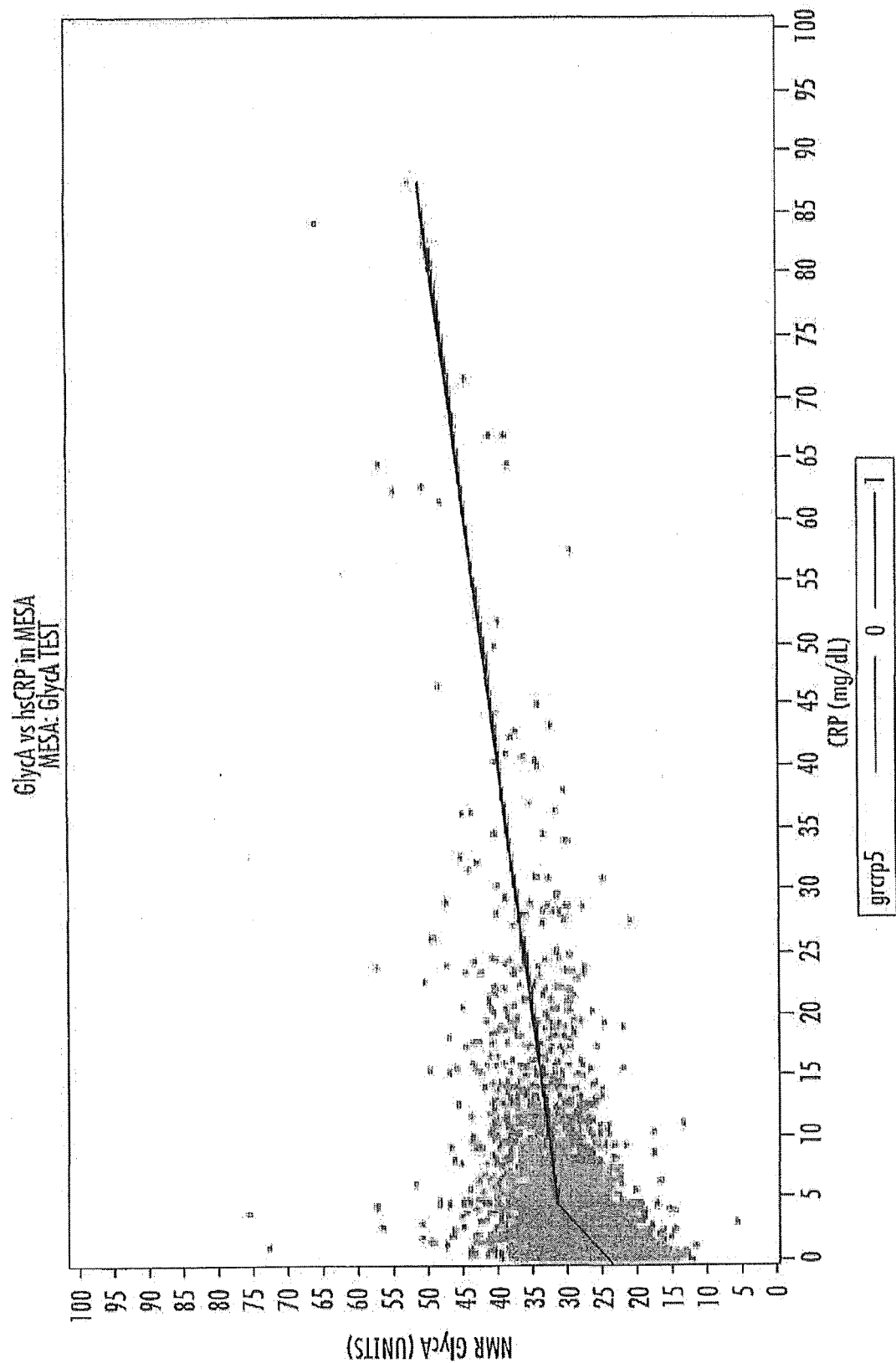
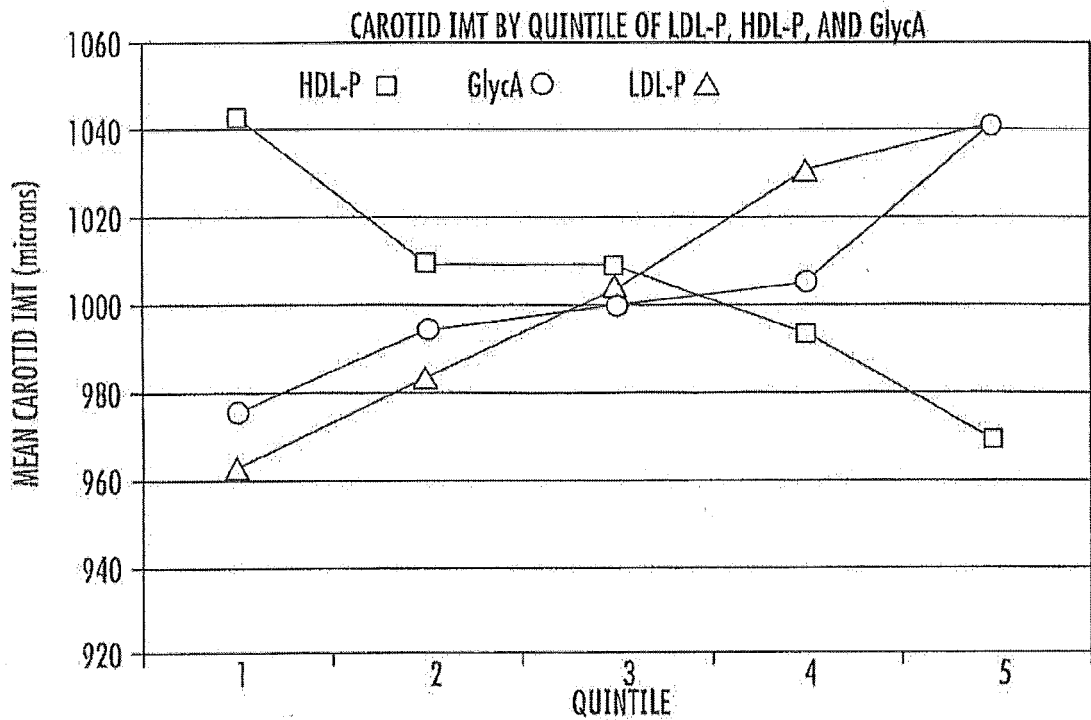


