

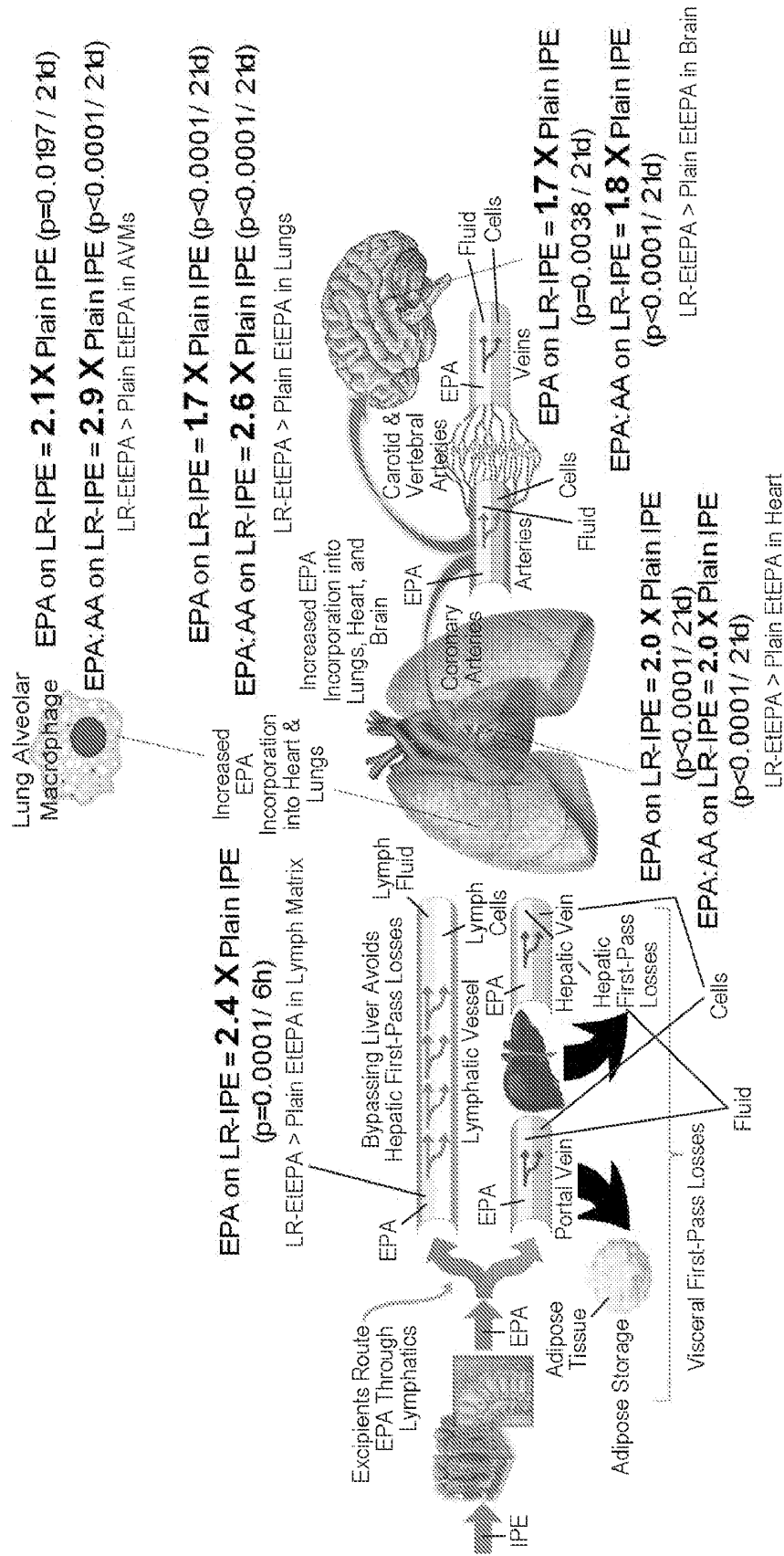


FIG. 1A

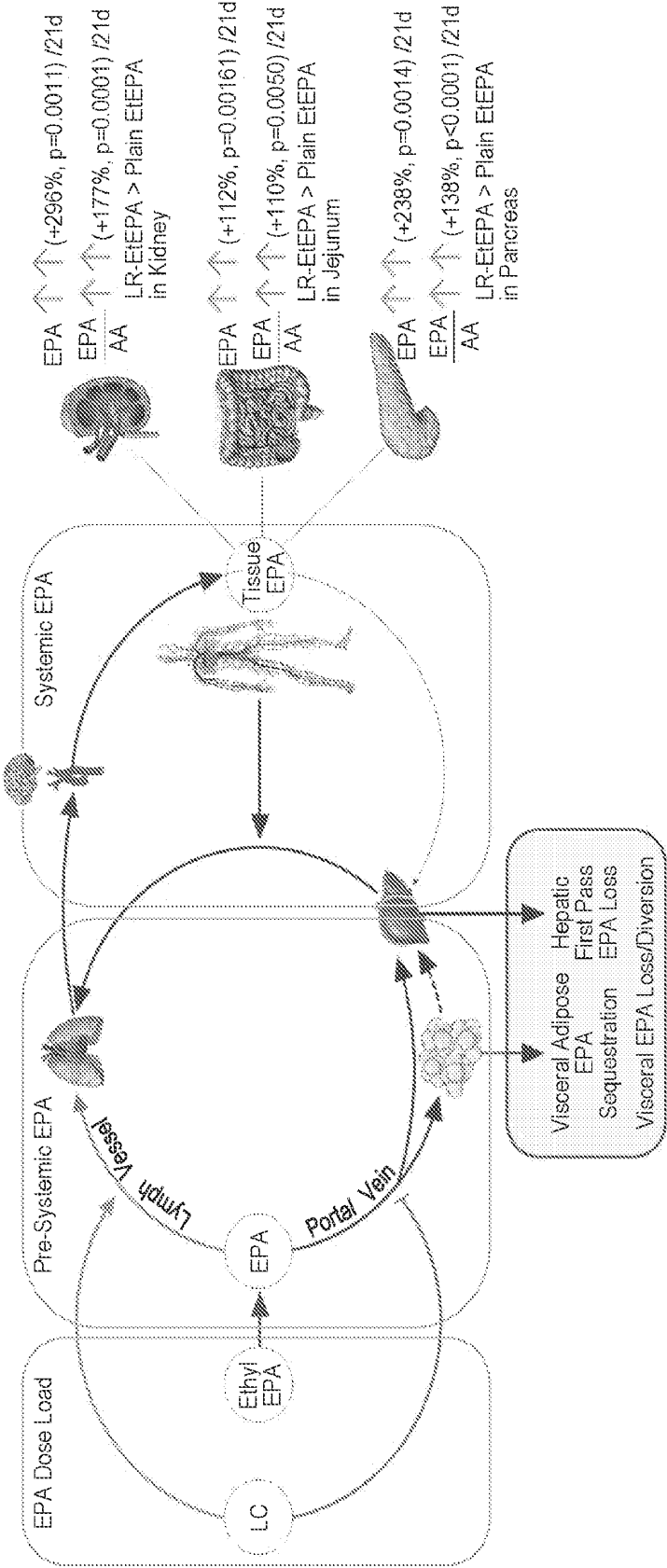


FIG. 1B

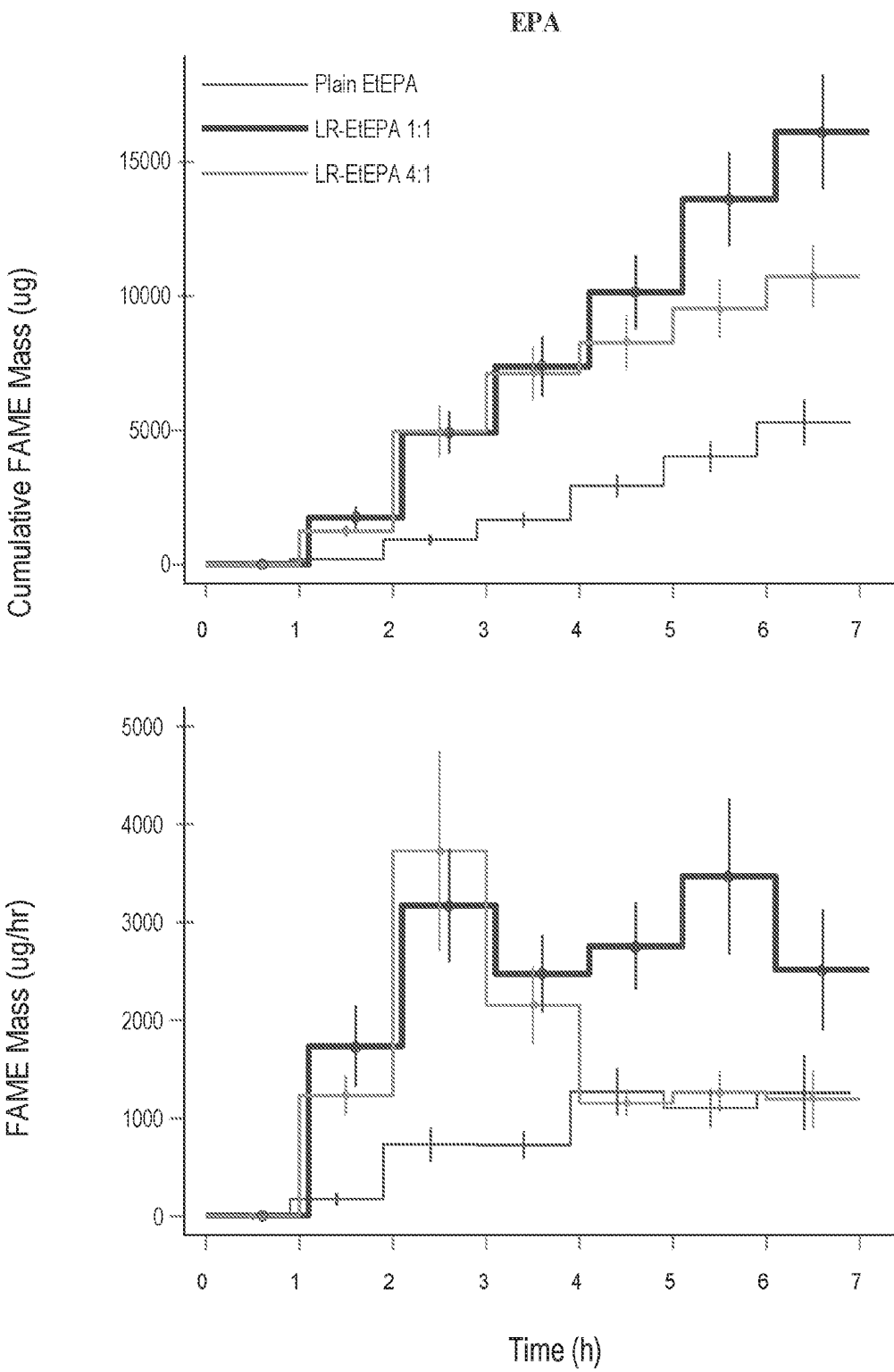
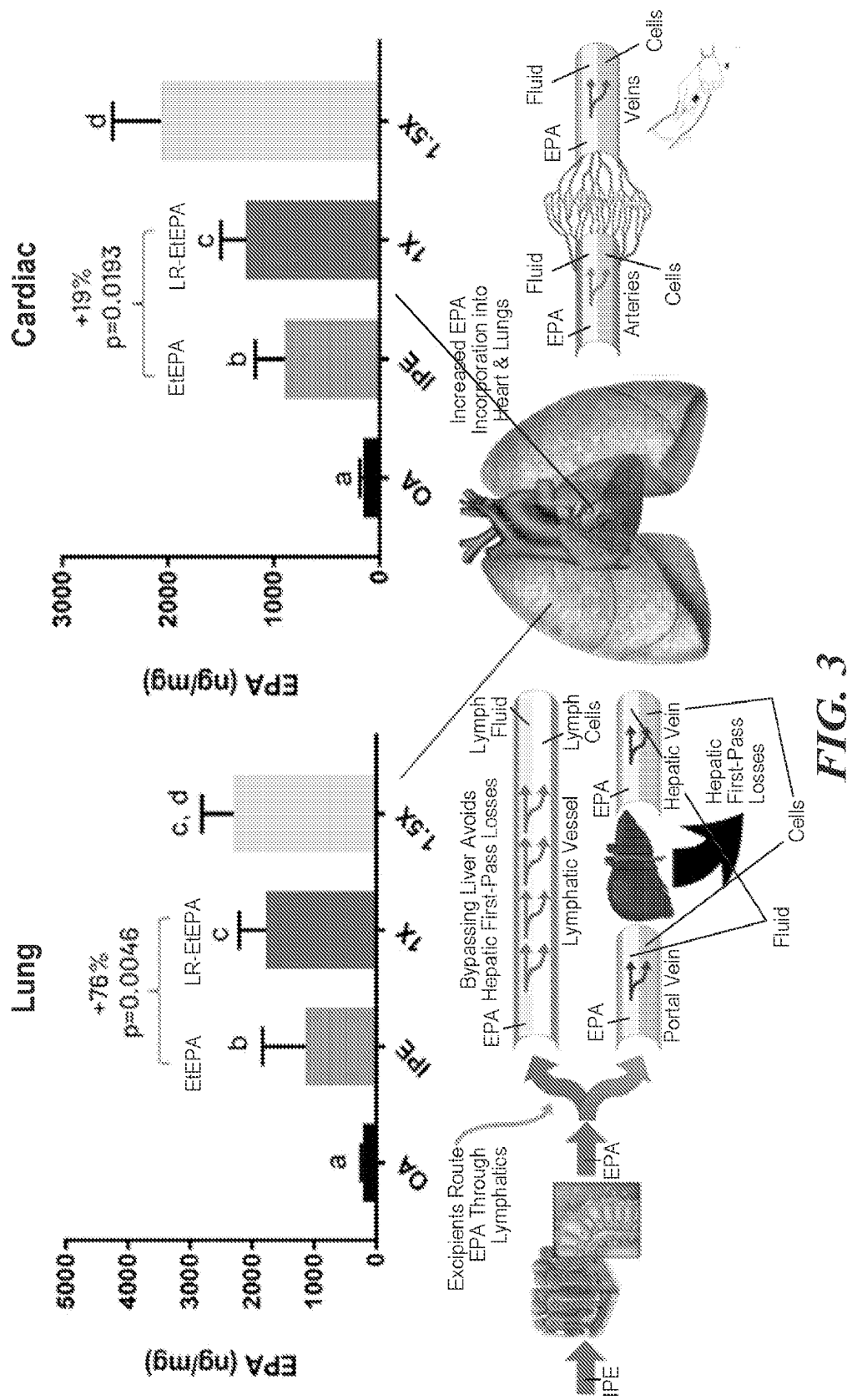


FIG. 2



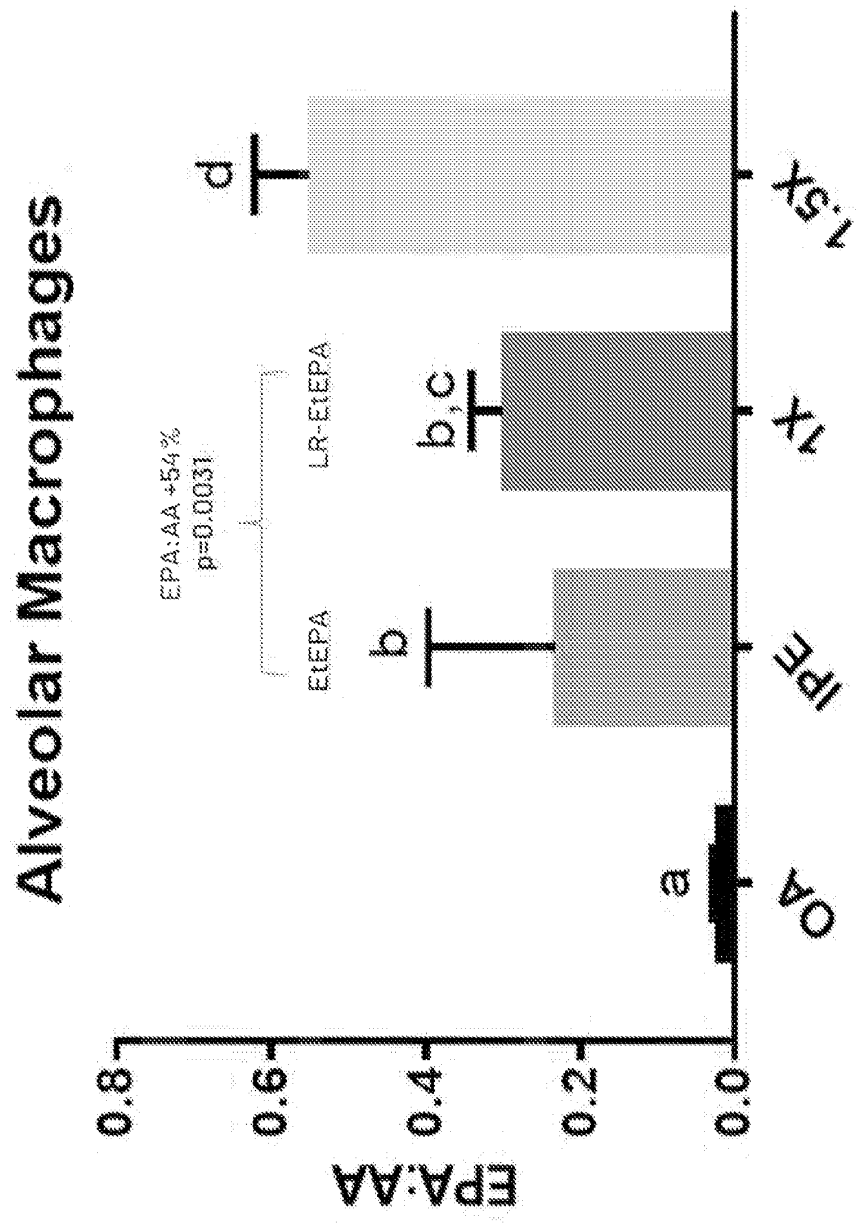
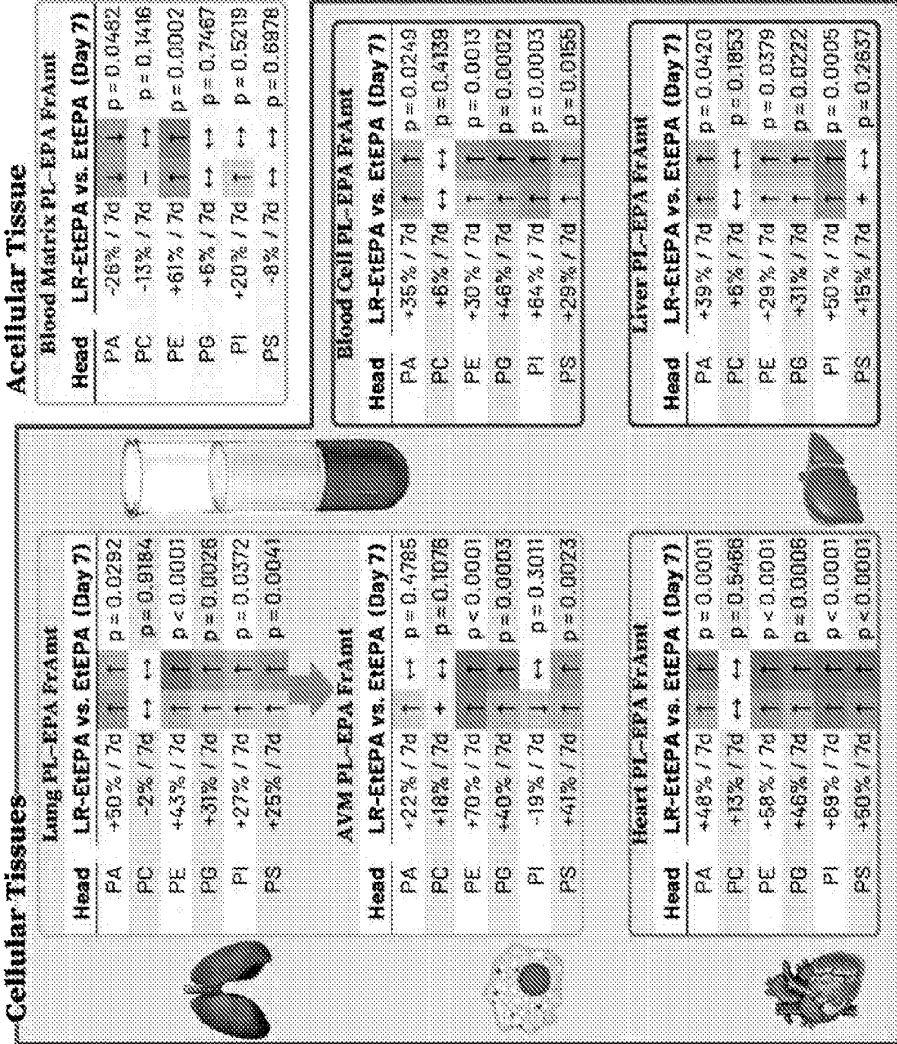


FIG. 4

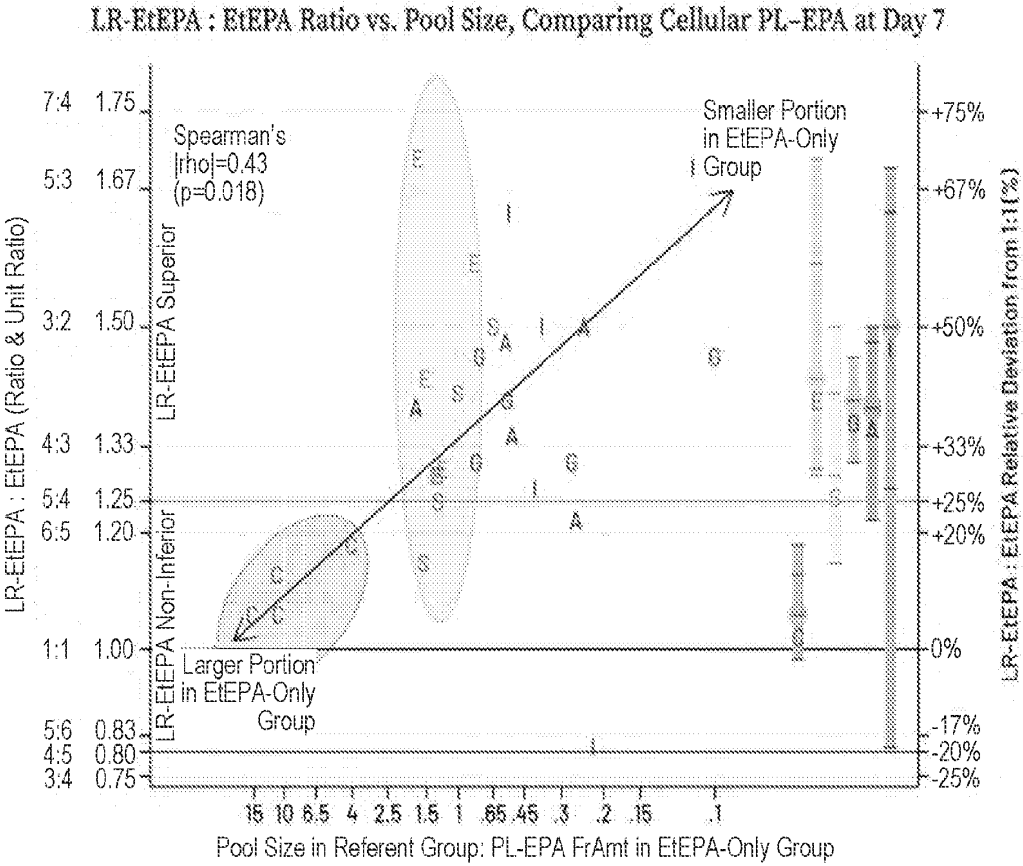
LR-EtEPA vs EtEPA for EPA Fractional Amount (FrAmt, 100th) on Day 7