FIG. 14

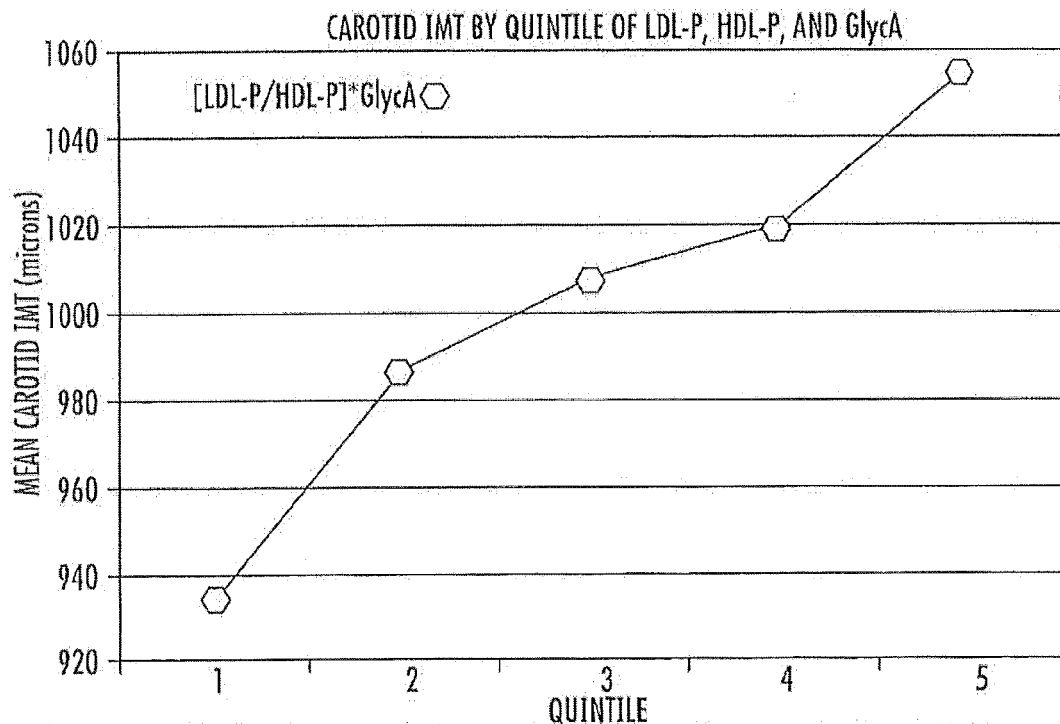
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FROM LINEAR REGRESSION MODELS ADJUSTED FOR AGE, SEX, ETHNICITY, SBP, HYPERTENSION MEDICATION, DIABETES, BMI, AND SMOKING.

FIG. 15A

MESA, UNPUBLISHED DATA



FROM LINEAR REGRESSION MODELS ADJUSTED FOR AGE, SEX, ETHNICITY, SBP, HYPERTENSION MEDICATION, DIABETES, BMI, AND SMOKING.

FIG 15B

MESA, UNPUBLISHED DATA

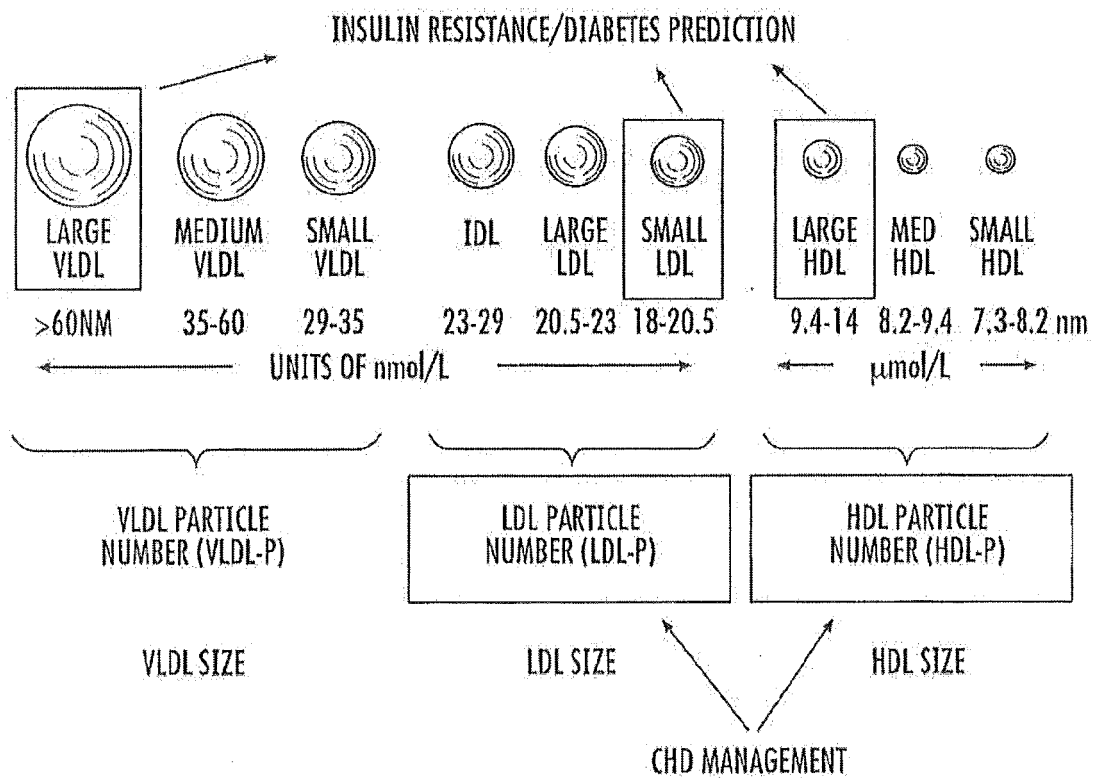
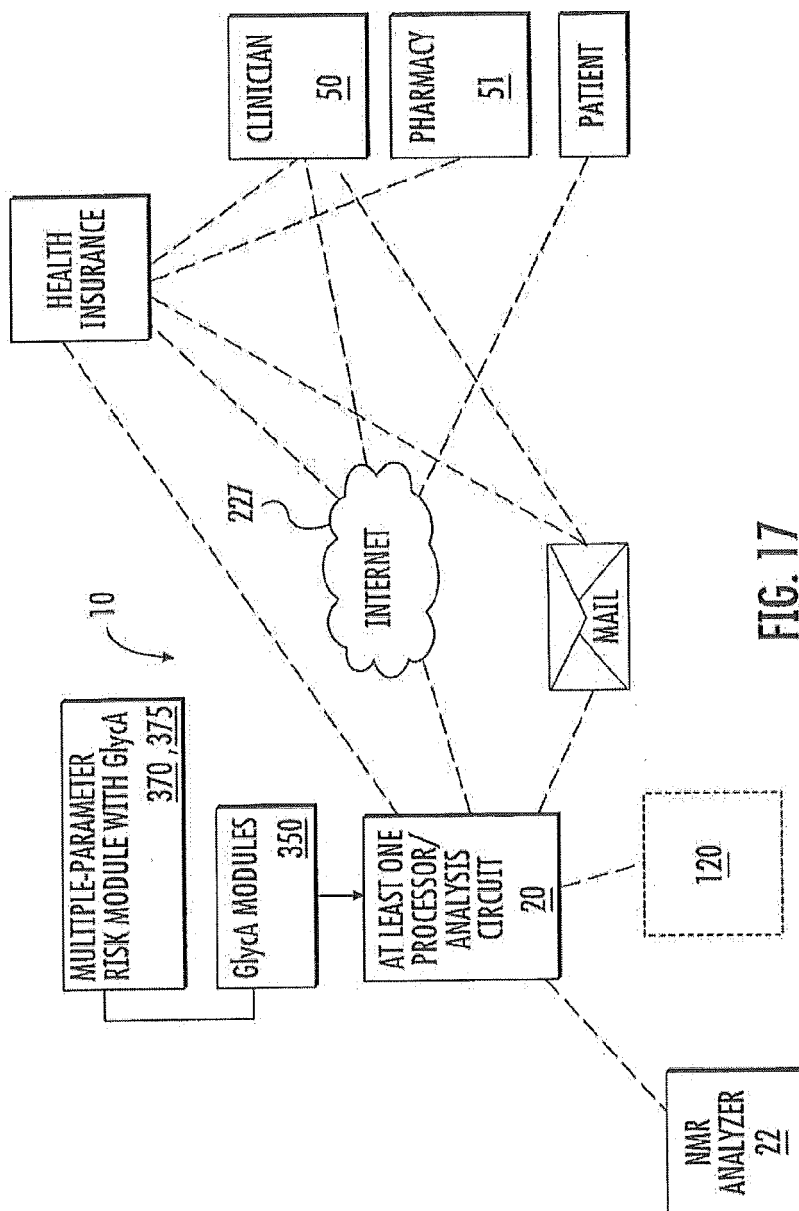