Key to Phospholipid Head Groups:

- PA = Phosphatidic Acid
- PC = Phosphatidyl Choline
- PE = Phosphatidyl Ethanolamine
- PG = Phosphatidyl Glycerol
- PI = Phosphatidyl Inositol
- PS = Phosphatidyl Serine

FIG. 5



Key	Phospho-lipid	Substituent (X)
A	PA	Hydrogen -H
C	PC	Choline <chem>CC[N+](C)(C)C</chem>
E	PE	Ethanolamine <chem>CCN</chem>
G	PG	Glycerol <chem>CC(O)CO</chem>
I	PI	Inositol <chem>C1C(C(C(C(C(C1O)O)O)O)O)O</chem>
S	PS	Serine <chem>C(C(=O)[O-])N</chem>

FIG. 6

Vector Plot of LR-EtEPA : EtEPA Ratio, Comparing Lung PL-EPA at Day 7

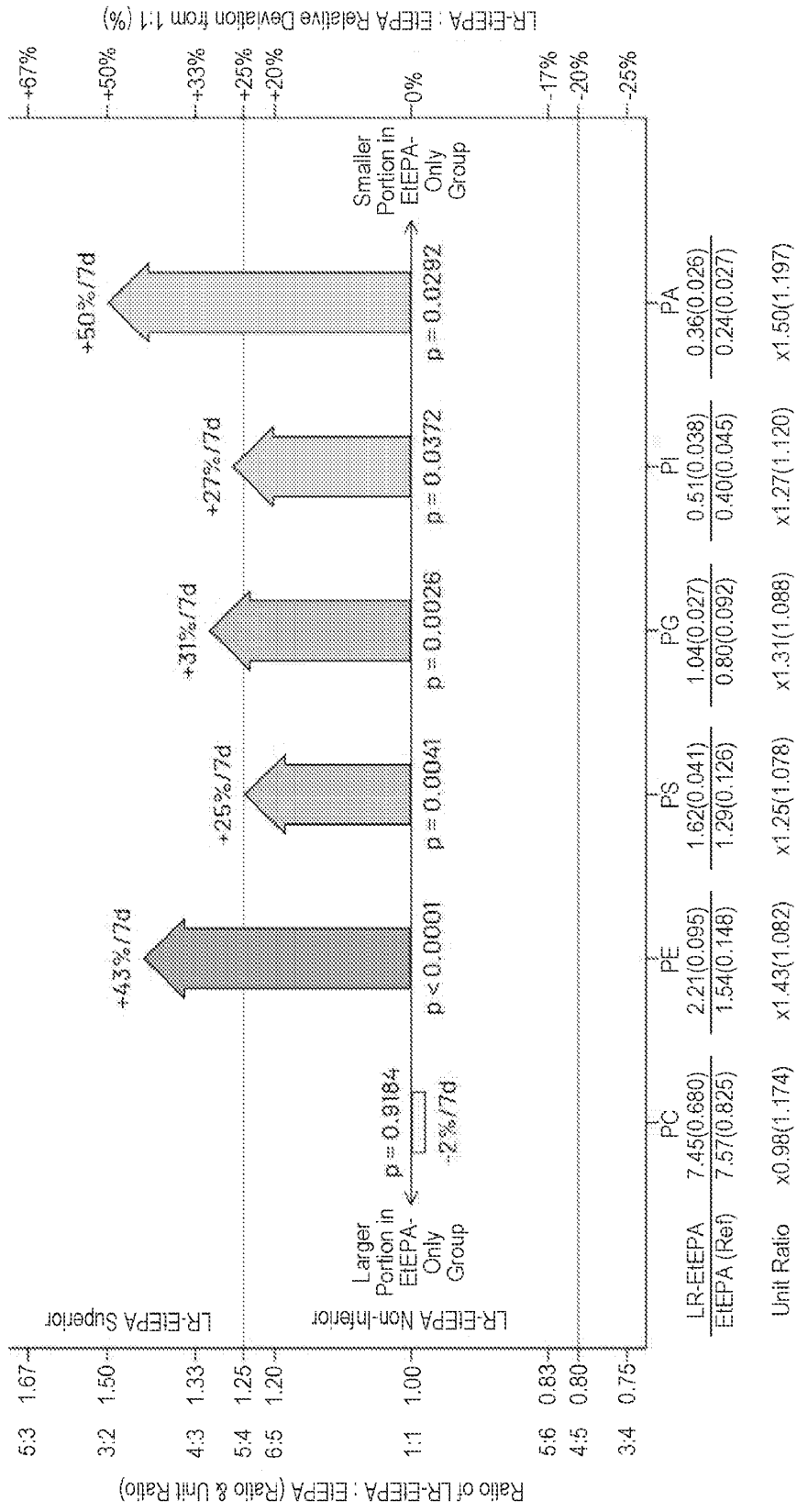


FIG. 7

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Vector Plot of LR-EtEPA : EtEPA Ratio, Comparing Alveolar Macrophage PL-EPA at Day 7

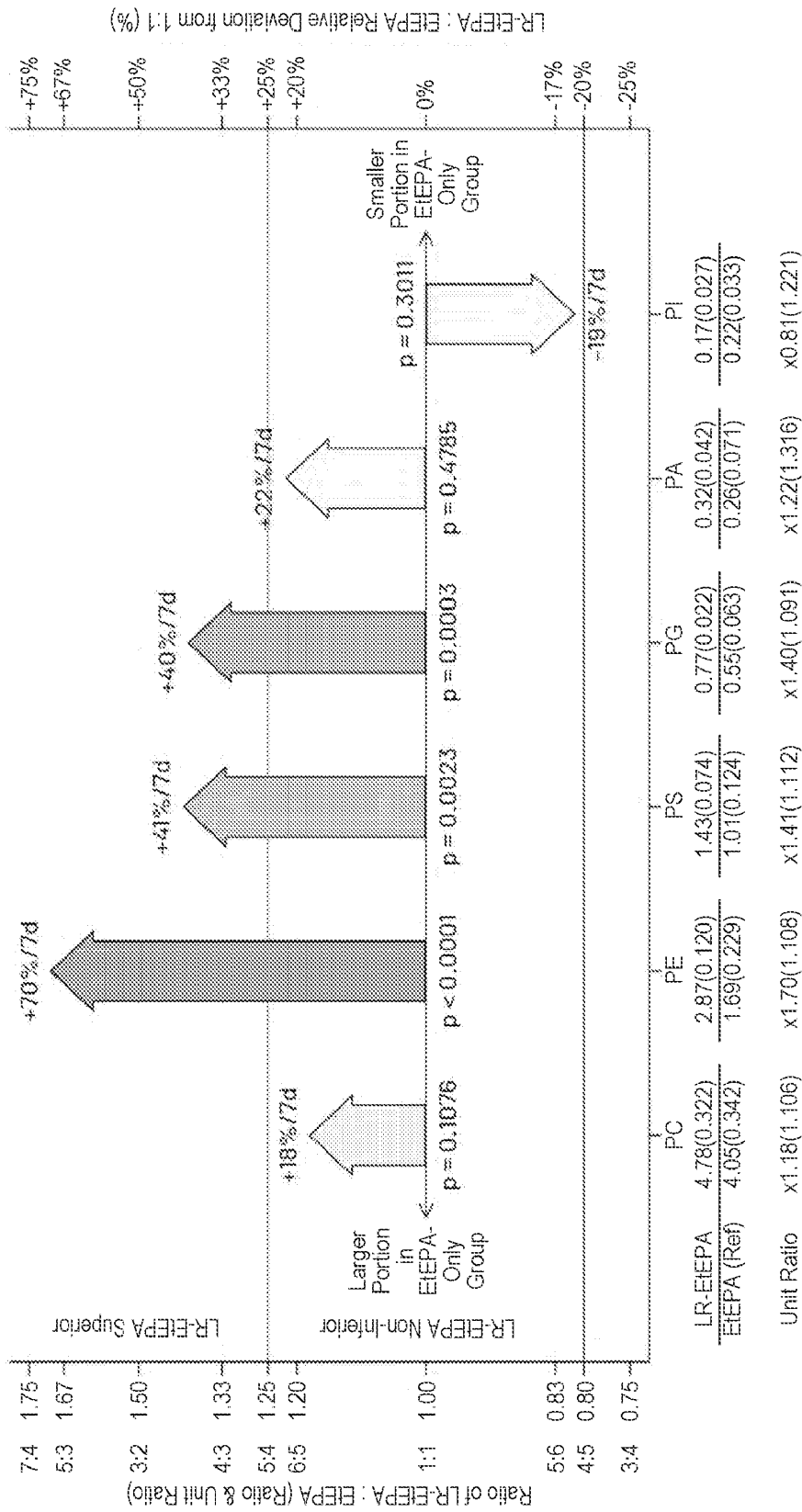


FIG. 8

Vector Plot of LR-EIEPA : EIEPA Ratio, Comparing Heart PL-EPA at Day 7

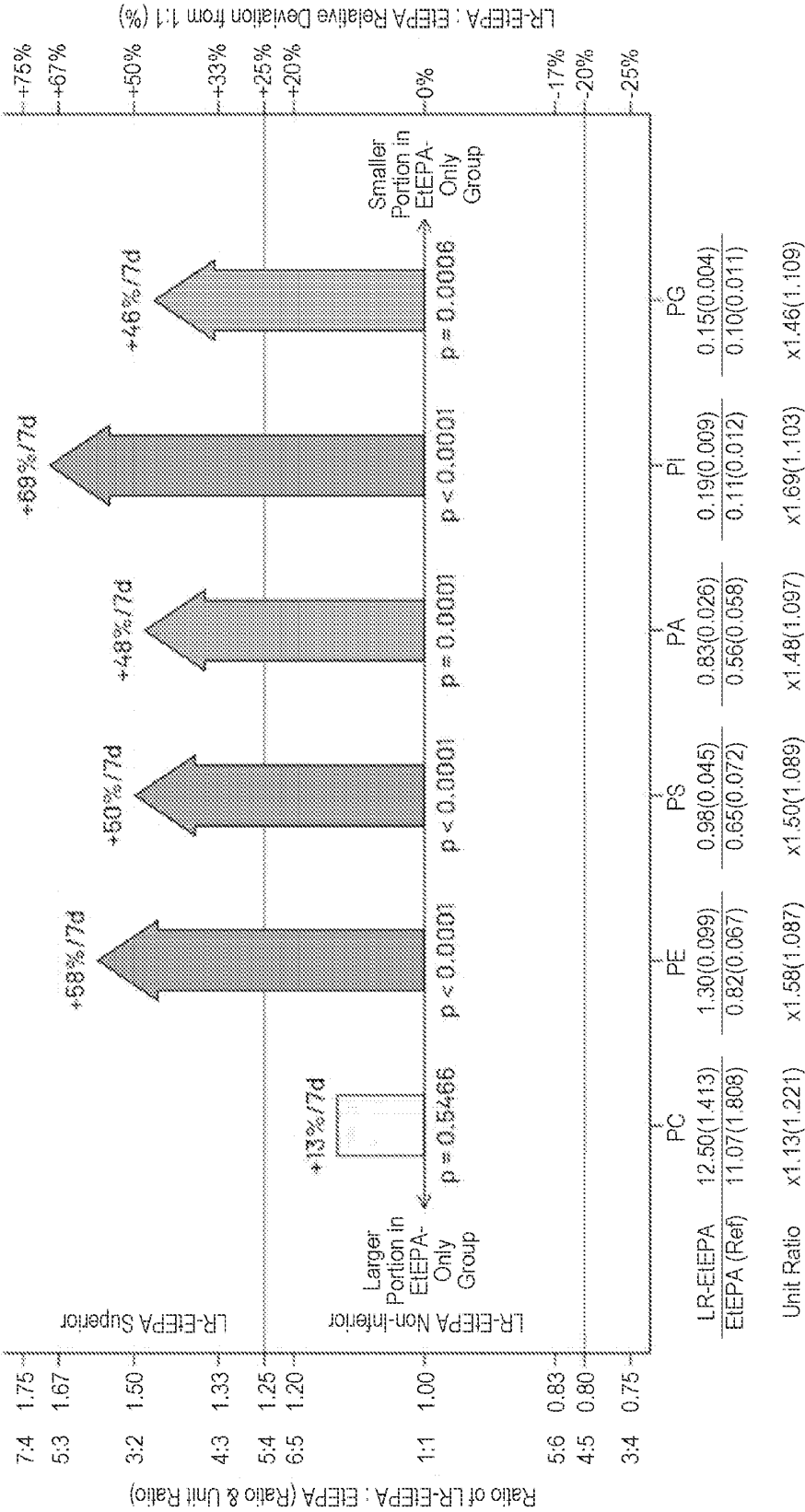


FIG. 9

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Vector Plot of LR-EtEPA : EtEPA Ratio, Comparing Blood Matrix PL-EPA at Day 7

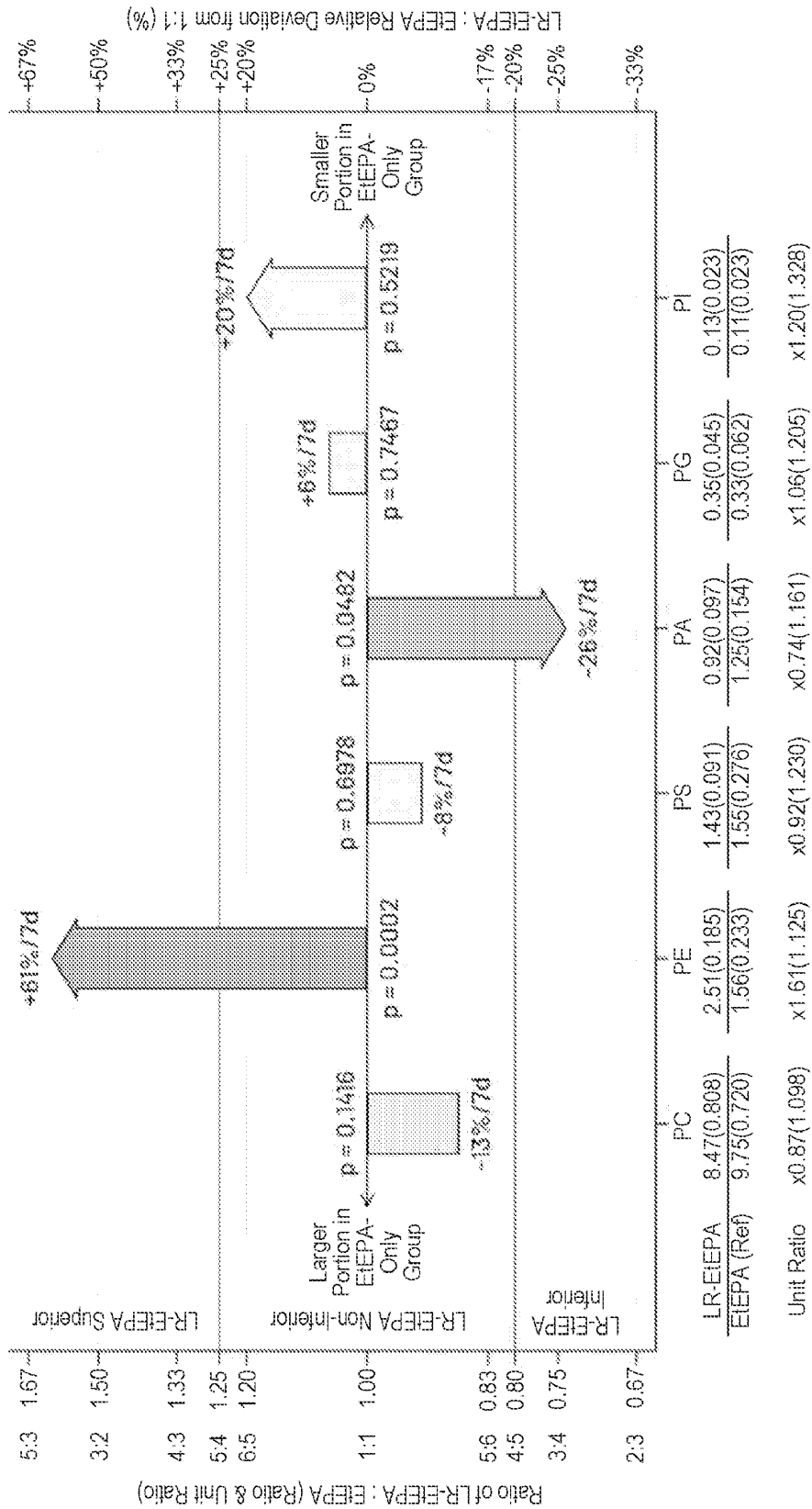


FIG. 10

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Vector Plot of LR-EIEPA : EIEPA Ratio, Comparing Blood Cell PL-EPA at Day 7

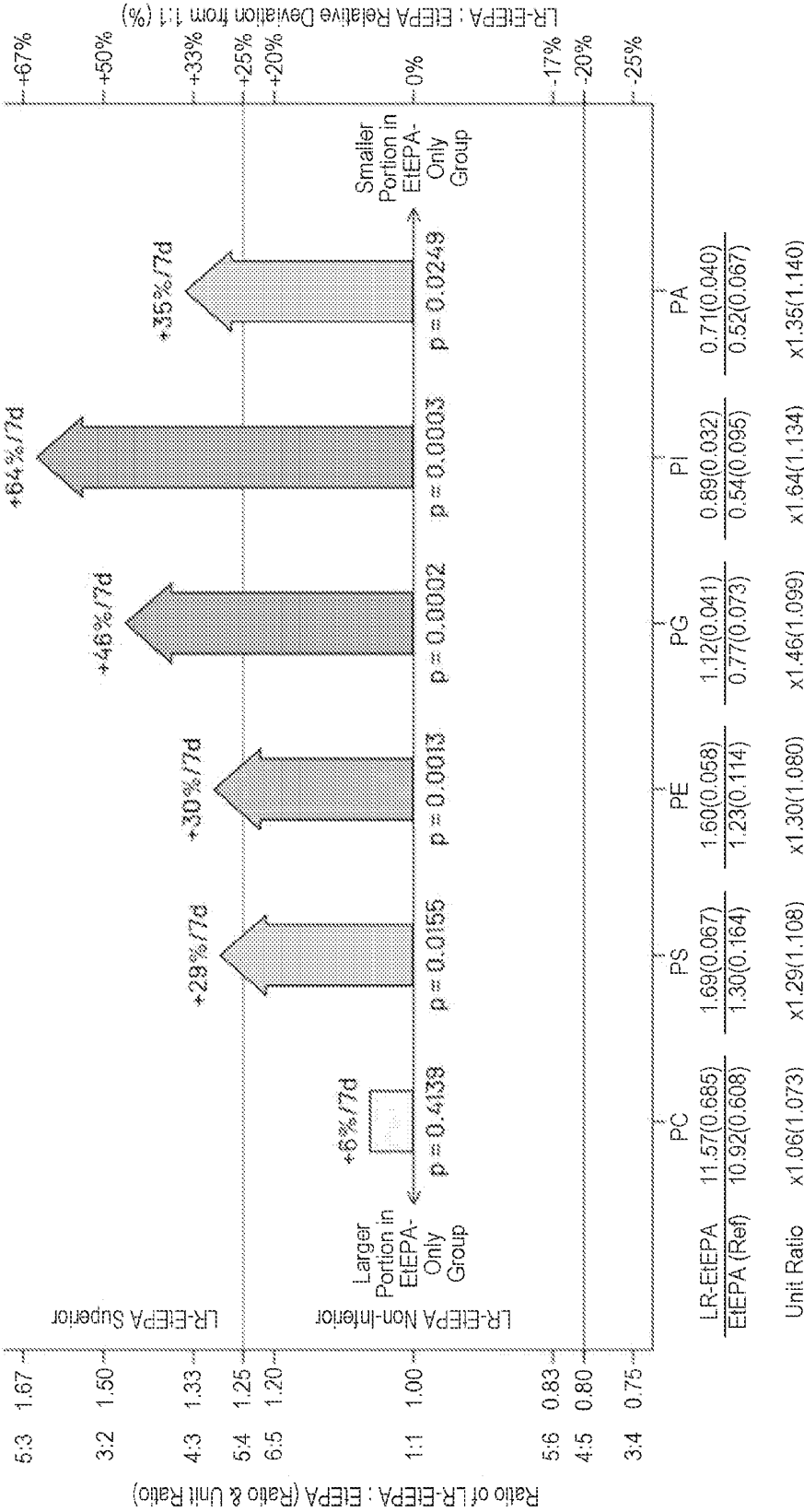
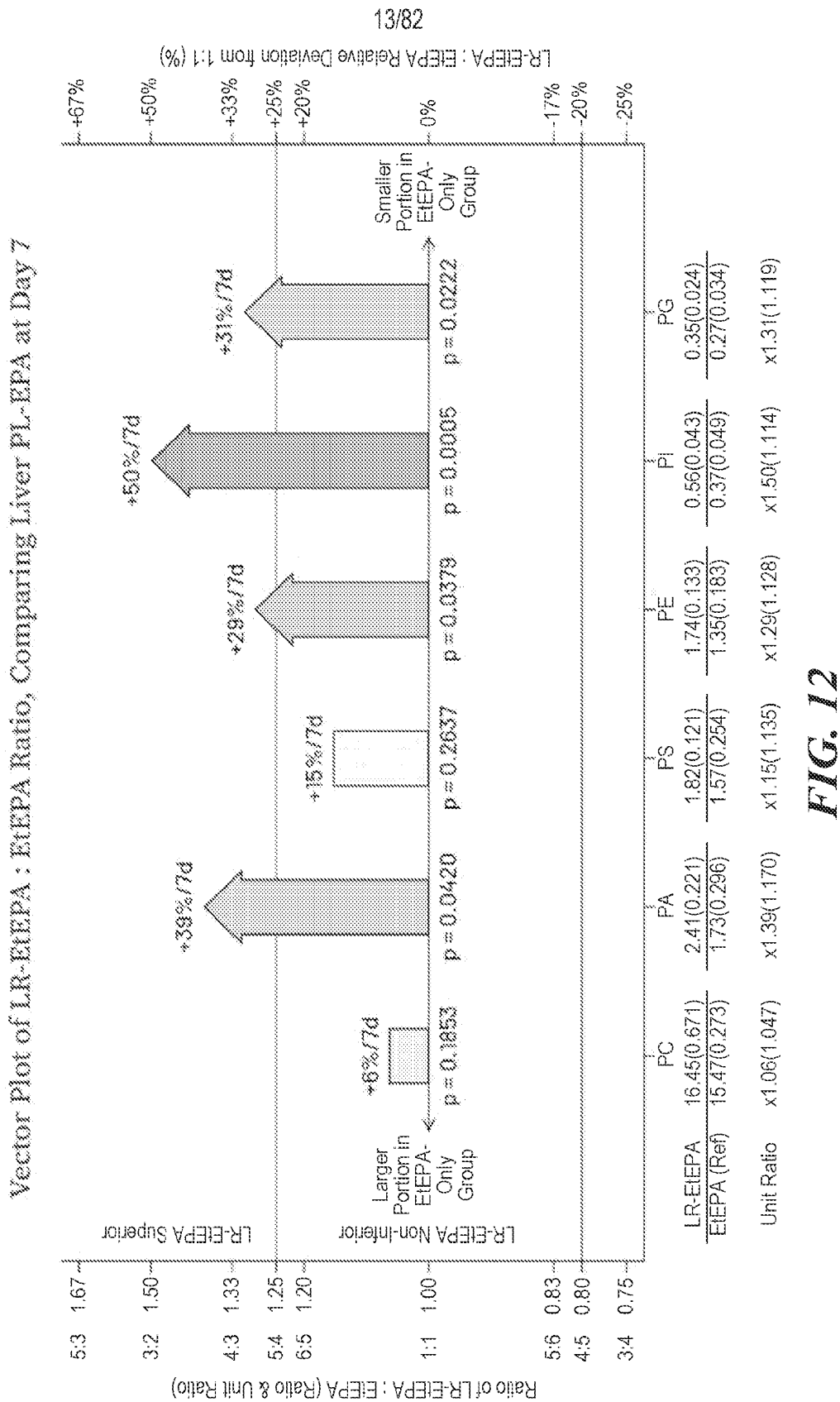