FIG. 16



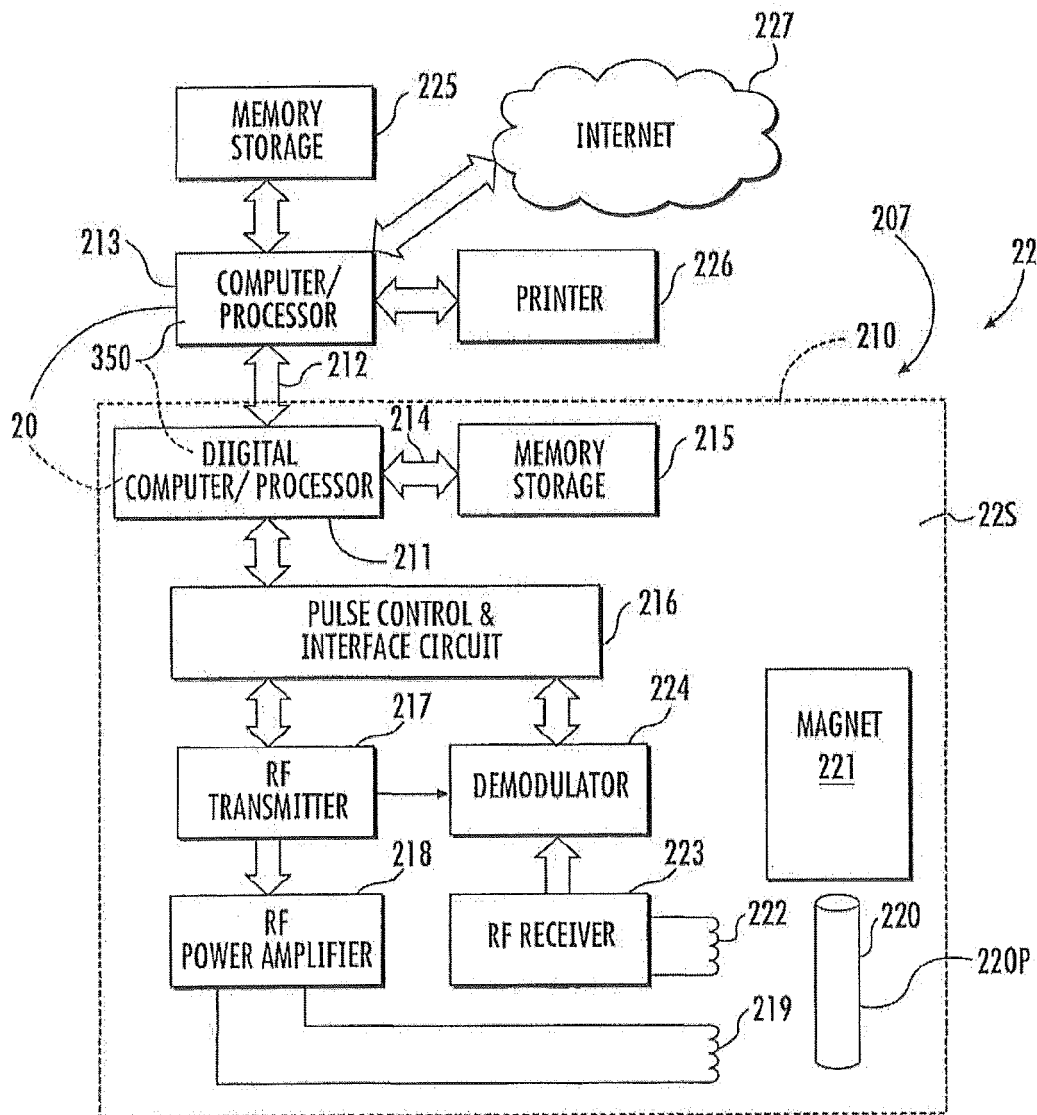


FIG. 18

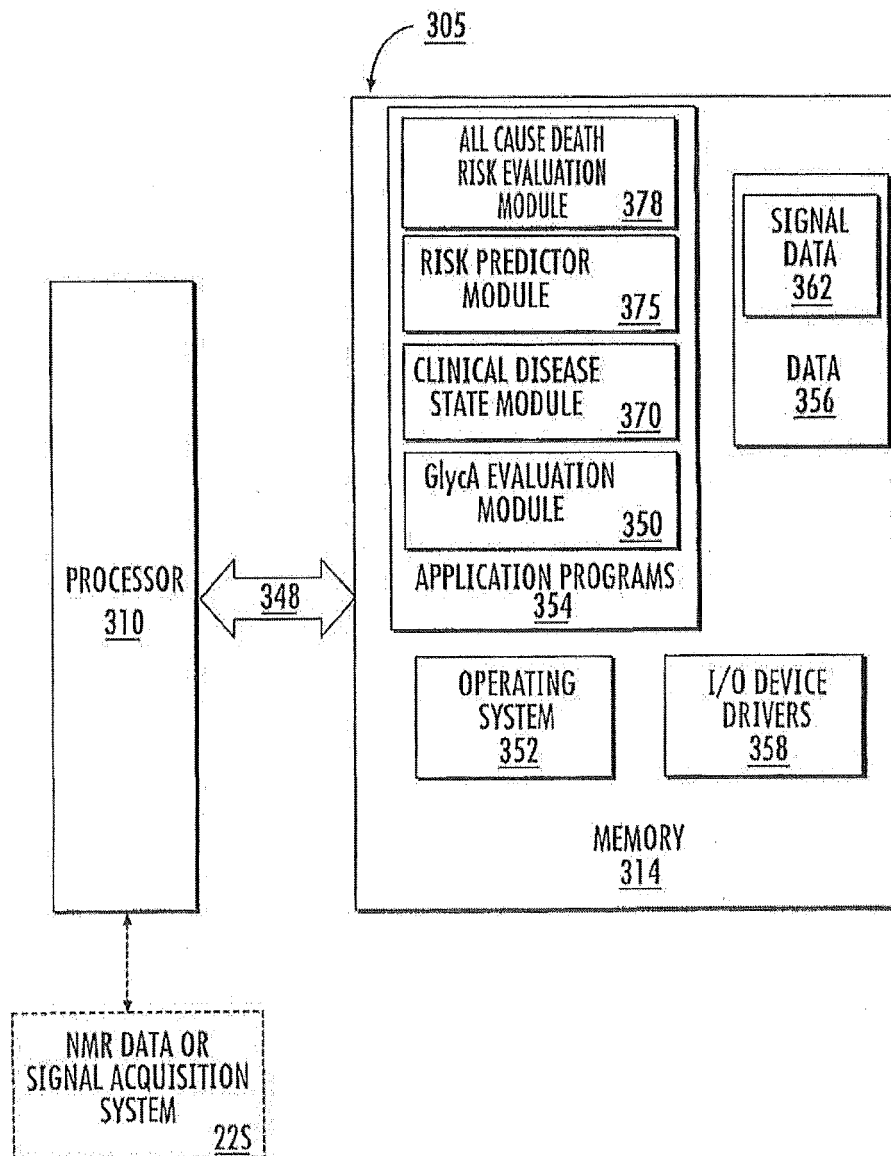


FIG. 19

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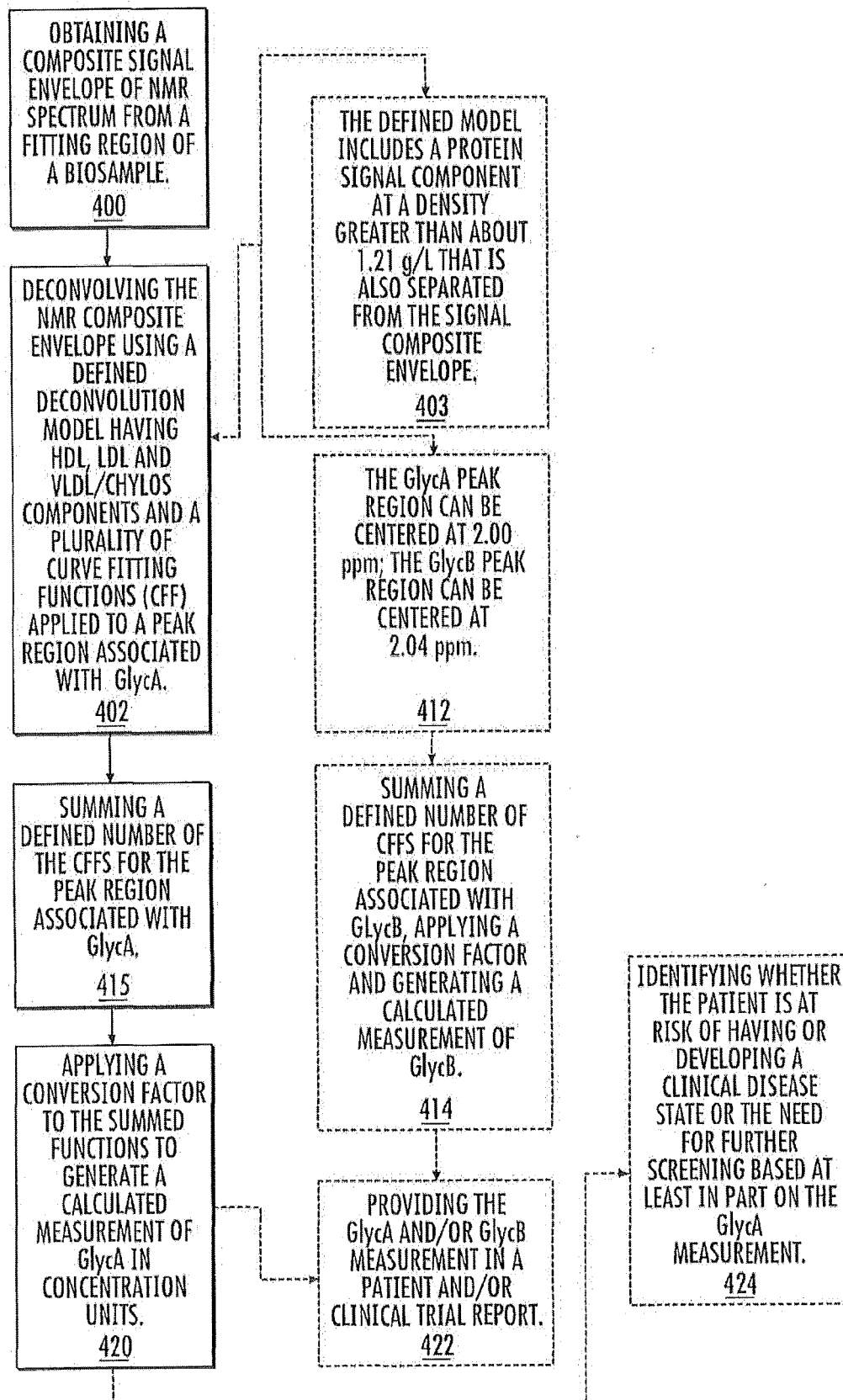


FIG 20

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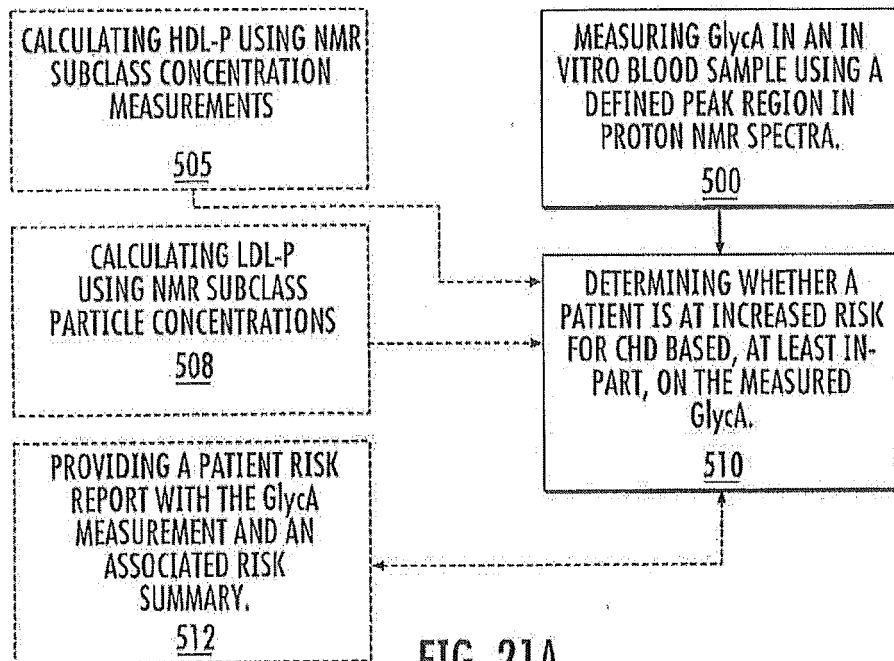