FIG. 11



LR-EtEPA vs EtEPA for EPA to ARA Ratio Fractional Amount (FrAmt, 100th) on Day 7

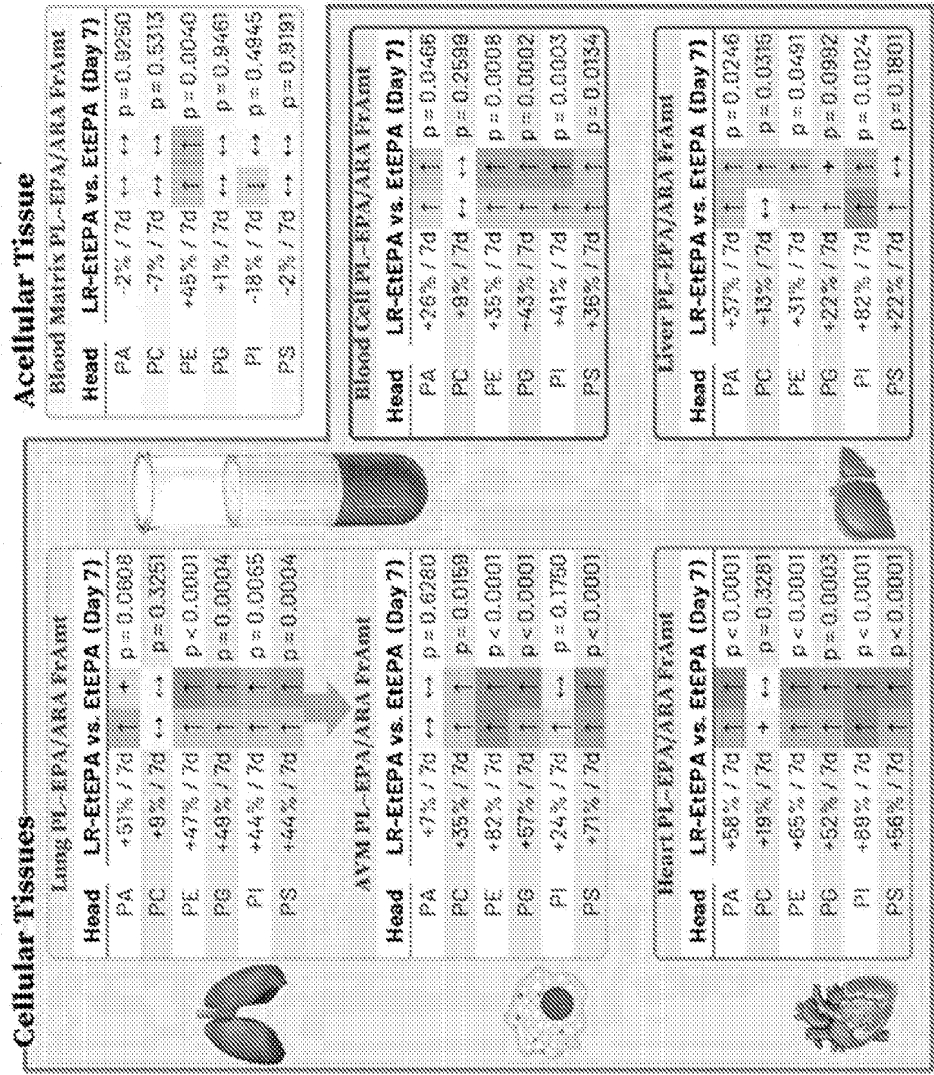


FIG. 13

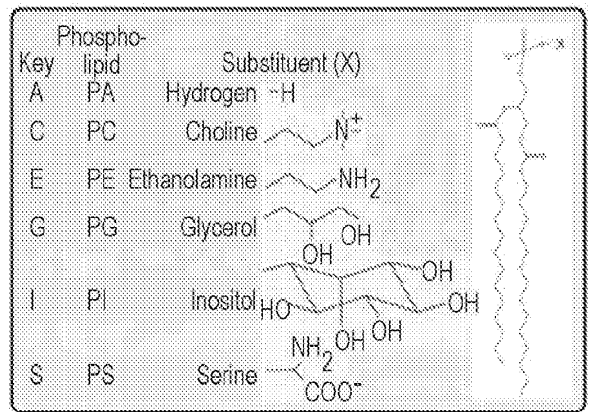
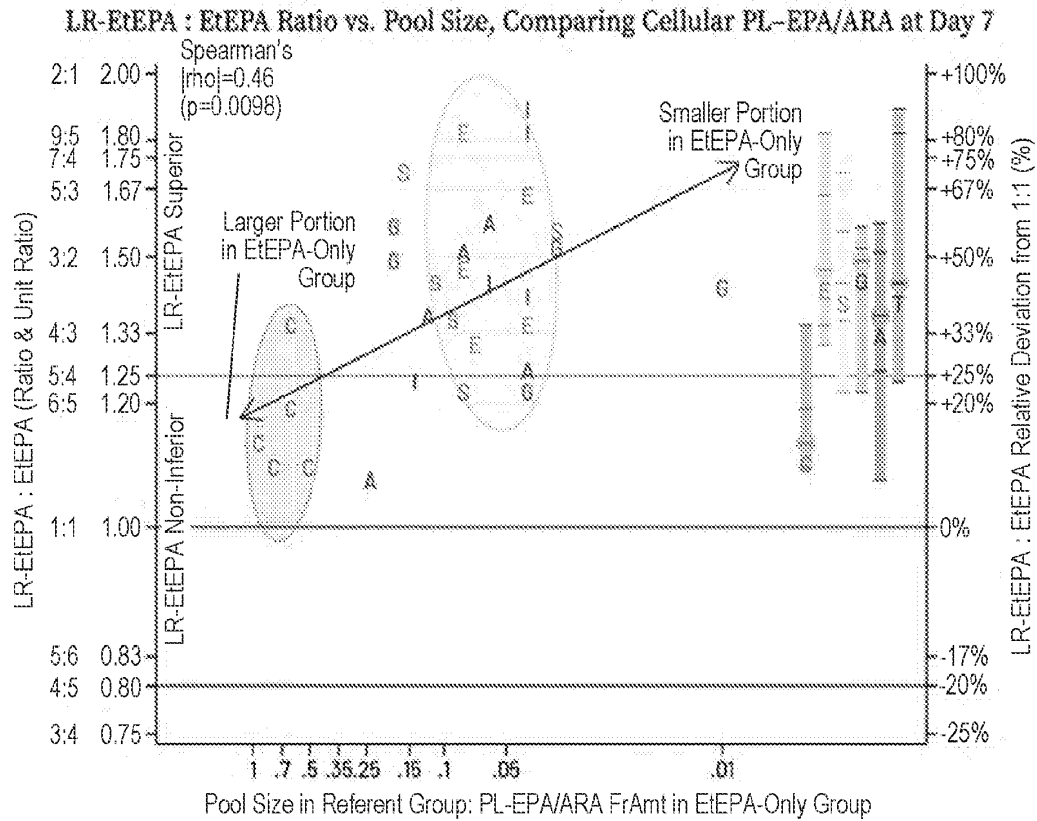
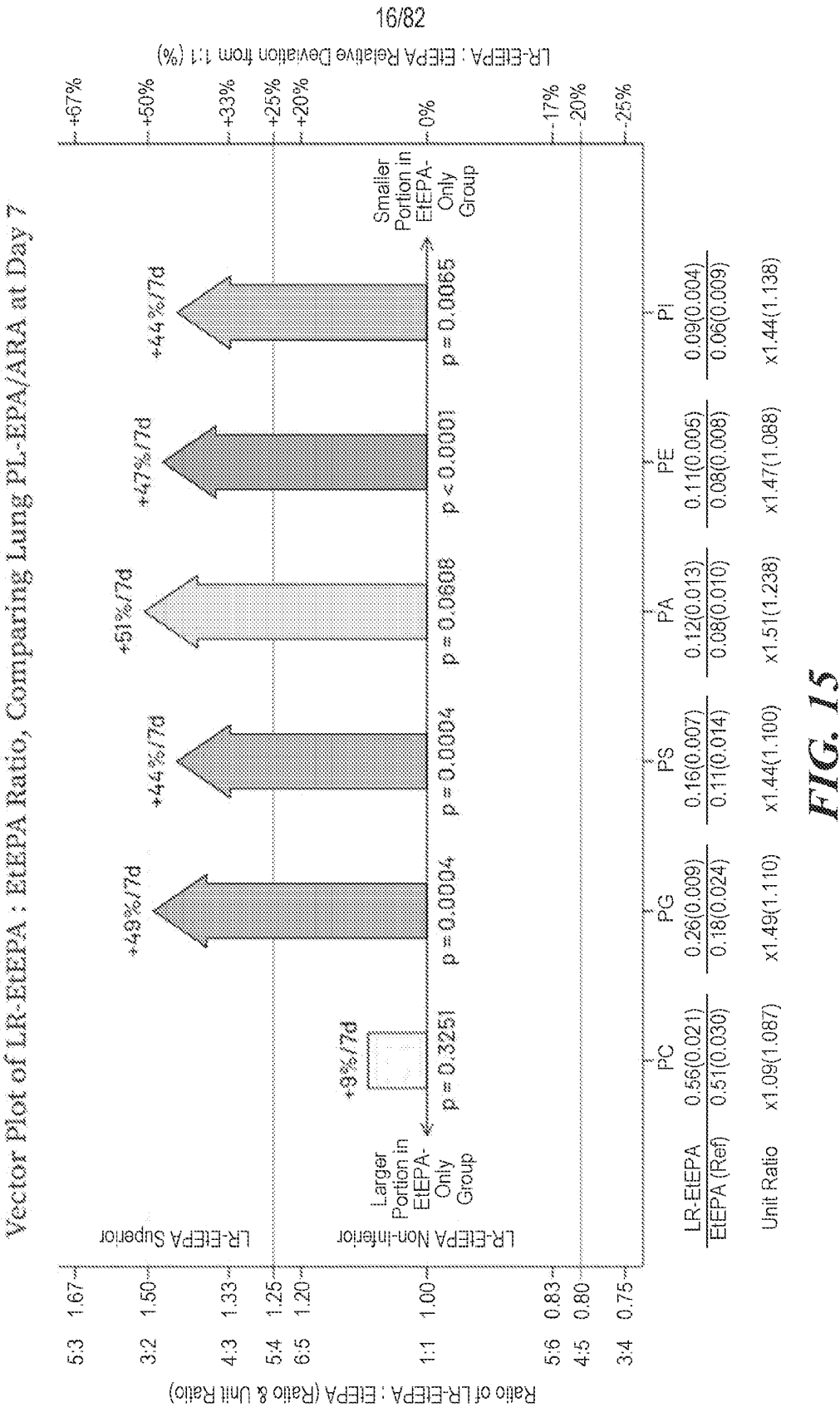


FIG. 14



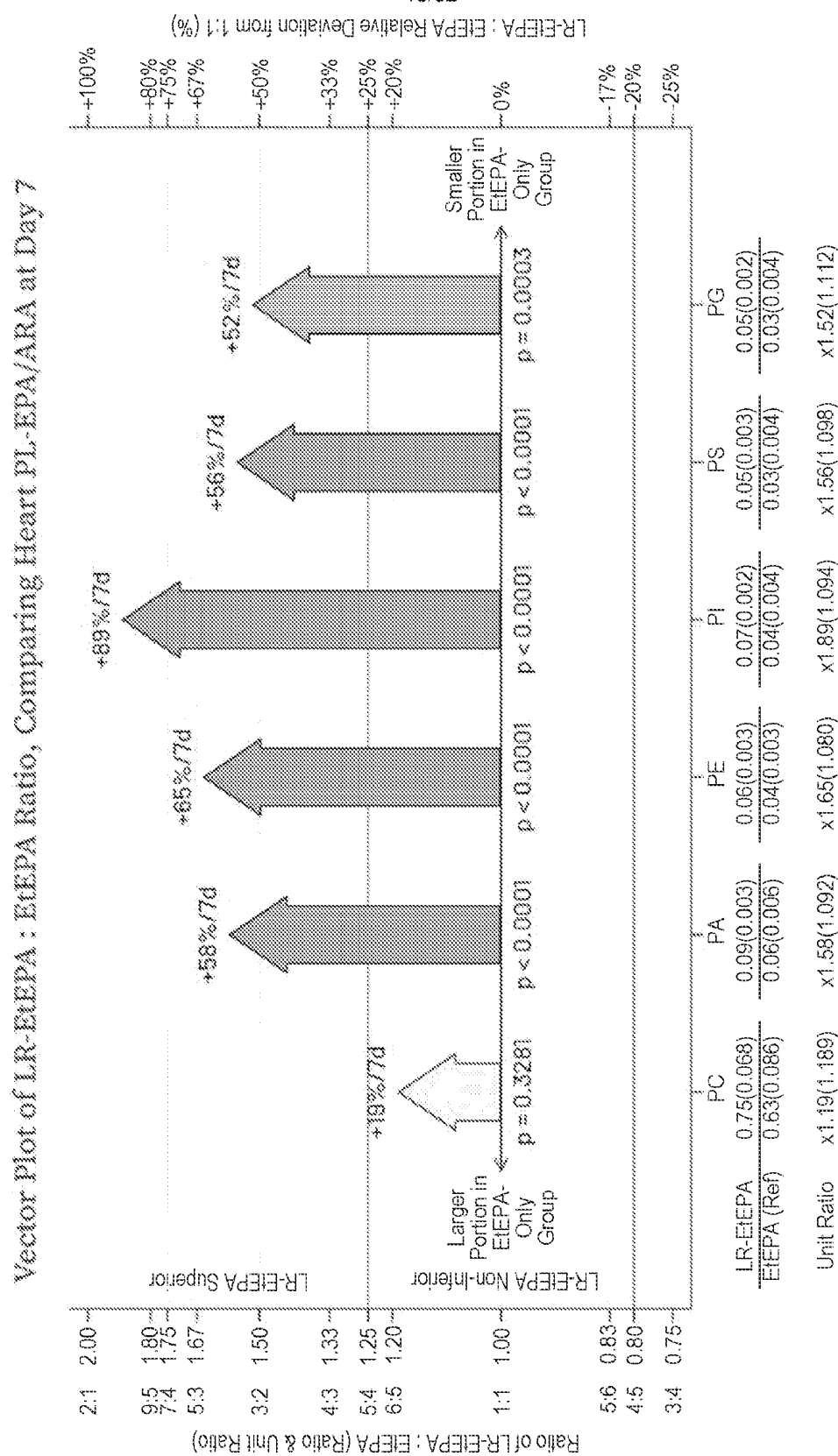


FIG. 17

Vector Plot of LR-EtEPA : EtEPA Ratio, Comparing Blood Matrix PL-EPA/ARA at Day 7