FIG. 21A

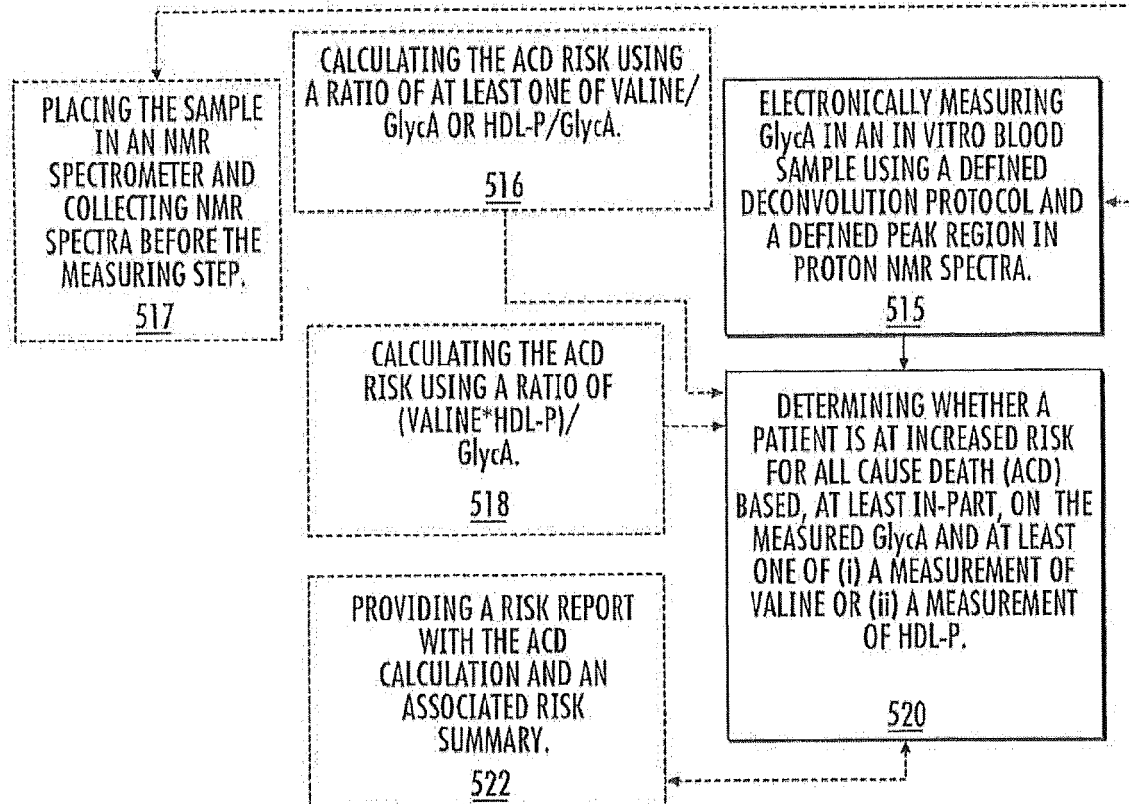


FIG. 21B

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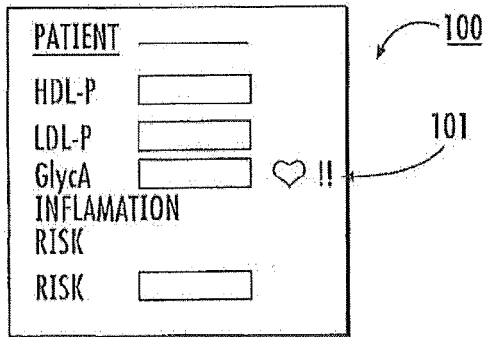


FIG. 22A

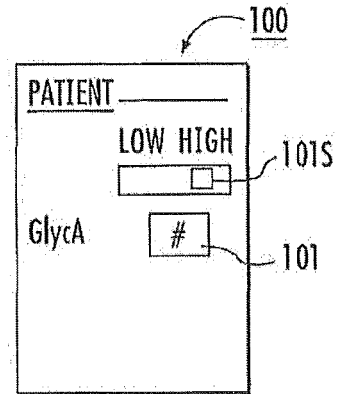


FIG. 22B

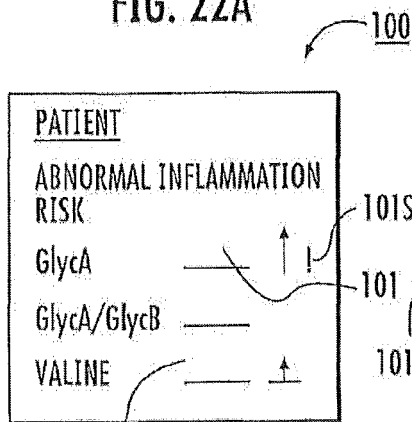


FIG. 22C

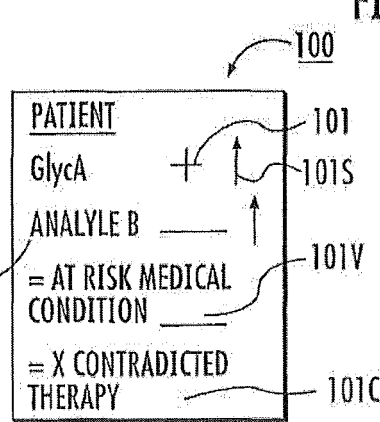


FIG. 22D

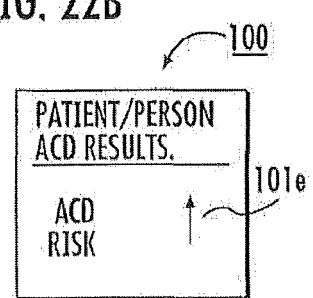


FIG. 22E

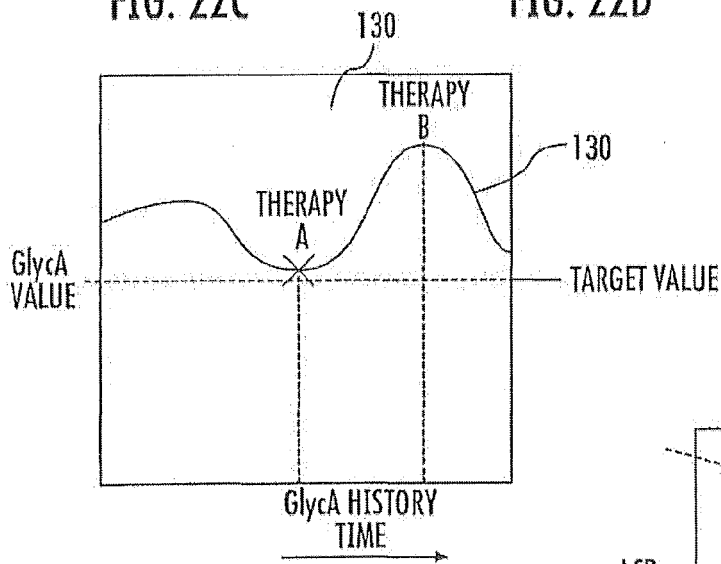


FIG. 23A

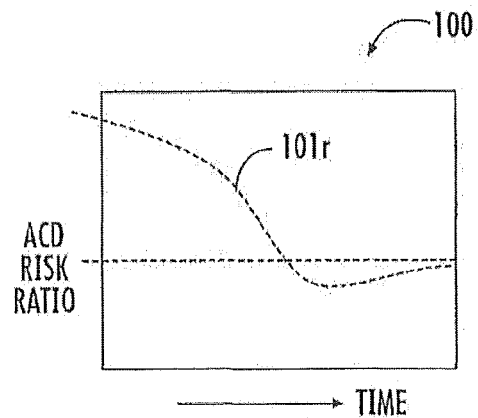


FIG. 23B

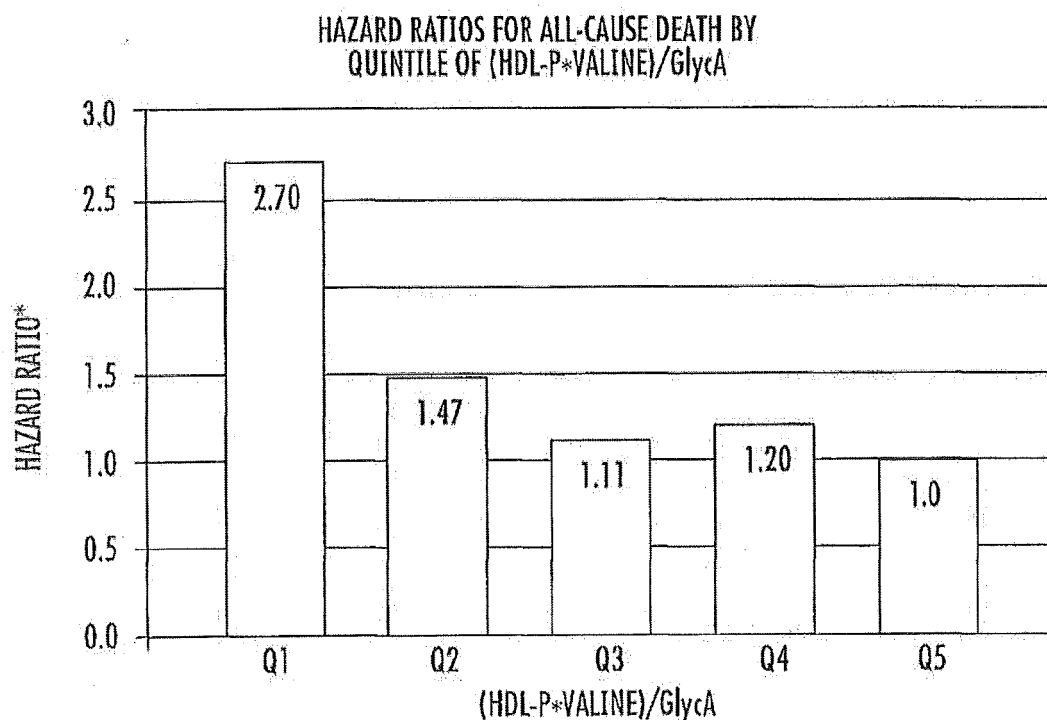
PREDICTION OF ALL-CAUSE DEATH IN MESA (n=5712)*

PARAMETER	MODEL χ^2	c STATISTIC	PARAMETER	PARAMETER χ^2	P
BASE MODEL COVARIATES	330.7	0.770			
+ TC/HDL-C	335.5	0.773		2.68	0.1
+ hsCRP	346.9	0.776		16.6	<0.0001
+ VALINE	348.5	0.777		-17.4	<0.0001
+ GlycA	354.0	0.778		23.9	<0.0001
+ HDL-P	347.7	0.777		-16.4	<0.0001
+ HDL-P/GlycA	367.4	0.782		-34.8	<0.0001
+ HDL-P*VALINE	360.7	0.780		-28.4	<0.0001
+ HDL-P*VALINE + GlycA	384.9	0.788	HDL-P*VALINE	-29.2	<0.0001
			GlycA	24.6	<0.0001
+HDL-P+VALINE+GlycA	388.5	0.789	HDL-P	-15.6	<0.0001
			VALINE	-16.9	<0.0001
			GlycA	24.4	<0.0001
+ (HDL-P*VALINE)/GlycA	382.2	0.786		-47.6	<0.0001

*PREDICTION OF ALL-CAUSE DEATH (n=346) FROM LOGISTIC REGRESSION ANALYSES (ADJUSTED).

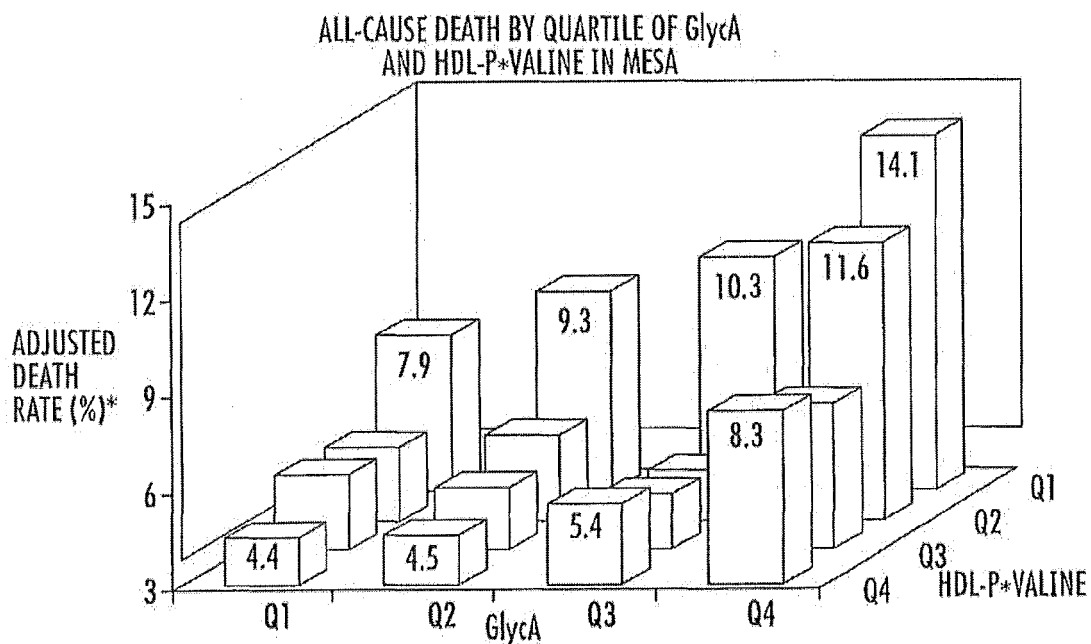
FIG. 24

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*HAZARD RATIOS FOR ALL-CAUSE DEATH (n=346) ARE FROM COX PROPORTIONAL HAZARDS REGRESSION ANALYSES ADJUSTED FOR AGE, GENDER, AND SMOKING.