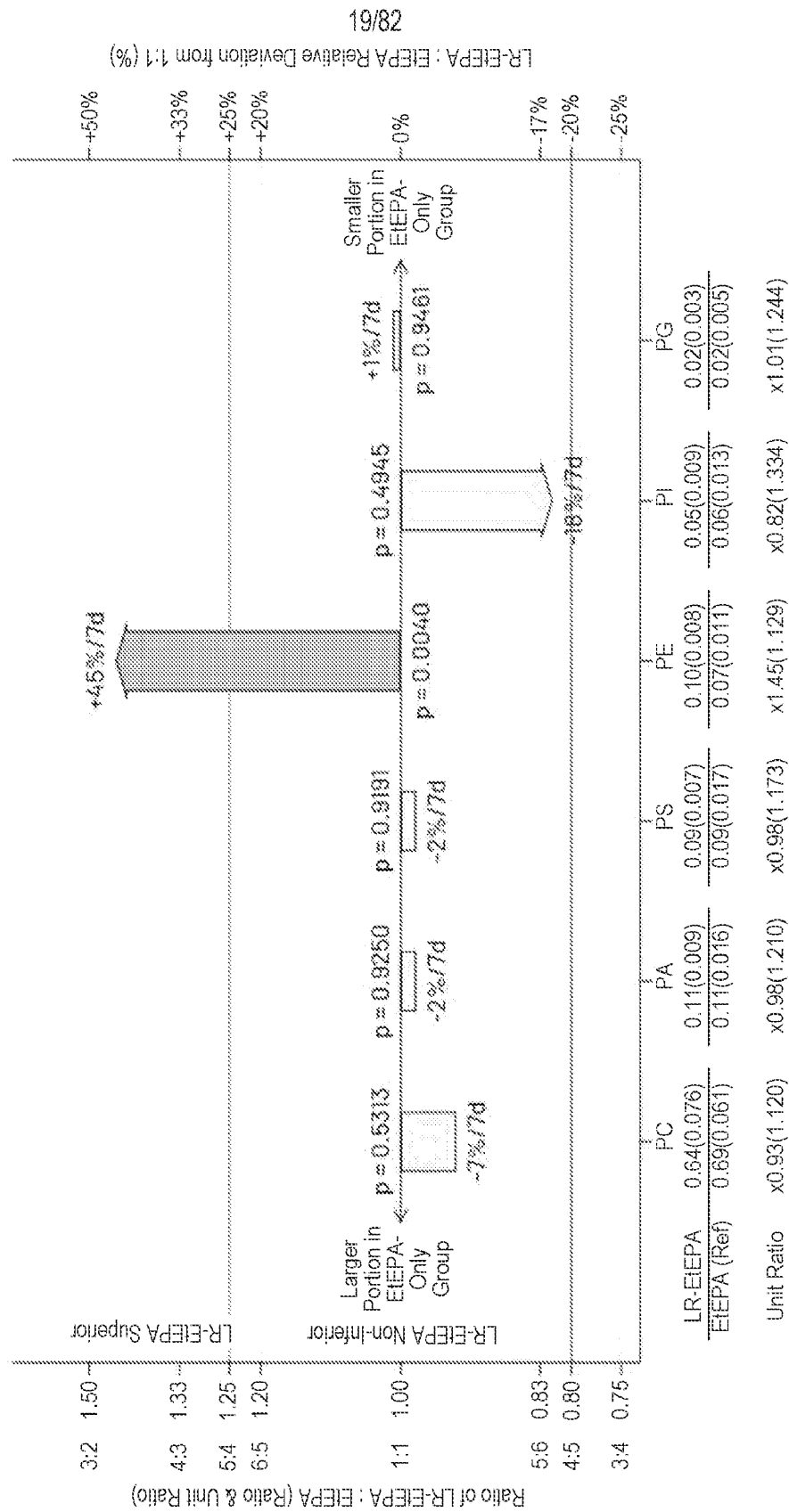


FIG. 18

Vector Plot of LR-EIEPA : EIEPA Ratio, Comparing Blood Cell PL-EPA/ARA at Day 7

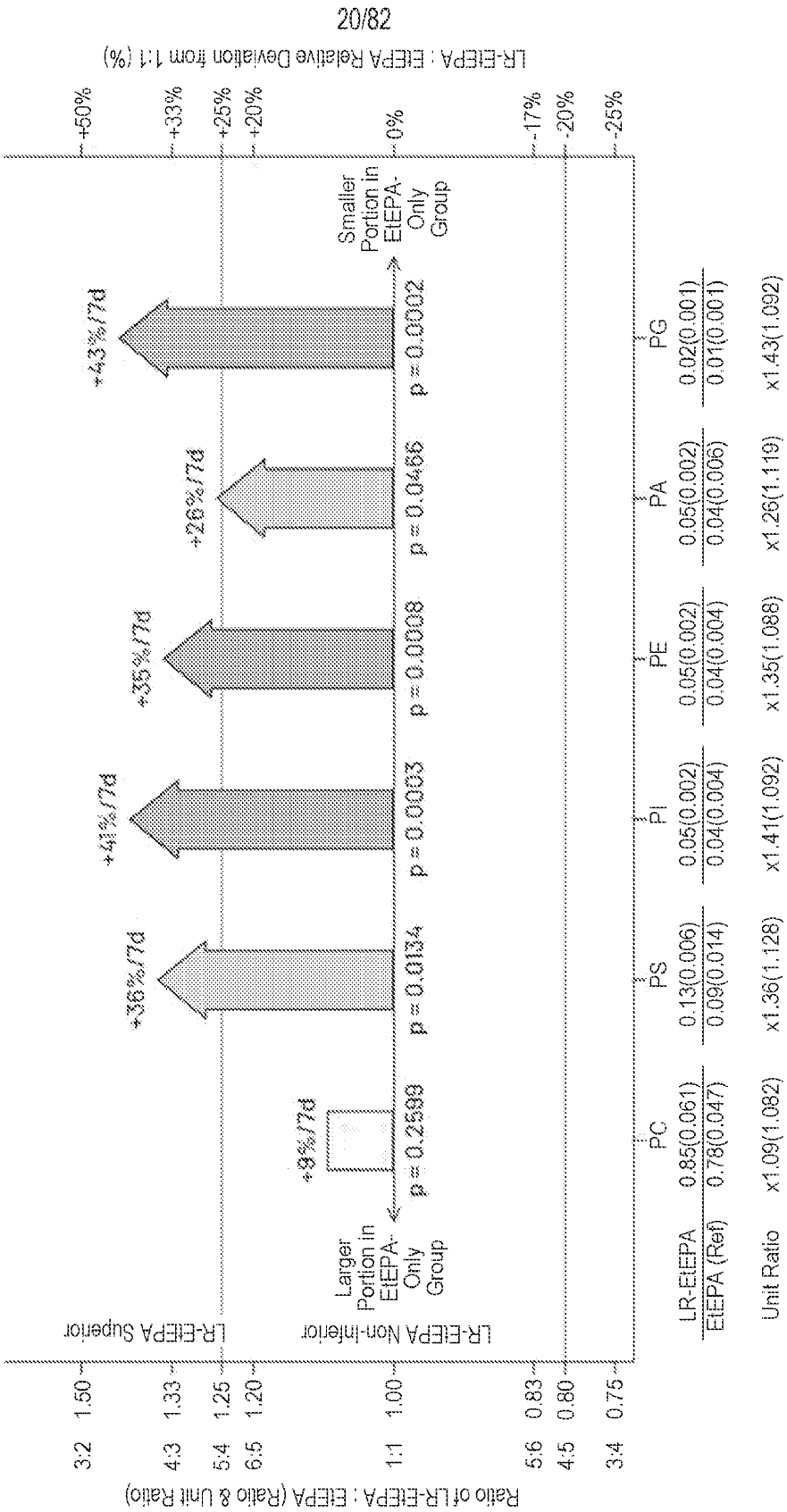


FIG. 19

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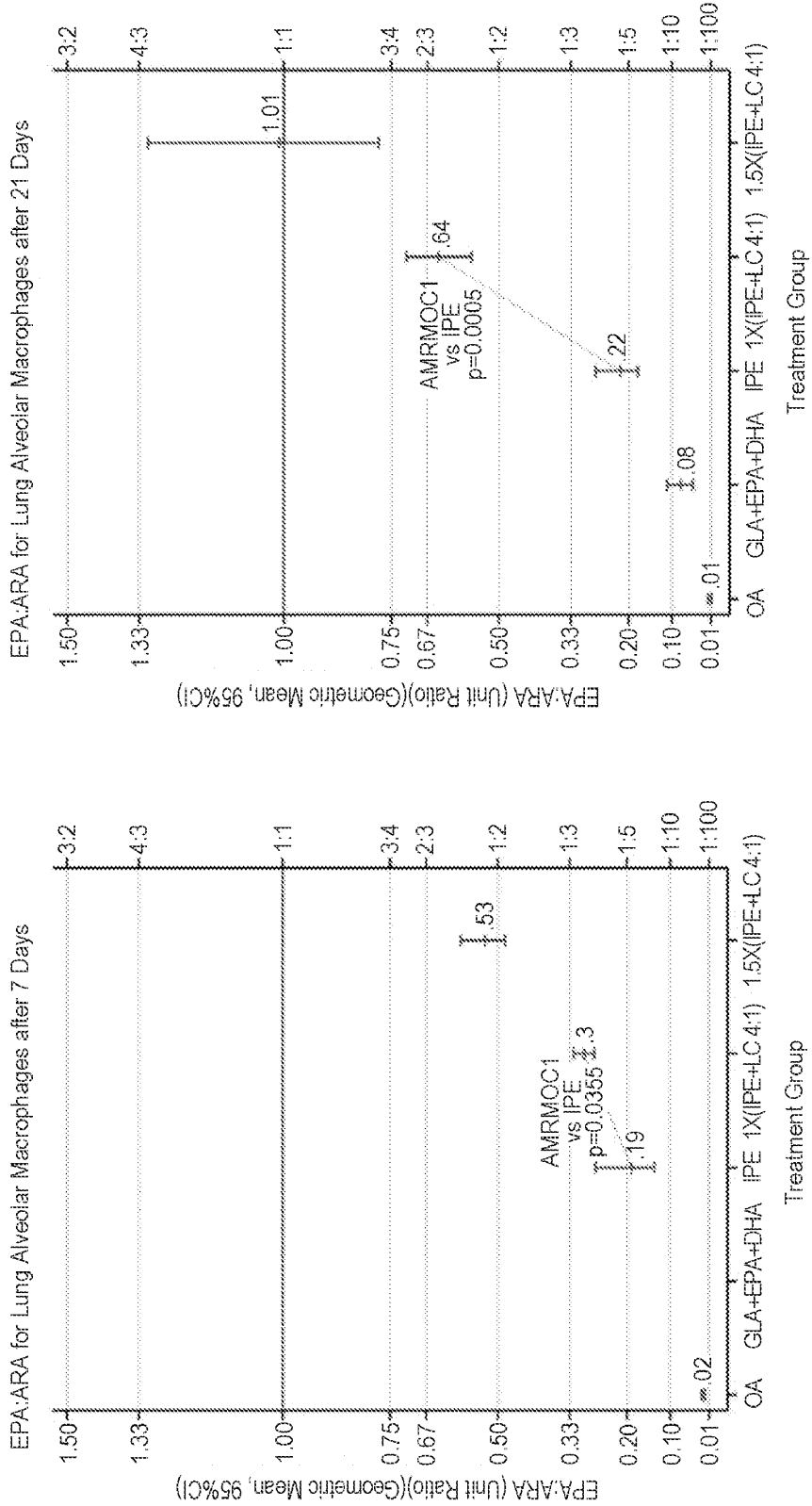


FIG. 21

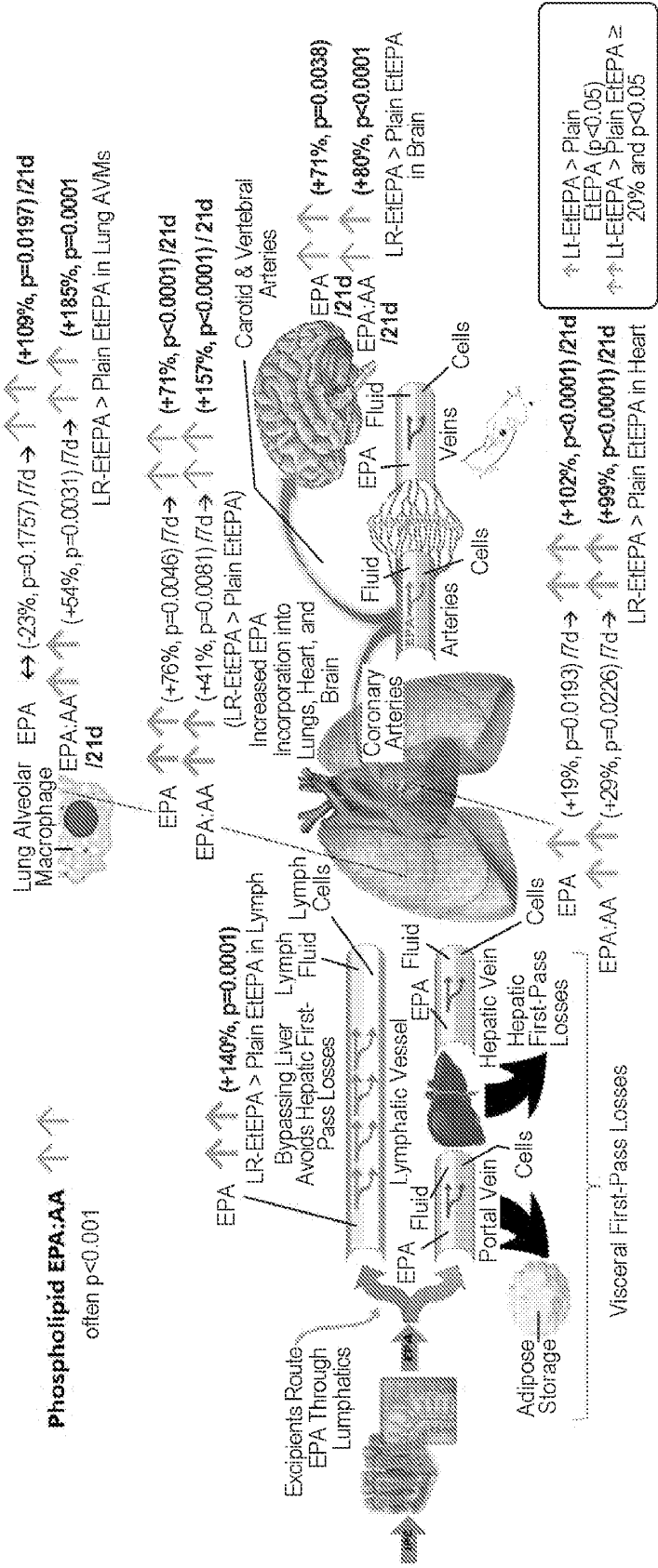


FIG. 22

Cell	Role of Cell in Atherosclerosis	Role of Cell in Pulmonary Disease	Role of Cell in Renal Disease	EPA-Oxylipins Attenuating Injury
Platelet	↑ clot → ischemia	↑ clot → DIC → overwhelming ischemia	both bleeding and thrombosis	Thromboxanes
Leukocyte	↑ vascular inflammation	↑ bronchiolar inflammation	↑ inflammation, cytokines, parenchymal injury	Leukotrienes Mono-alcohols Ketones
Macrophage	↑ unstable plaque → ischemia	↑ alveolar collapse → hypoxia → respiratory failure	↑ inflammation M1 ↑ ARA oxylipins M2 ↑ EPA oxylipins	Mono-alcohols Epoxides Di-alcohols
Endothelial Cell	↑ vasoconstriction	↑ broncho-constriction ↑ vasoconstriction	↑ inflammation & ↑ ROS → tissue damage & fibrosis	Prostanoids, Alcohols, Epoxides, Resolvins
Red Cell	↓ membrane fluidity, ↑ senescence, ↑ RDW, ↓ microvascular perfusion → microvascular ischemia & promote inflammatory/hemolytic anemias			Mono-alcohols Epoxides Di-alcohols

FIG. 23A

Cell	Role of Cell in Pulmonary Disease	Major Oxylipin Class Associated with Cell	Conditions Treated by Selected Oxylipins, Including from EPA
Platelet	↑ clot → DIC → over-whelming ischemia	Thromboxanes	Deep venous thrombosis, pulmonary embolism, ischemia, DIC, SIRS/sepsis/ARDS
Leukocyte	↑ bronchiolar inflammation	Leukotrienes Mono-alcohols Ketones	Bronchiectasis, asthma, COPD, SIRS/sepsis/ARDS
Macrophage	↑ alveolar collapse → hypoxia → respiratory failure	Prostanoids, Mono-, Di-Alcohols Epoxides, Resolvins	Inflammatory pulmonary disease, pulmonary vasculitis, pulmonary renal syndromes, SIRS/sepsis/ARDS
Endothelial Cell	↑ bronchoconstriction ↑ vasoconstriction	Prostanoids Alcohols, Epoxides, Resolvins	Pulmonary hypertension, SIRS/sepsis/ARDS

FIG. 23B

EPA:ARA per Ion Count Concentration by Treatment

in Lung Tissue After 21 Days

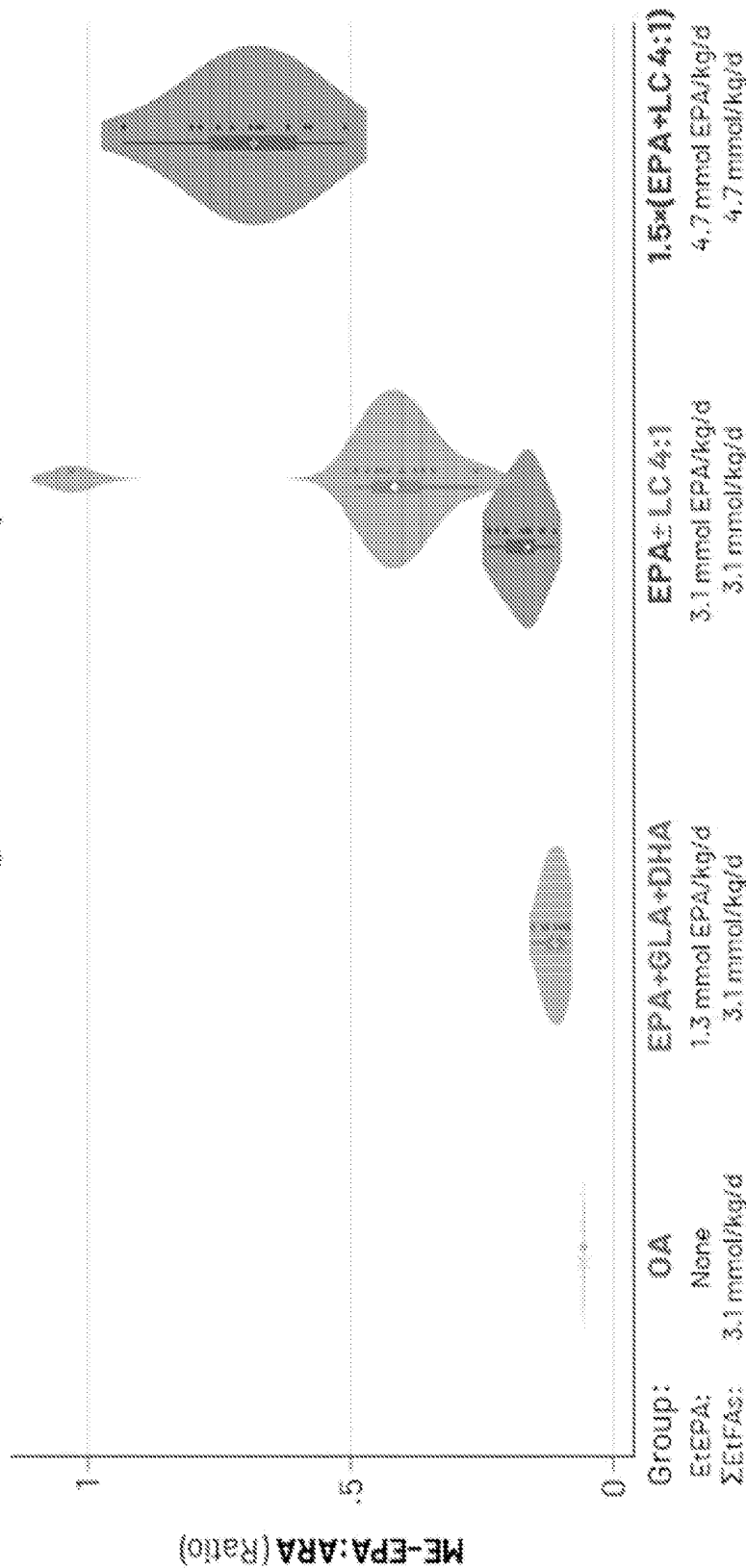


FIG. 24A

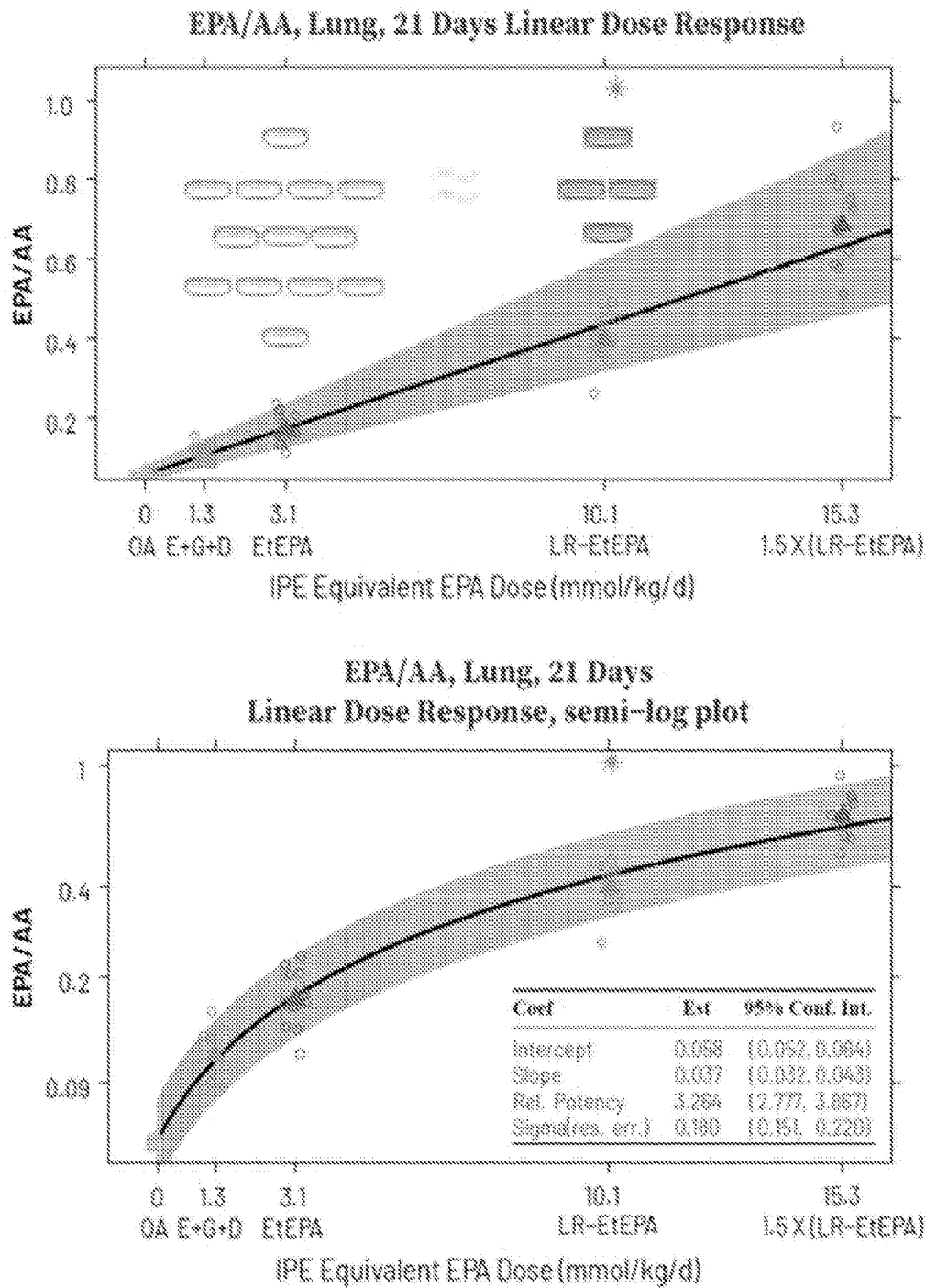


FIG. 24B

MOP:ARA per Ion Count Concentration by Treatment

in Lung Tissue After 21 Days

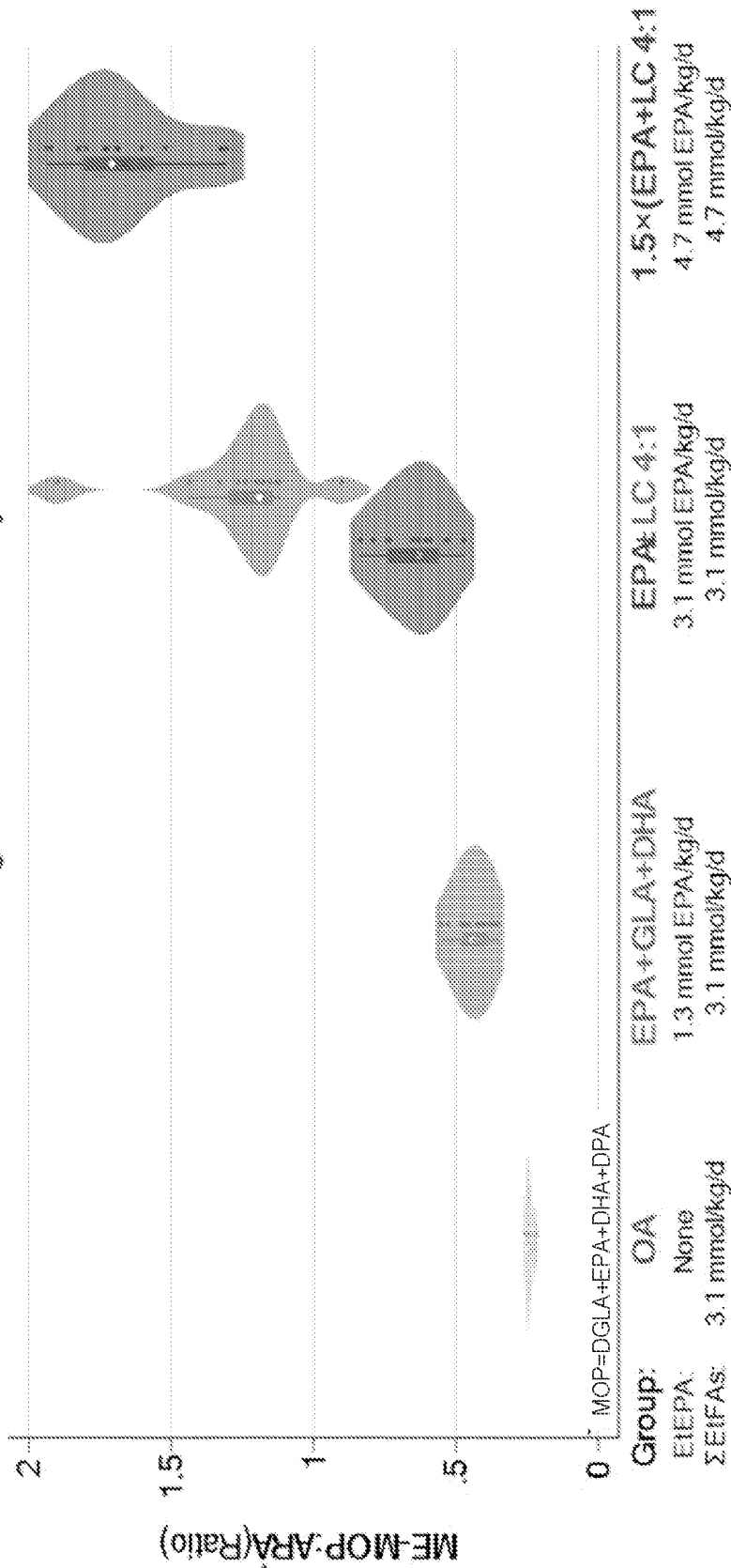


FIG. 24C

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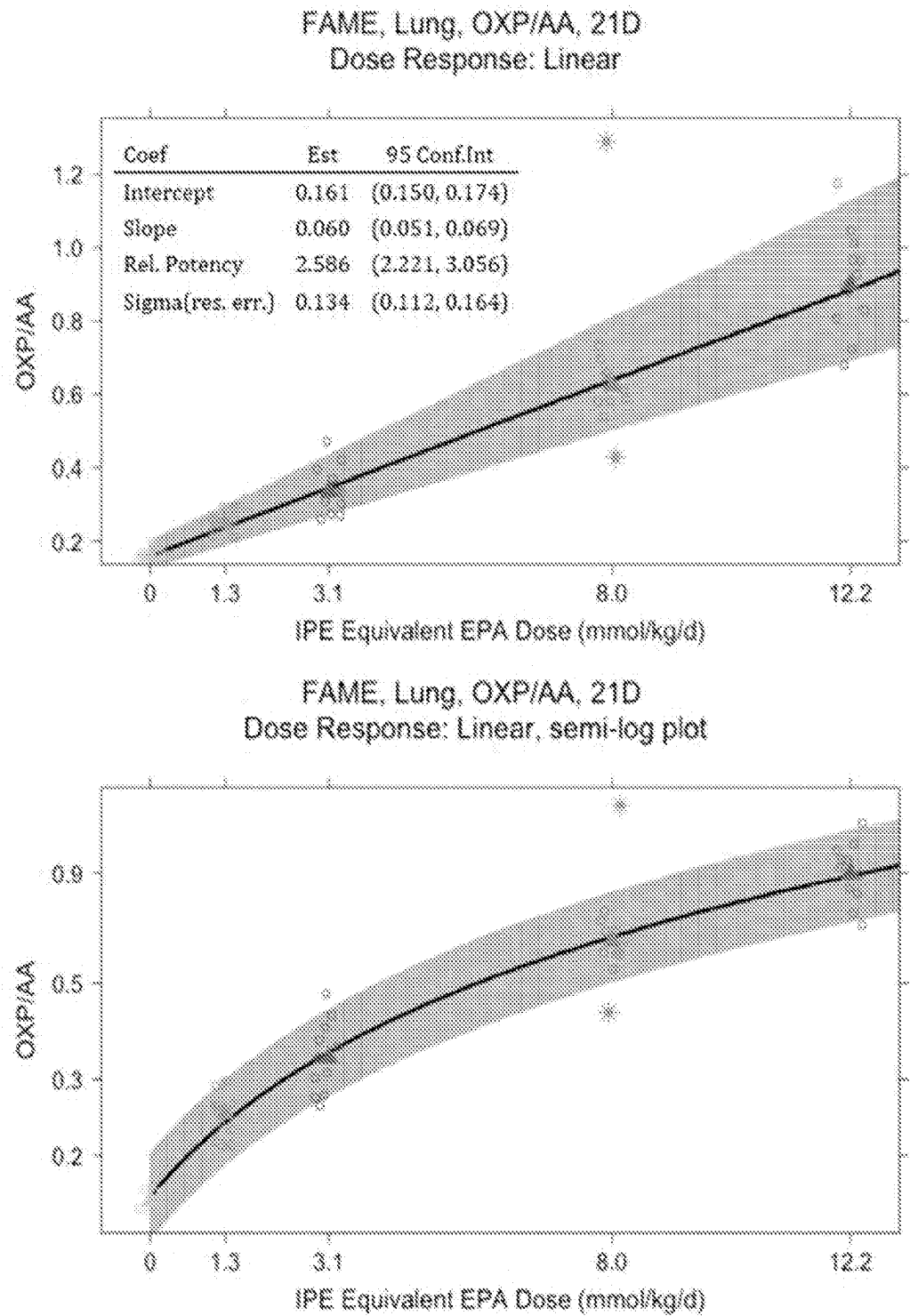


FIG. 24D

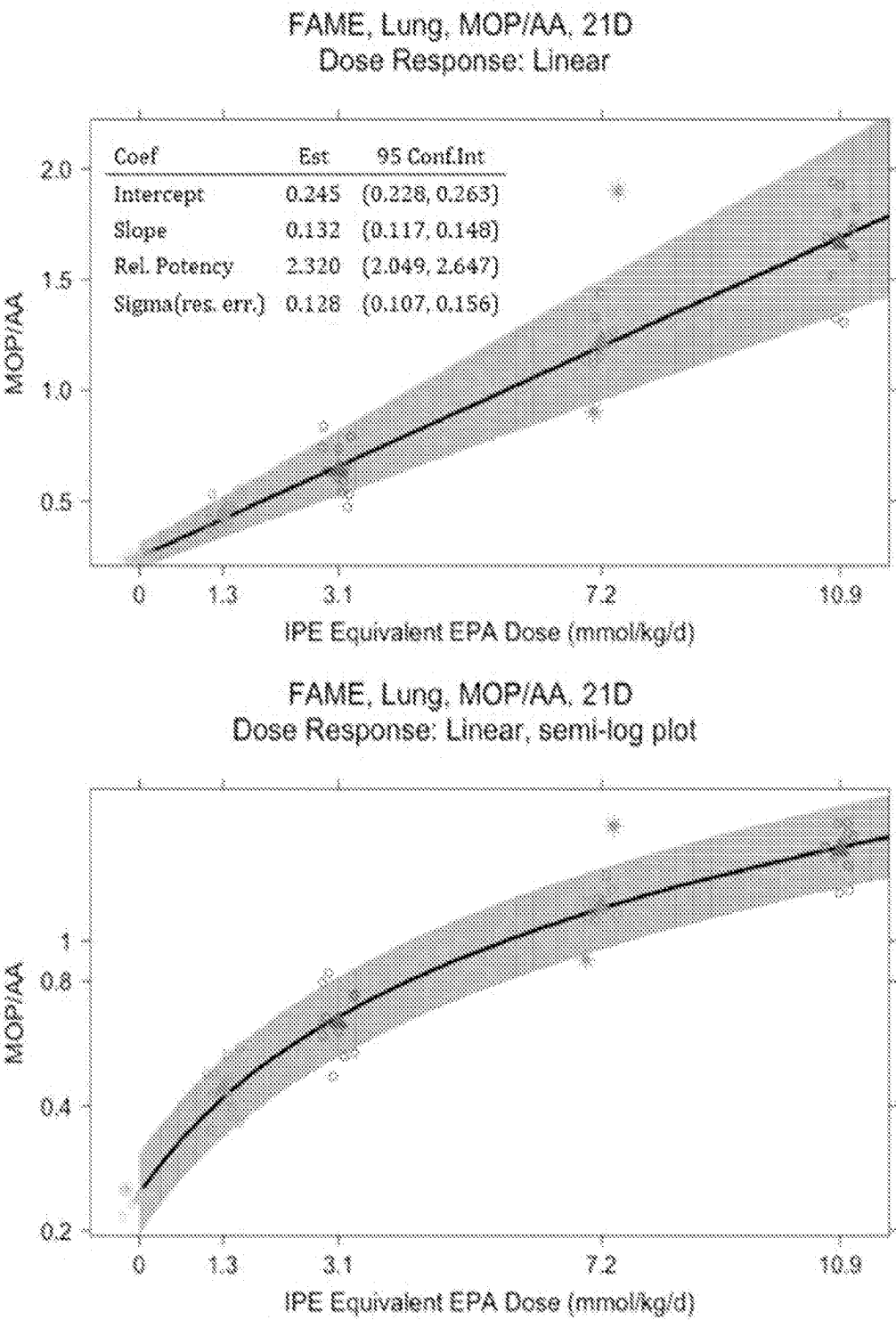


FIG. 24E

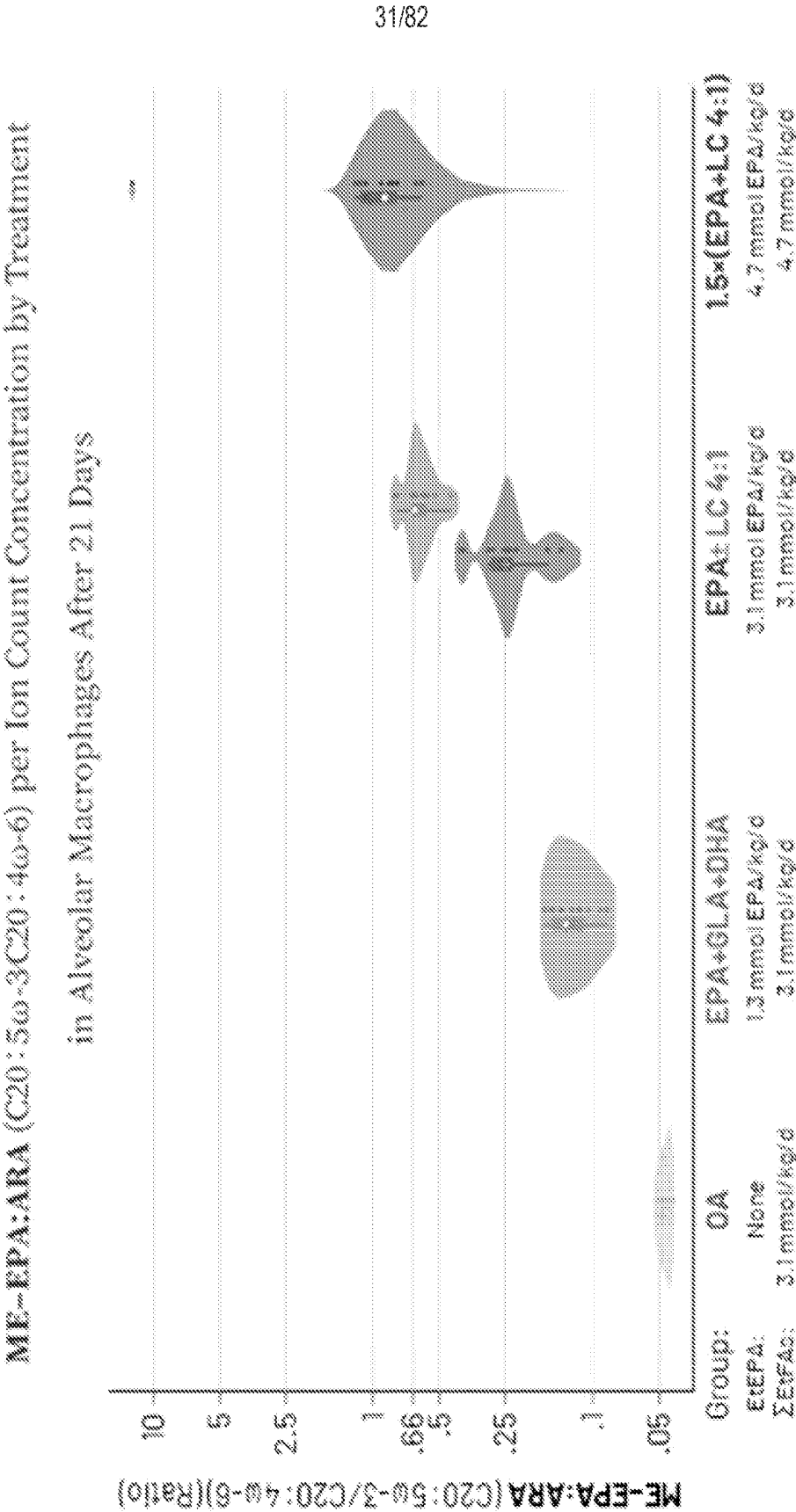


FIG. 25A

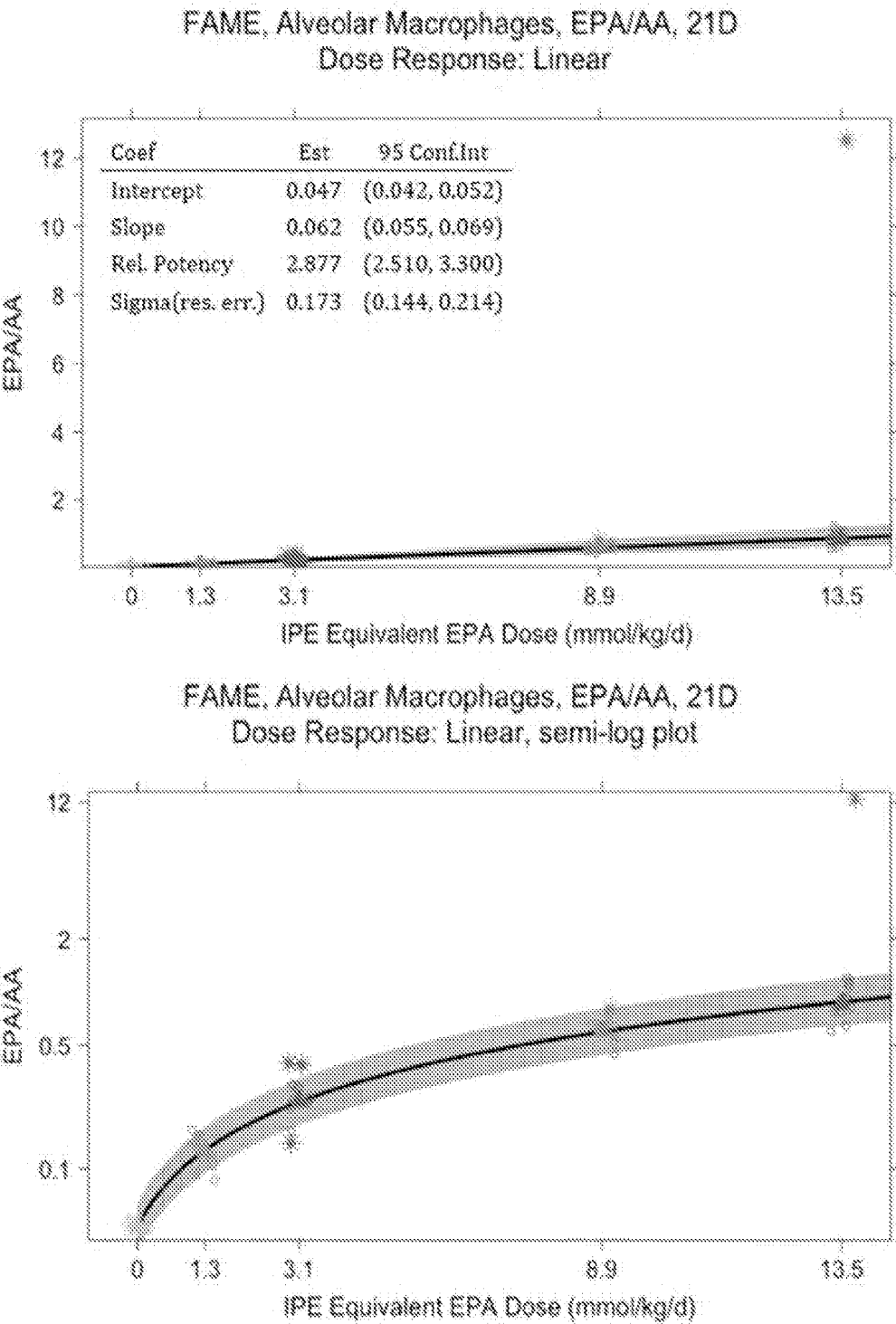


FIG. 25B

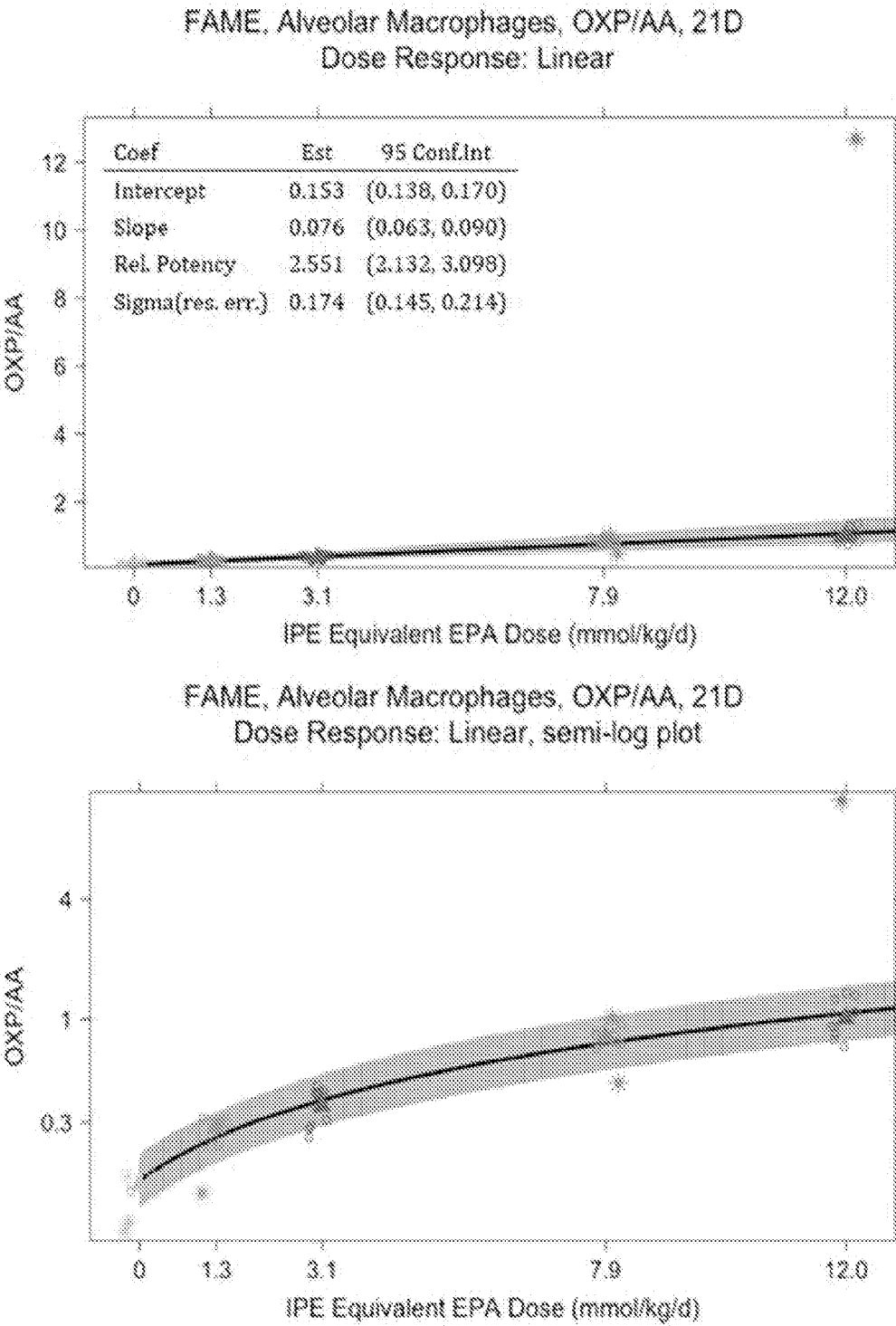


FIG. 25C

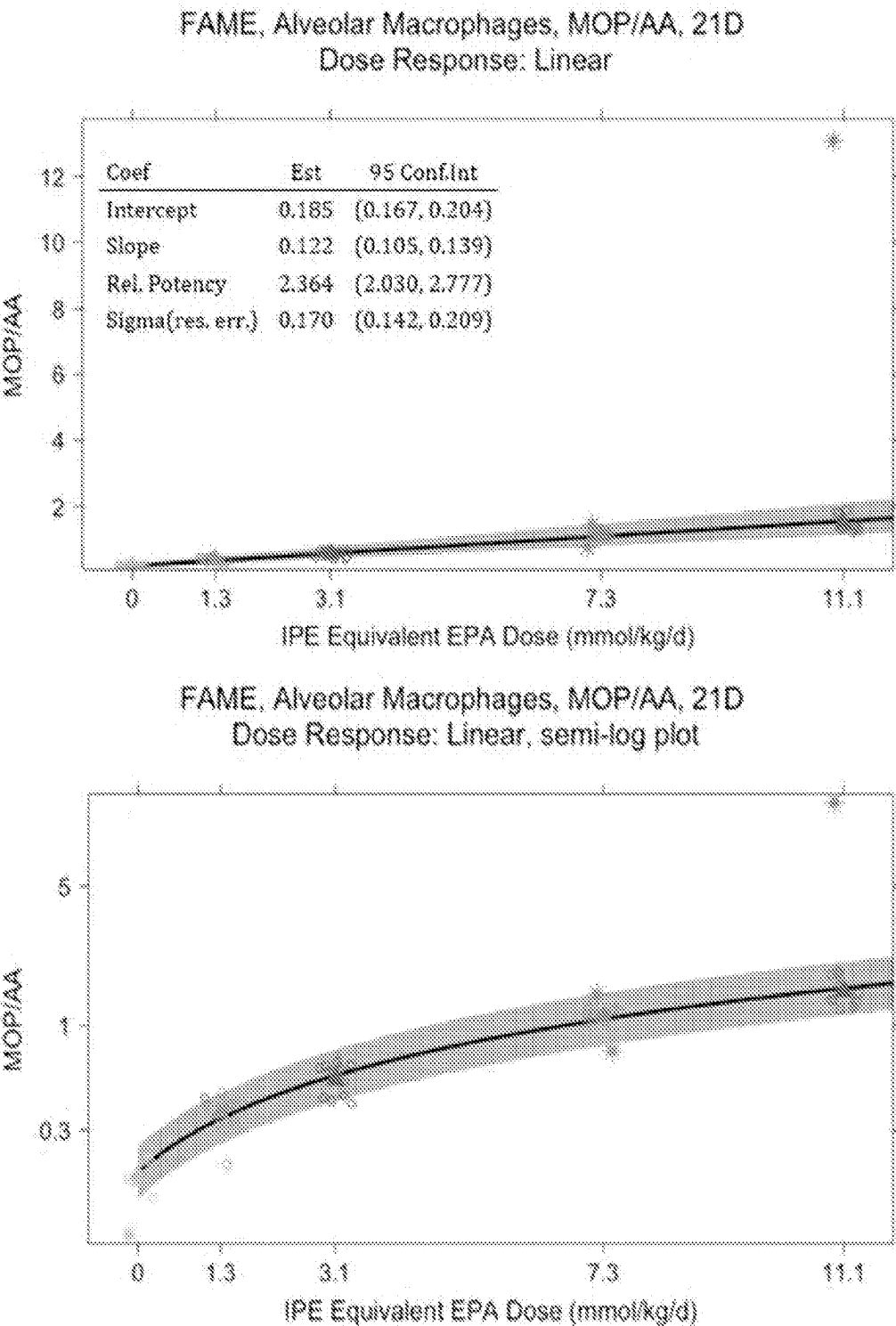


FIG. 25D

EPA:ARA per Ion Count Concentration by Treatment
in Cardiac Tissue After 21 Days

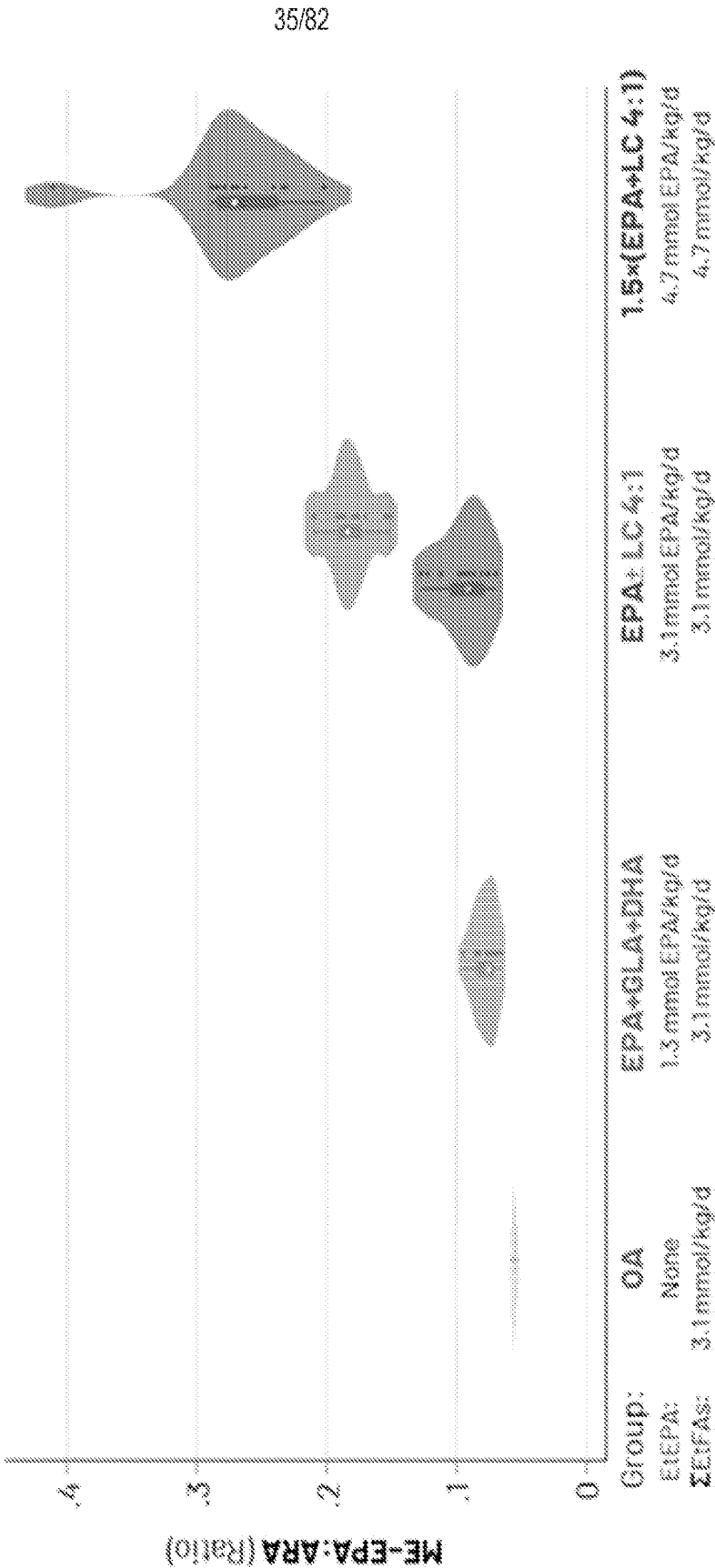


FIG. 26A