FIG. 25A

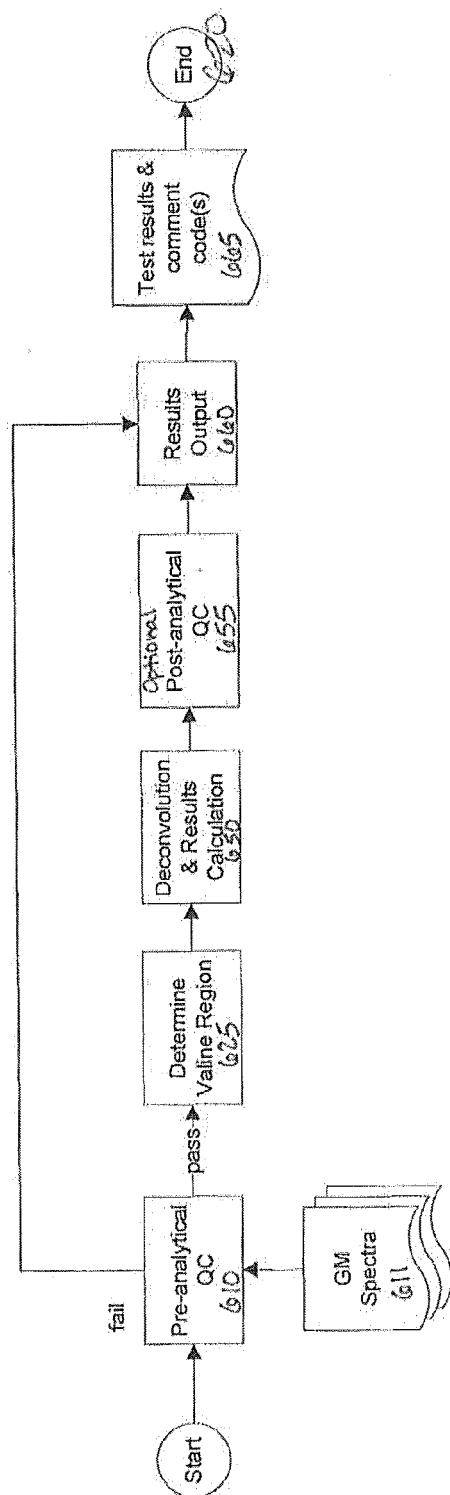


*DEATH RATE (%) DURING 7-YEAR FOLLOW-UP, ADJUSTED FOR AGE, GENDER, AND SMOKING

FIG. 25B

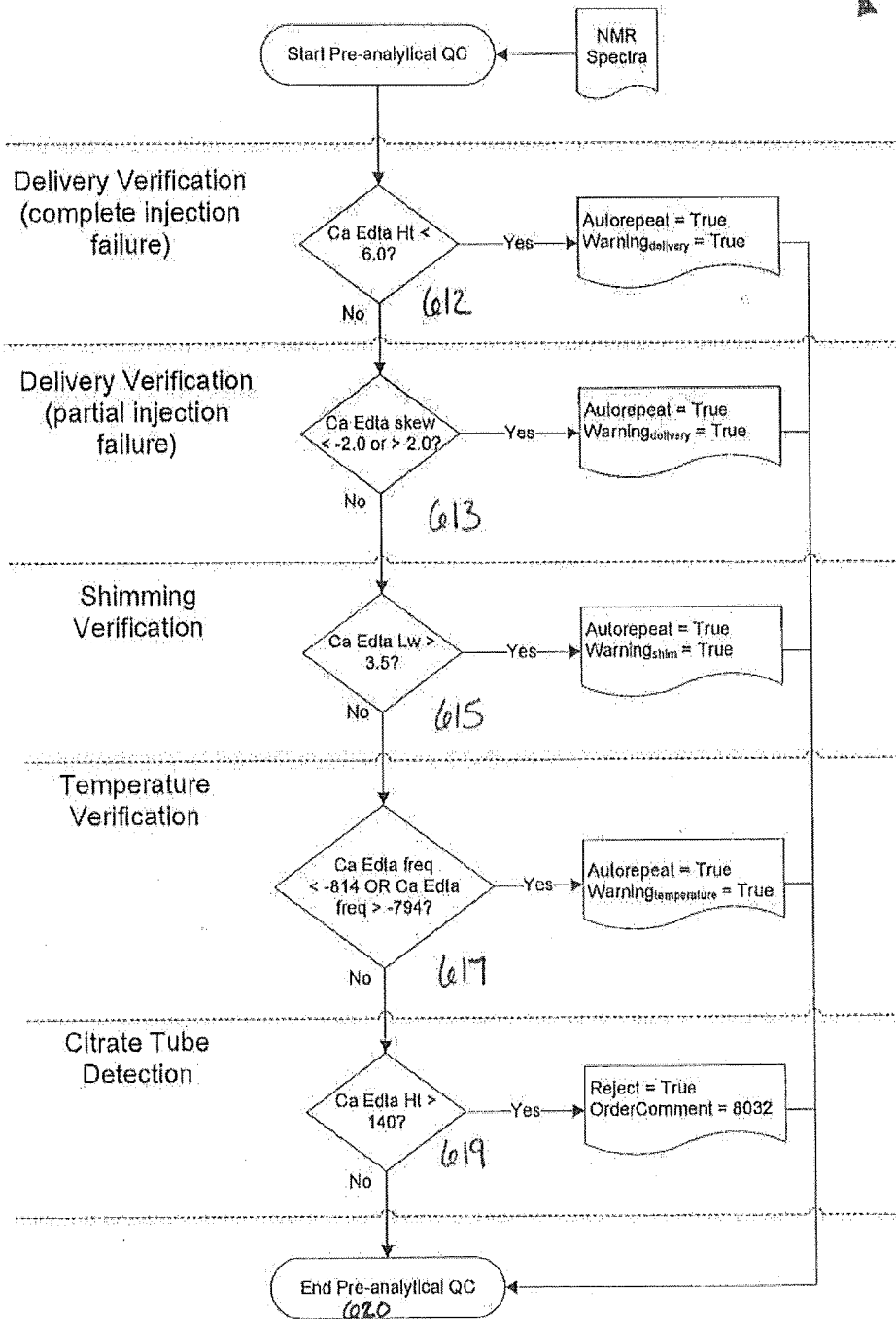
600

Fig. 26A



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Fig. 26B



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Fig. 26C