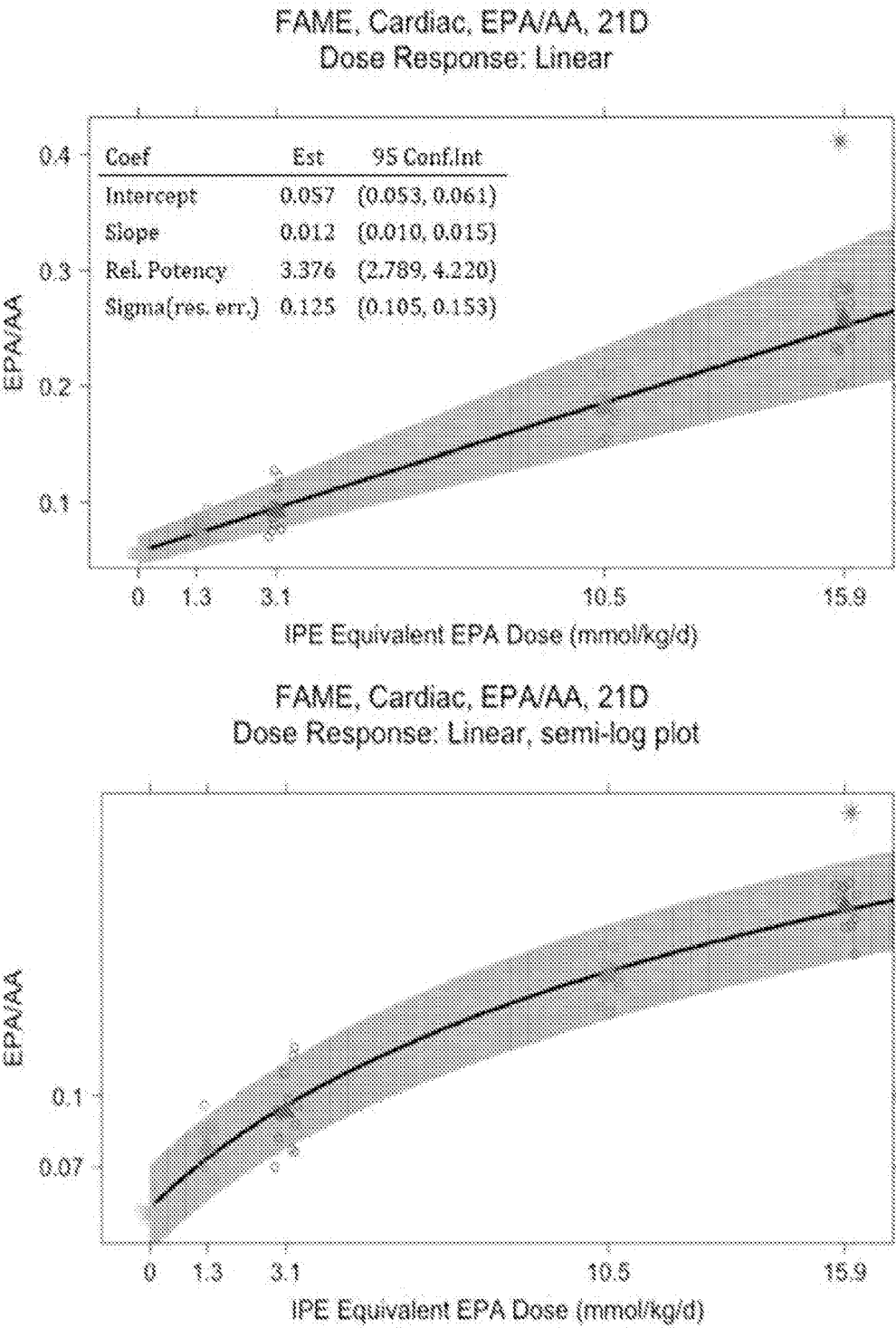


FIG. 26B

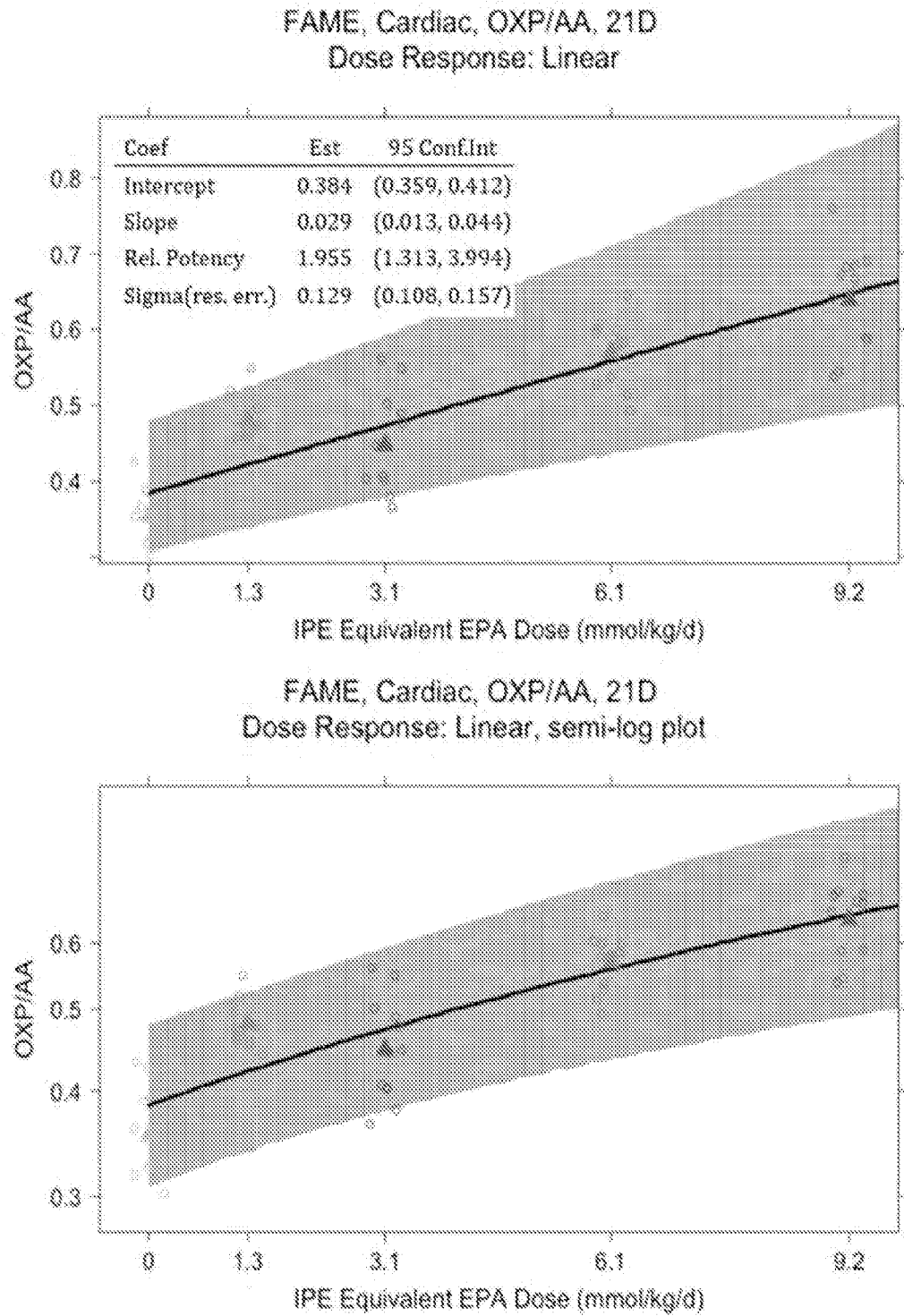


FIG. 26C

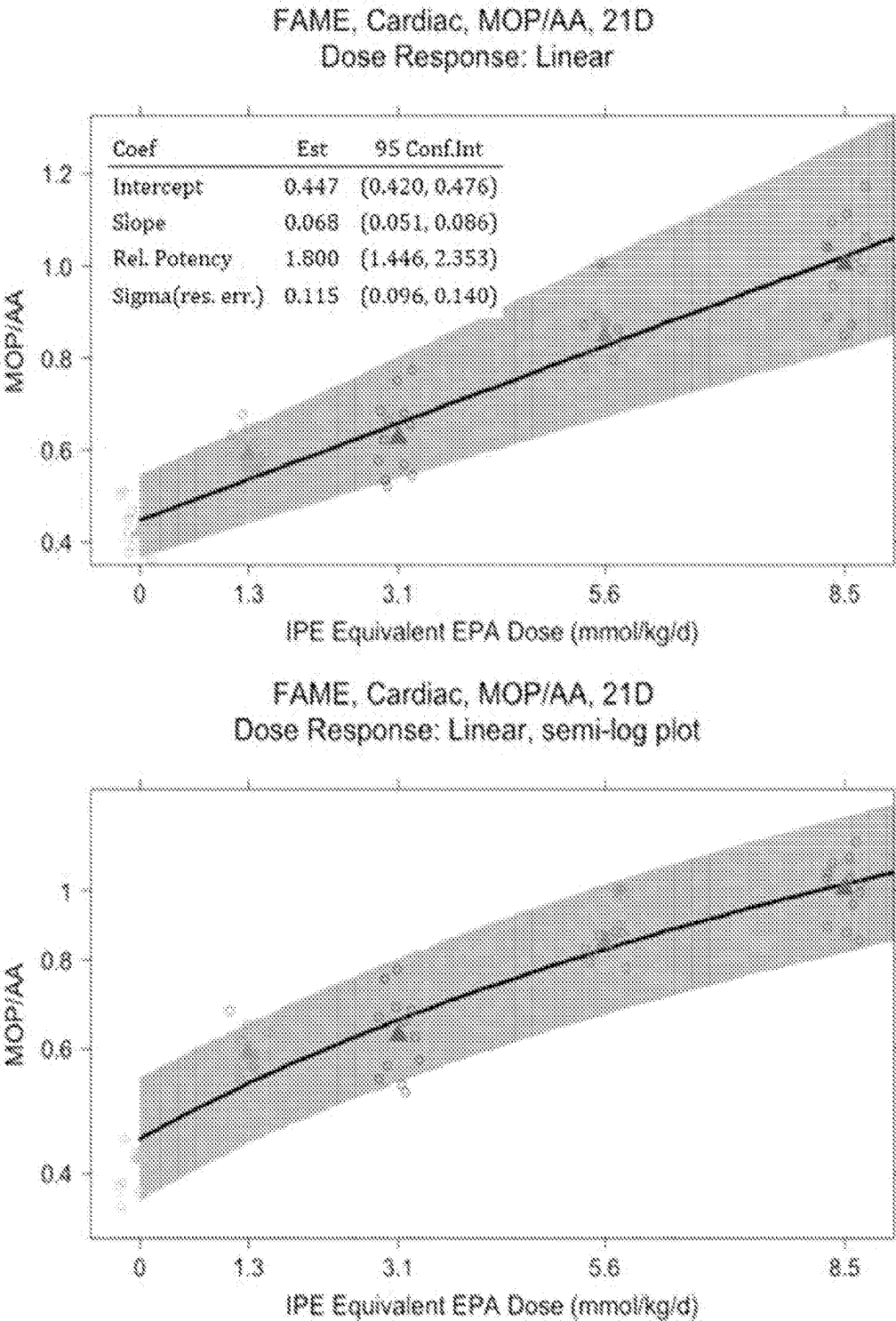


FIG. 26D

ME-EPA:ARA (C20:5ω-3/C20:4ω-6) per Ion Count Concentration (Std IC/kg)

by Treatment Group in Kidney Tissue After 21 Days

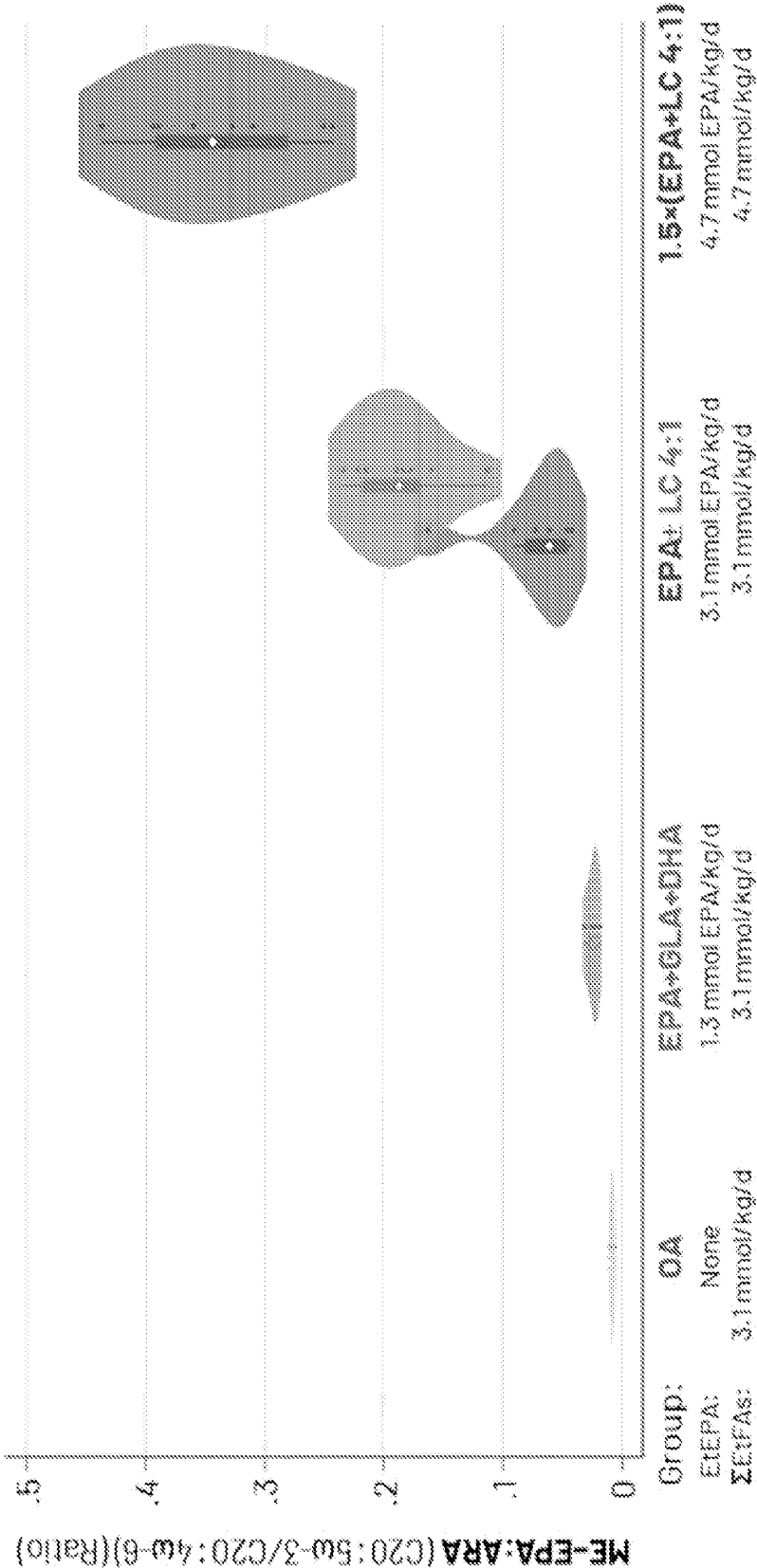


FIG. 27A

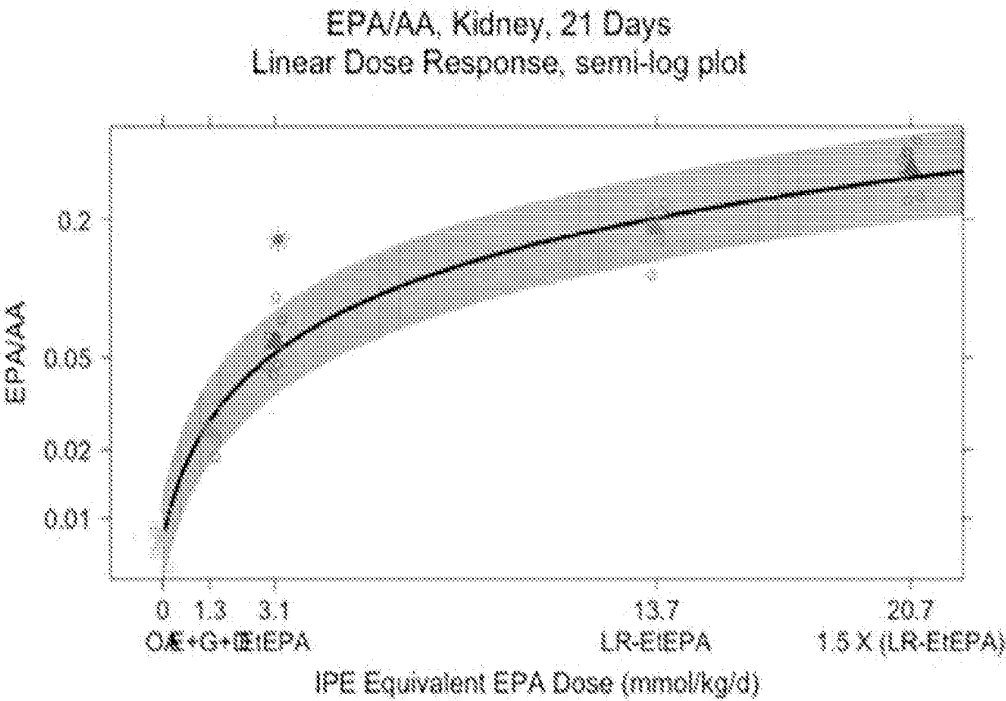
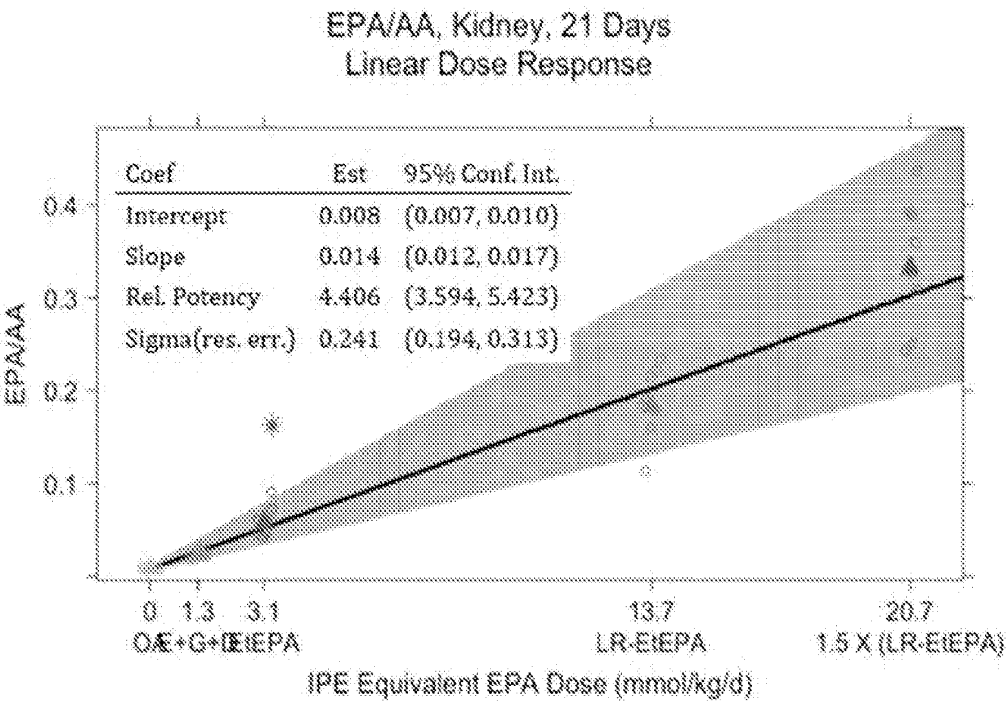


FIG. 27B

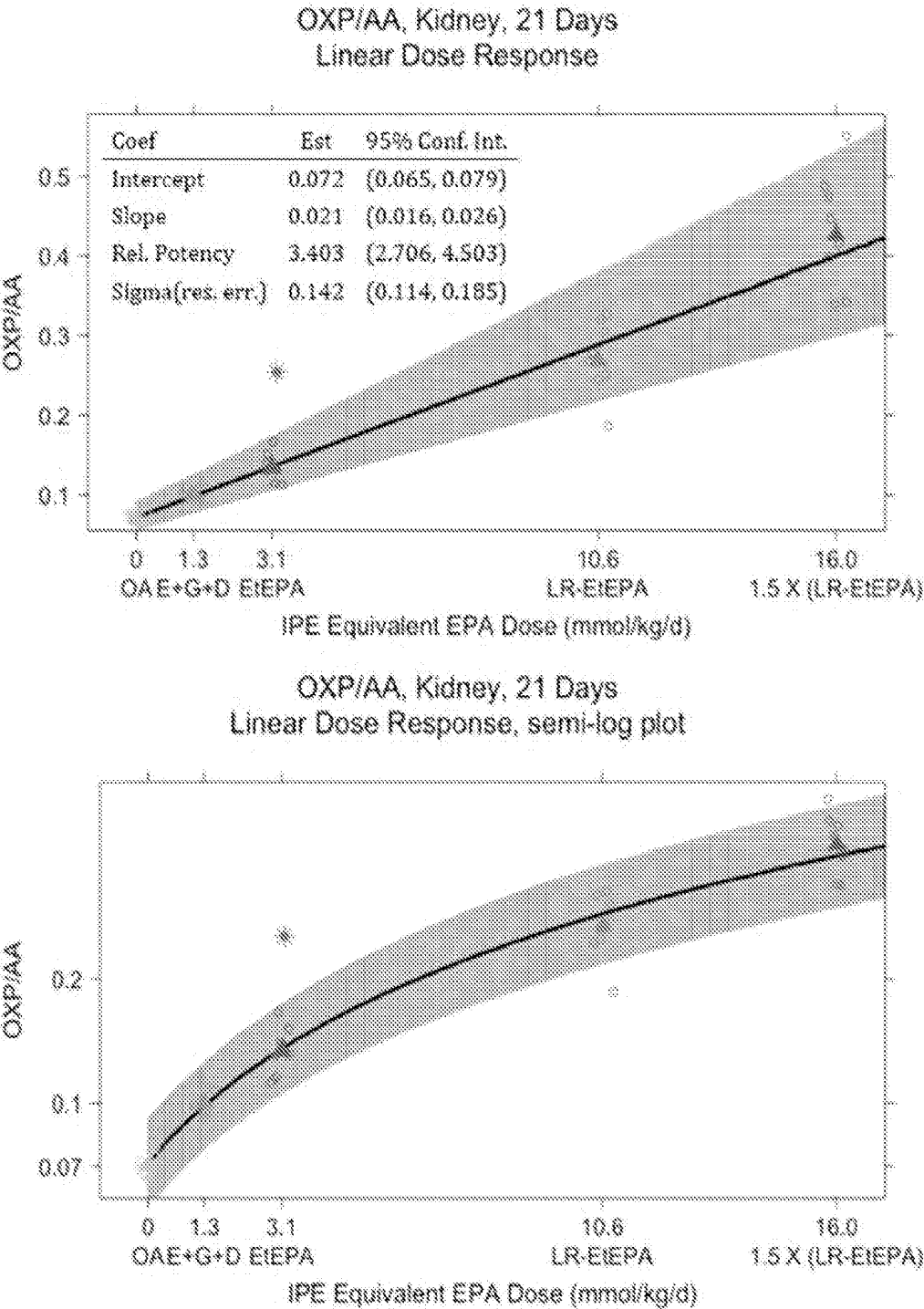


FIG. 27C

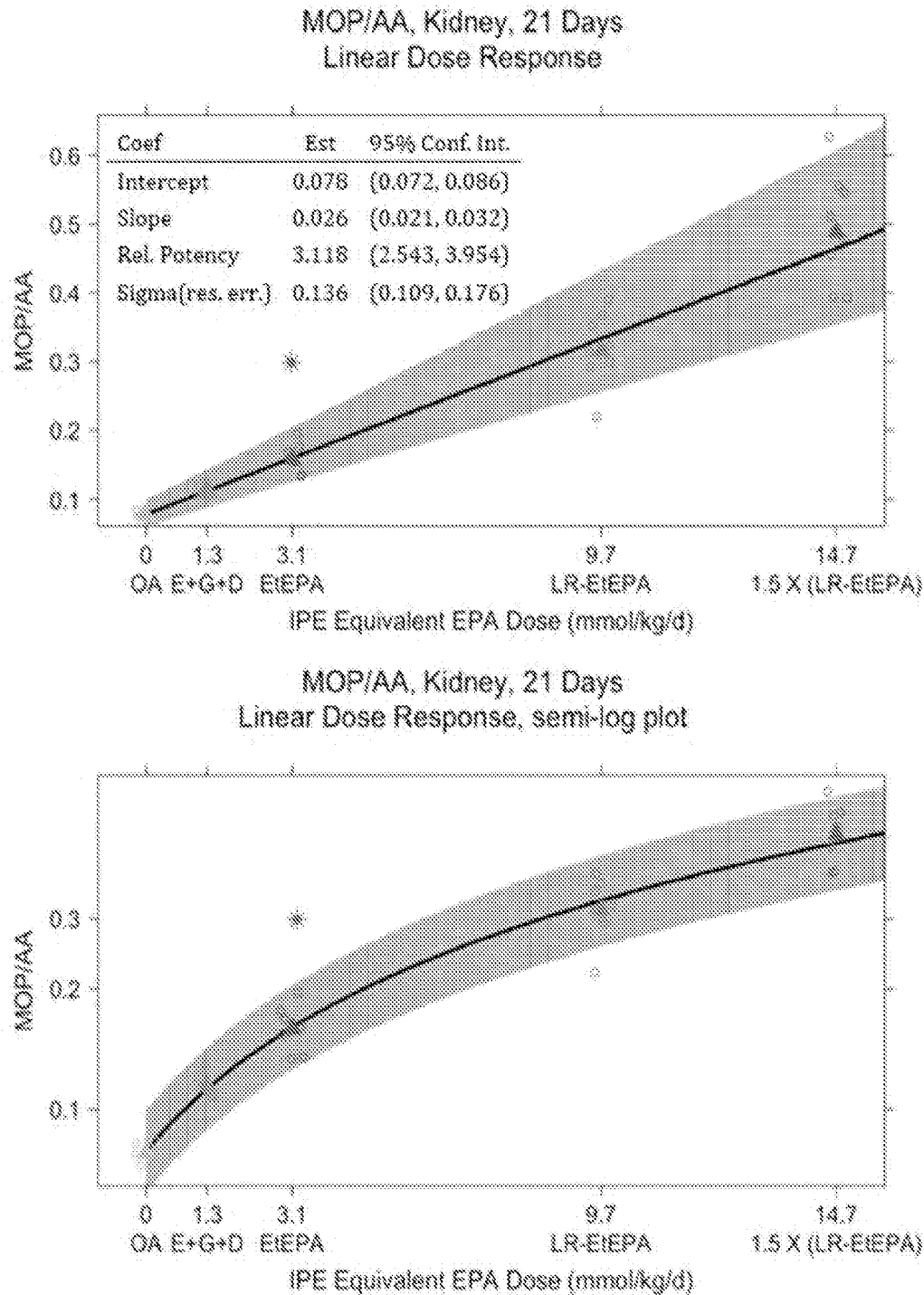


FIG. 27D

ME-EPA:ARA (C20:5ω-3/C20:4ω-6) per Ion Count Concentration (Std IC/kg)

by Treatment Group in Brain Tissue After 21 Days

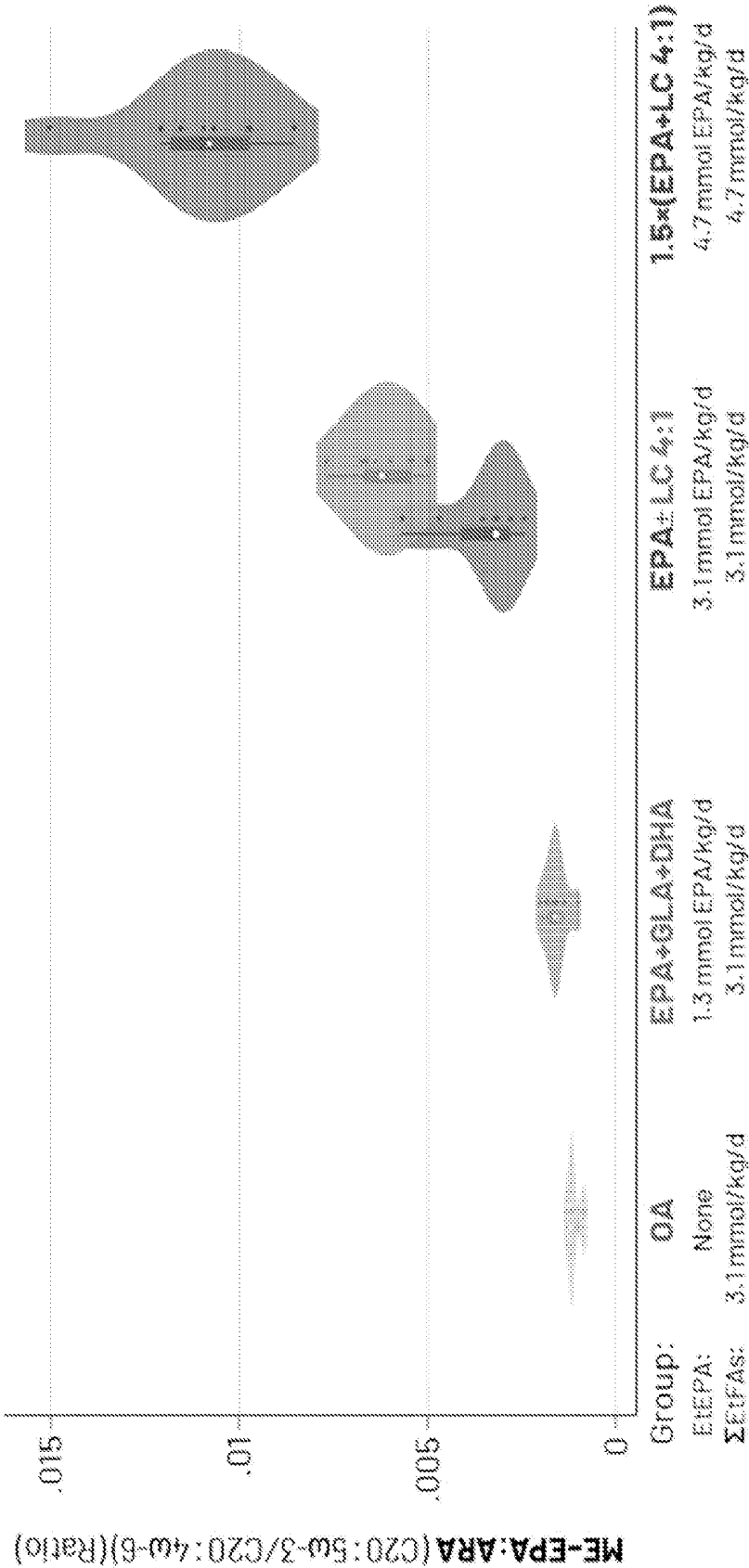


FIG. 28A

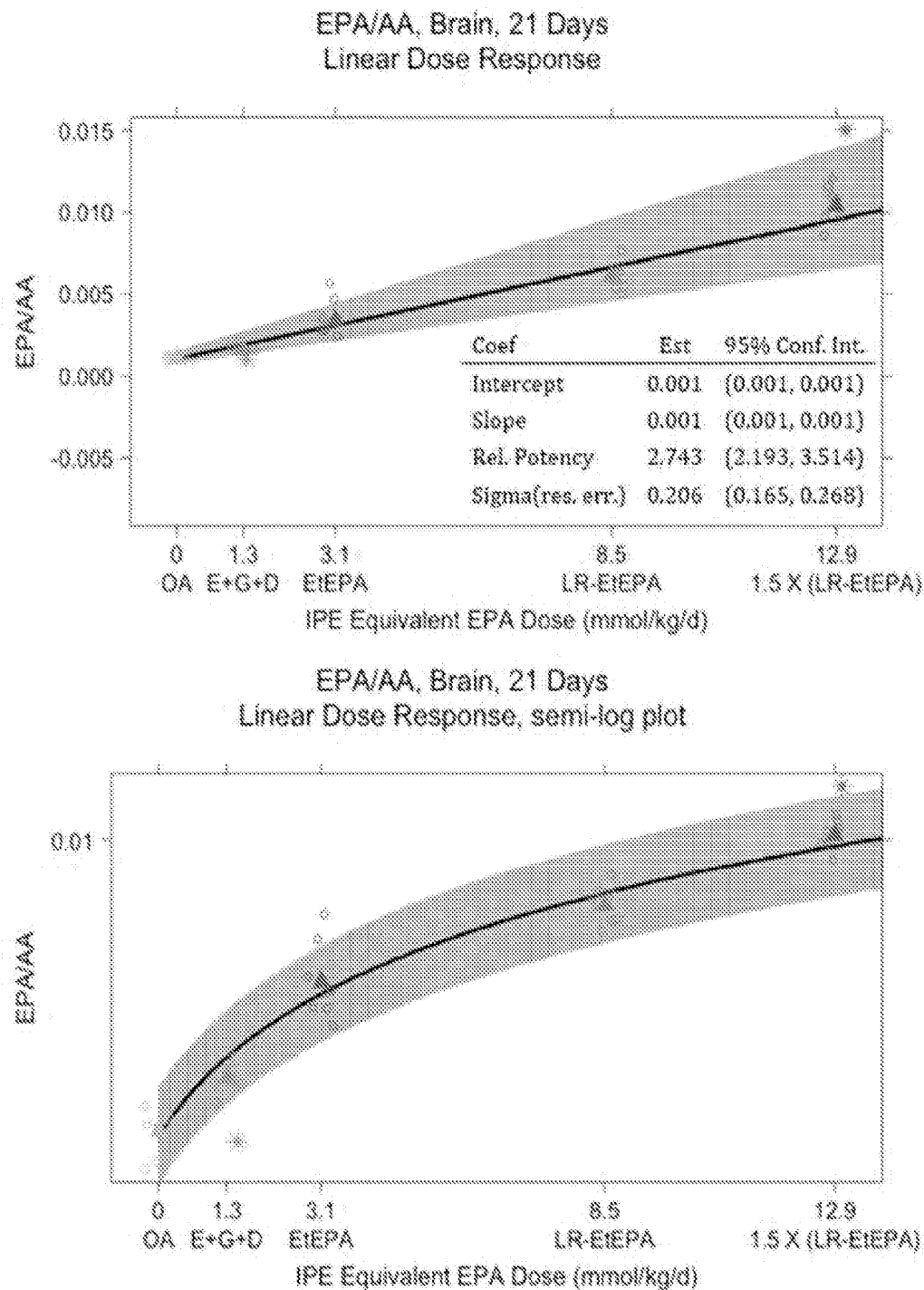


FIG. 28B

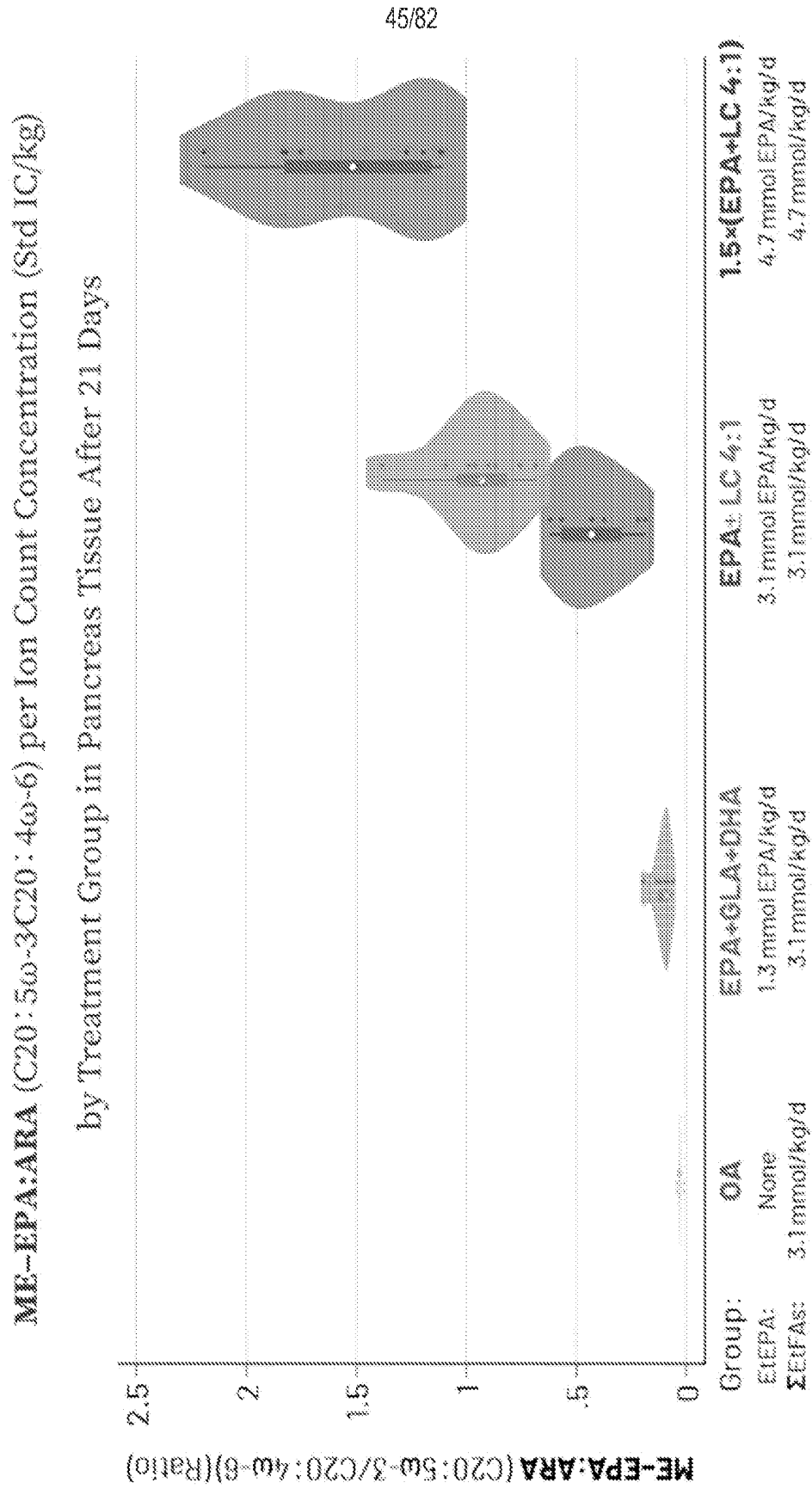
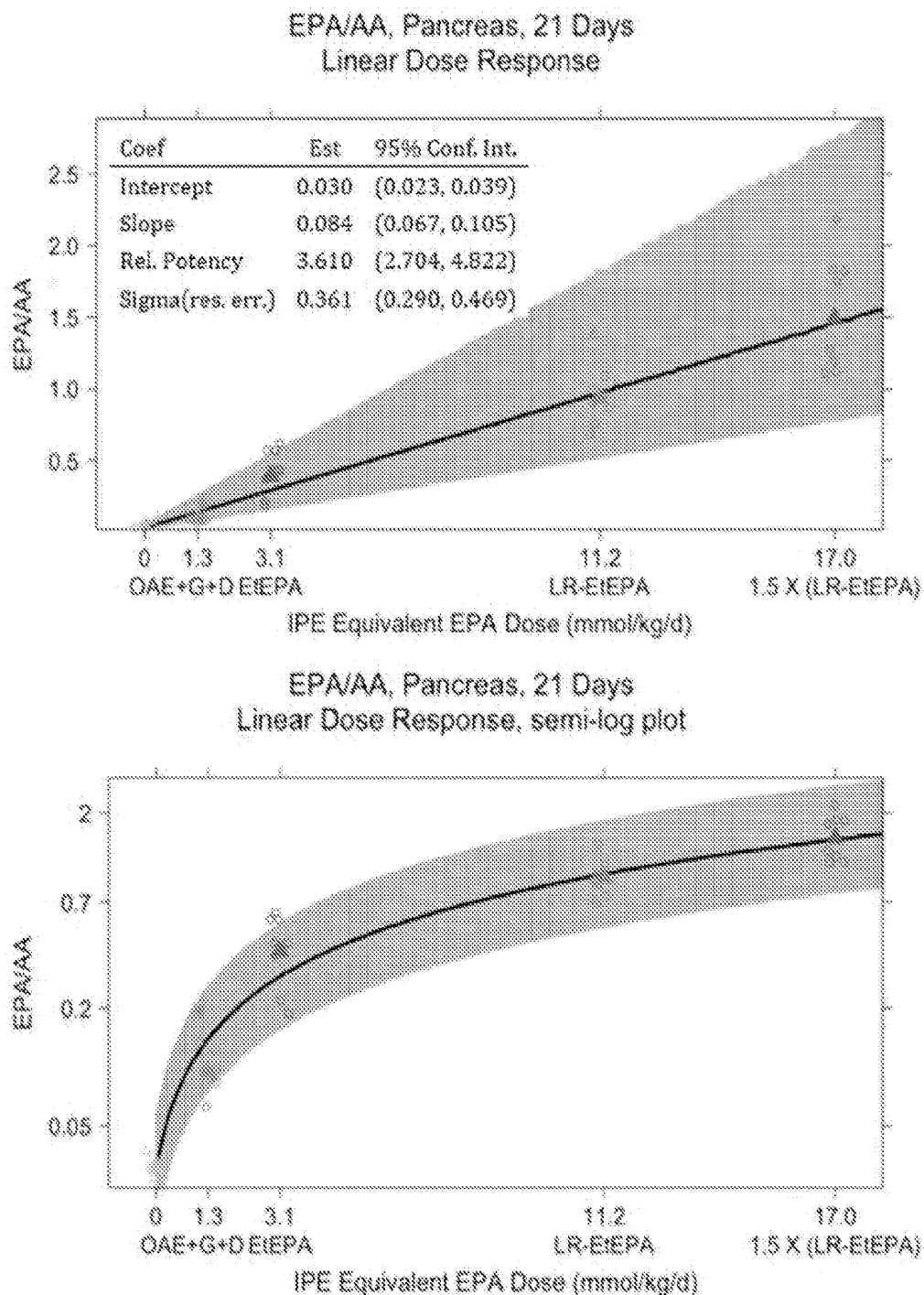


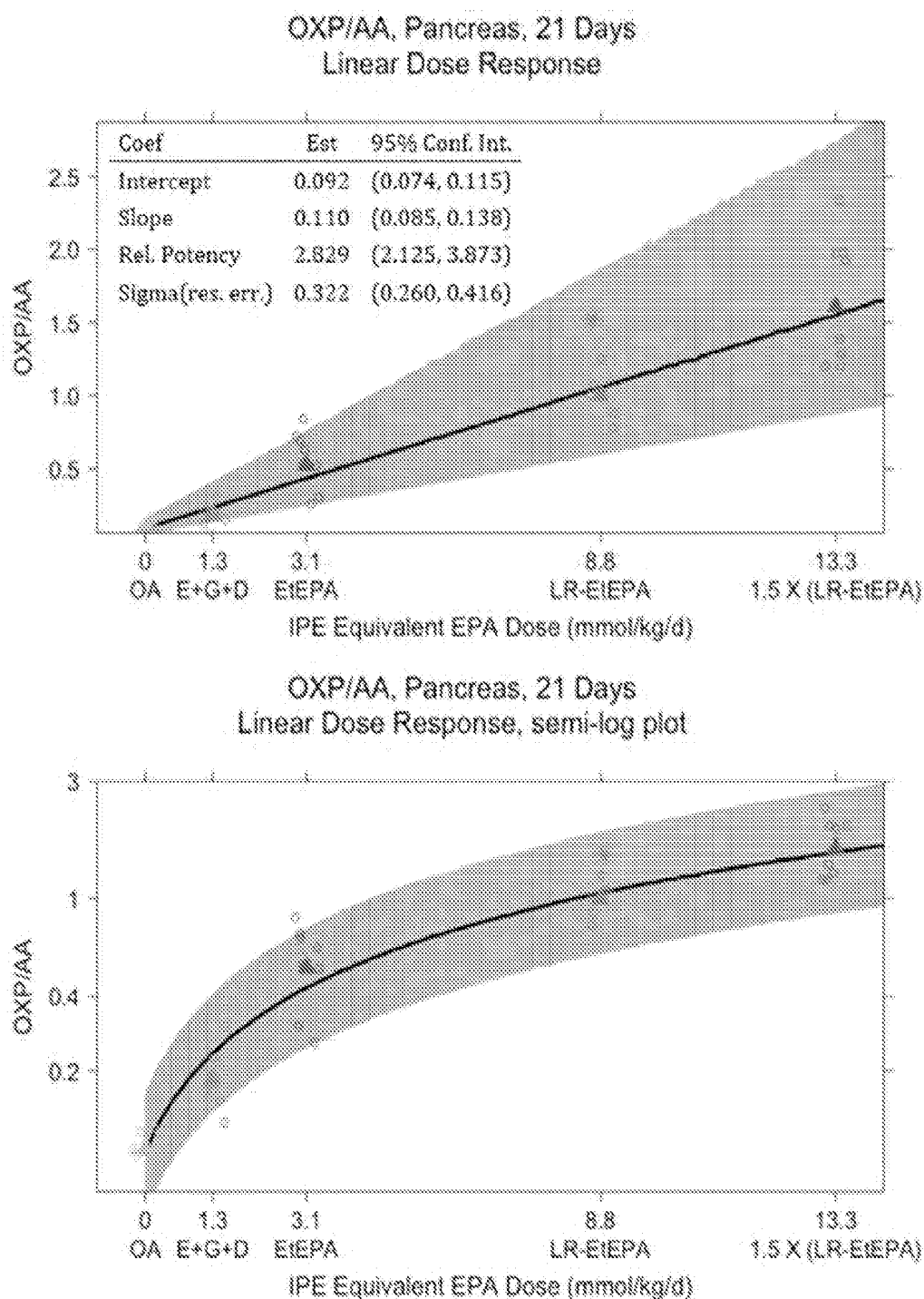
FIG. 29A

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**FIG. 29B**

SUBSTITUTE SHEET (RULE 26)

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**FIG. 29C**

SUBSTITUTE SHEET (RULE 26)

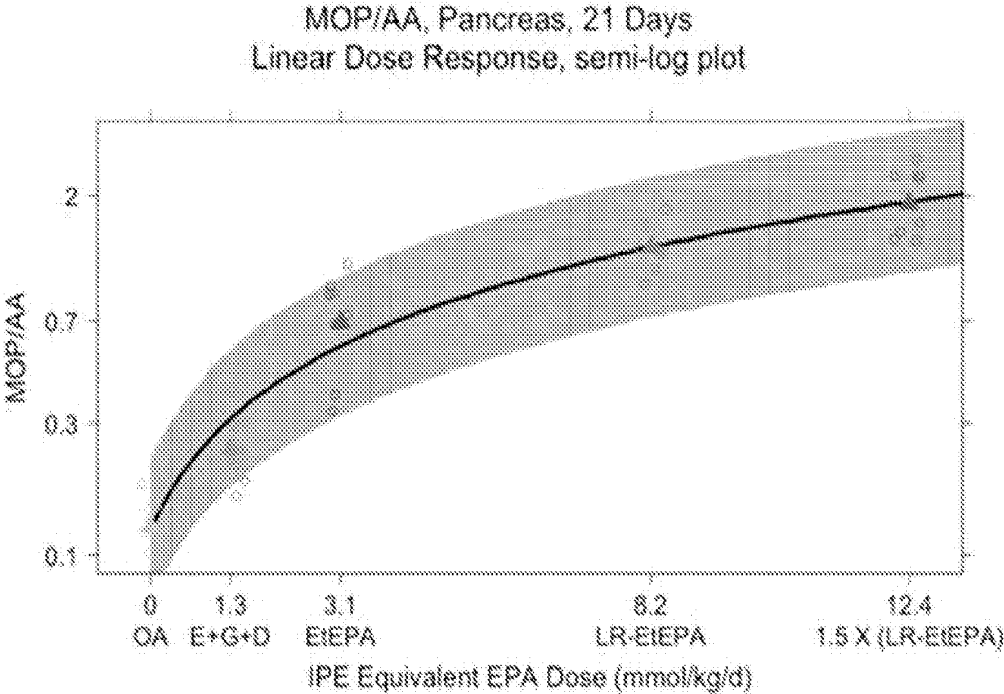
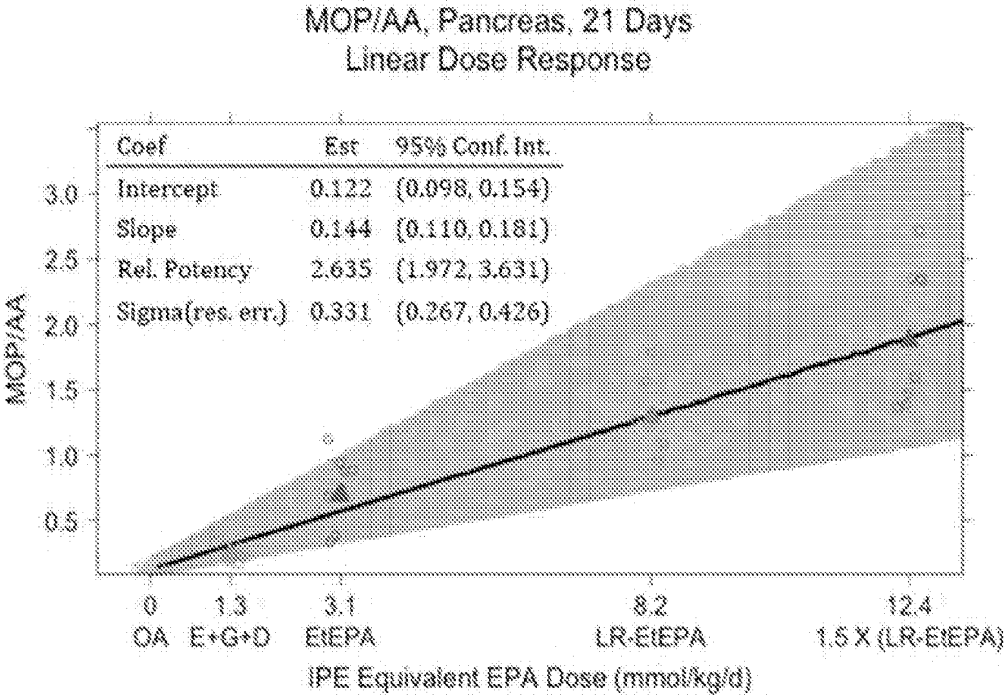


FIG. 29D

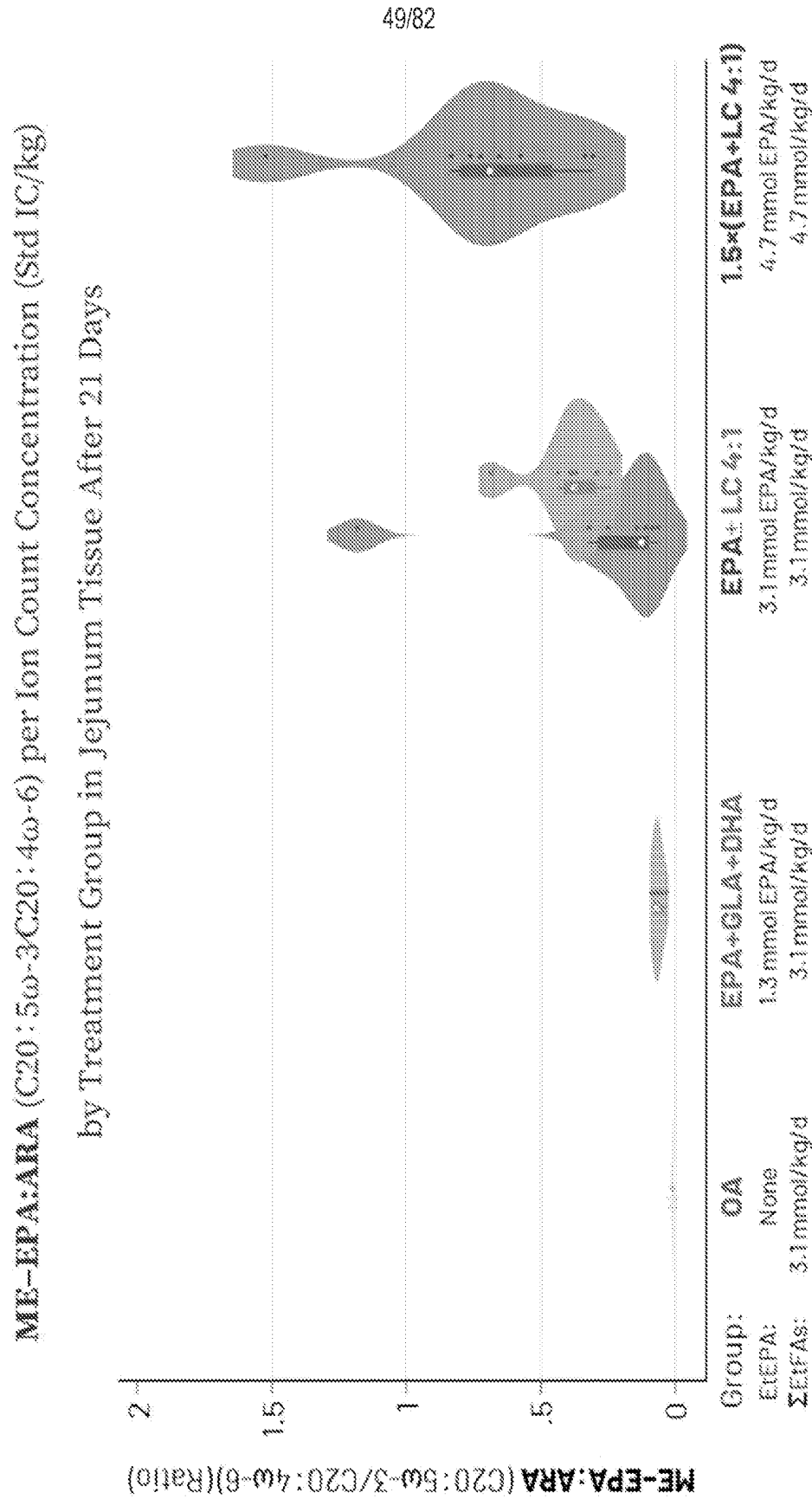


FIG. 30A

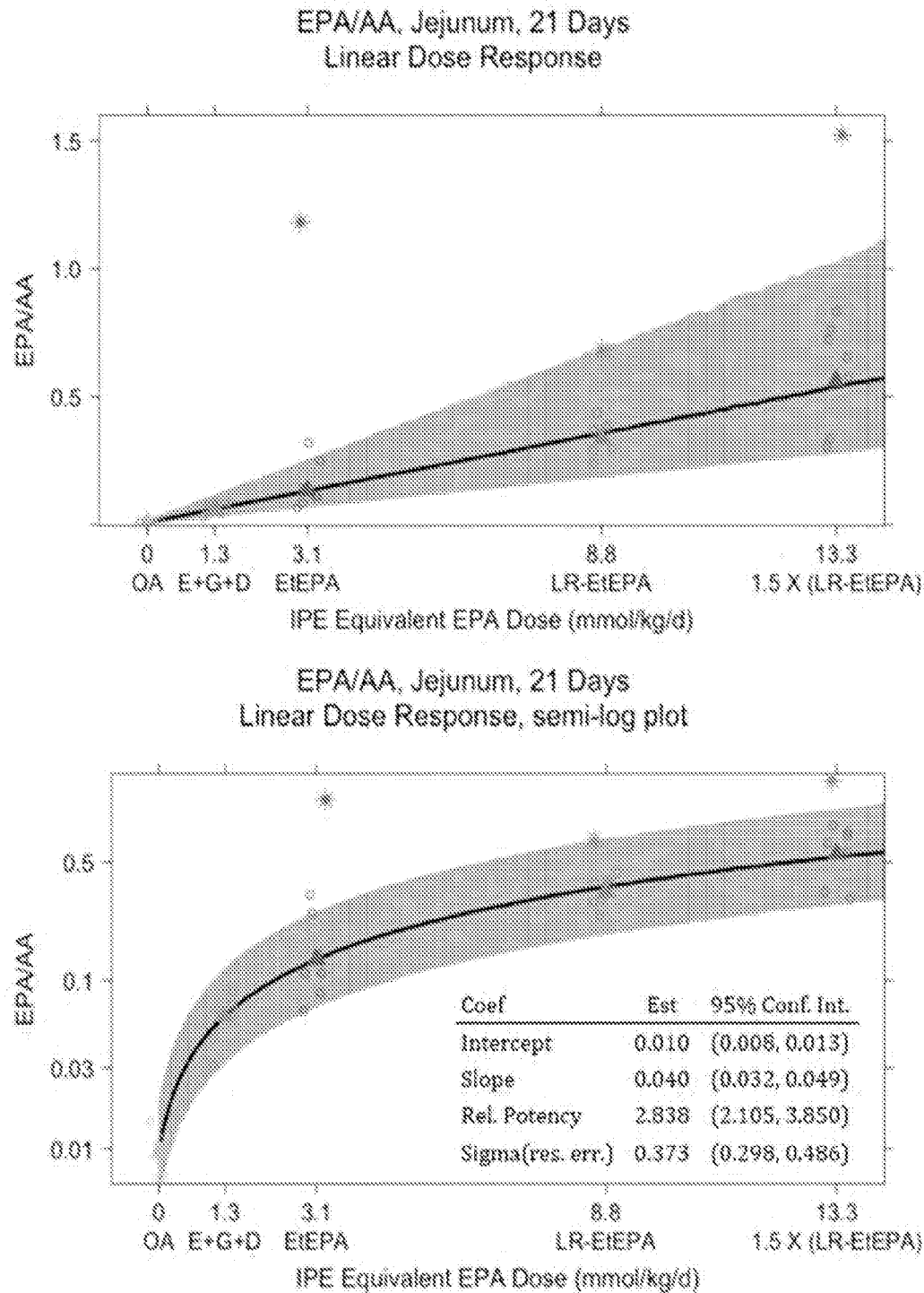


FIG. 30B

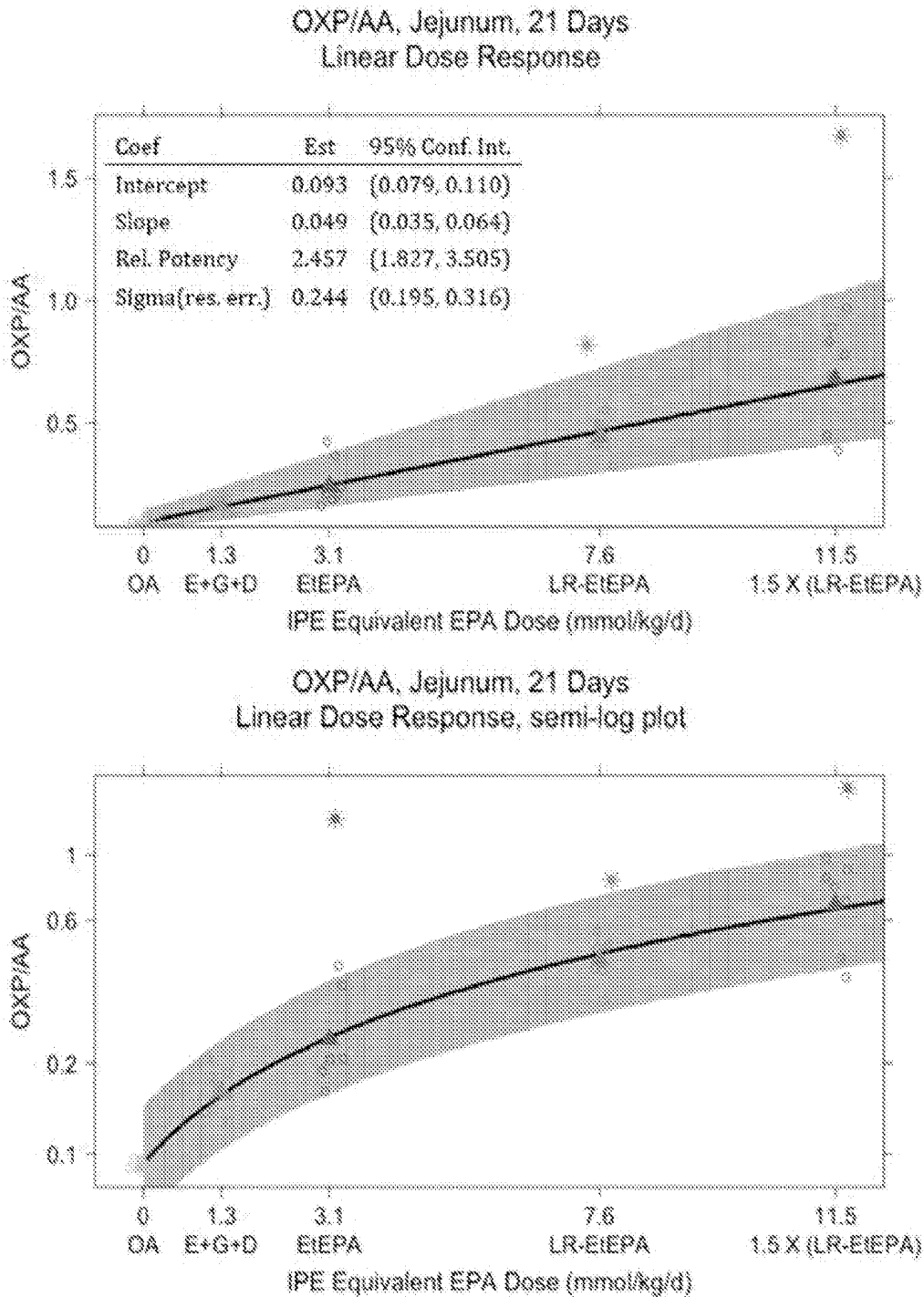
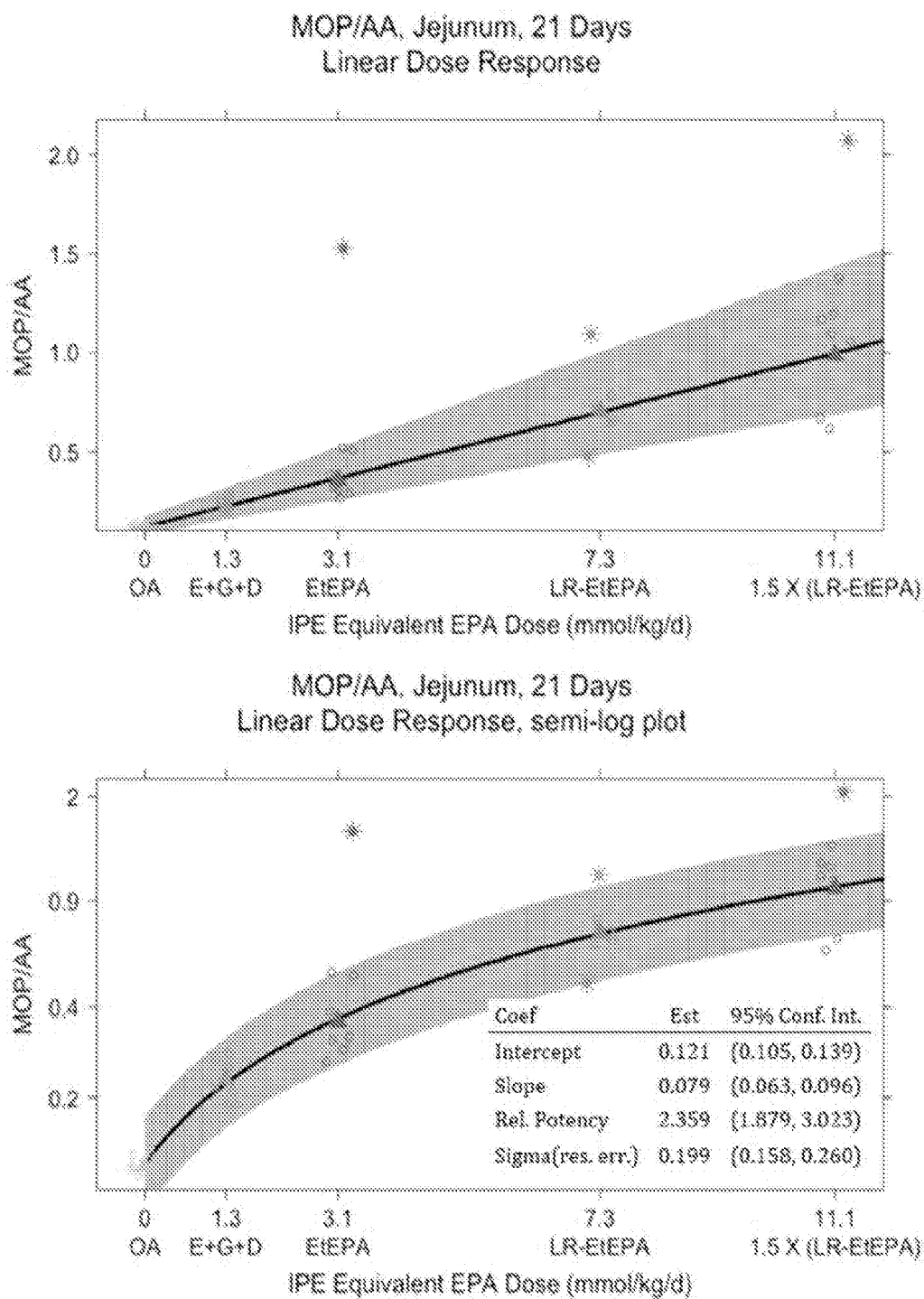


FIG. 30C

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**FIG. 30D**

SUBSTITUTE SHEET (RULE 26)

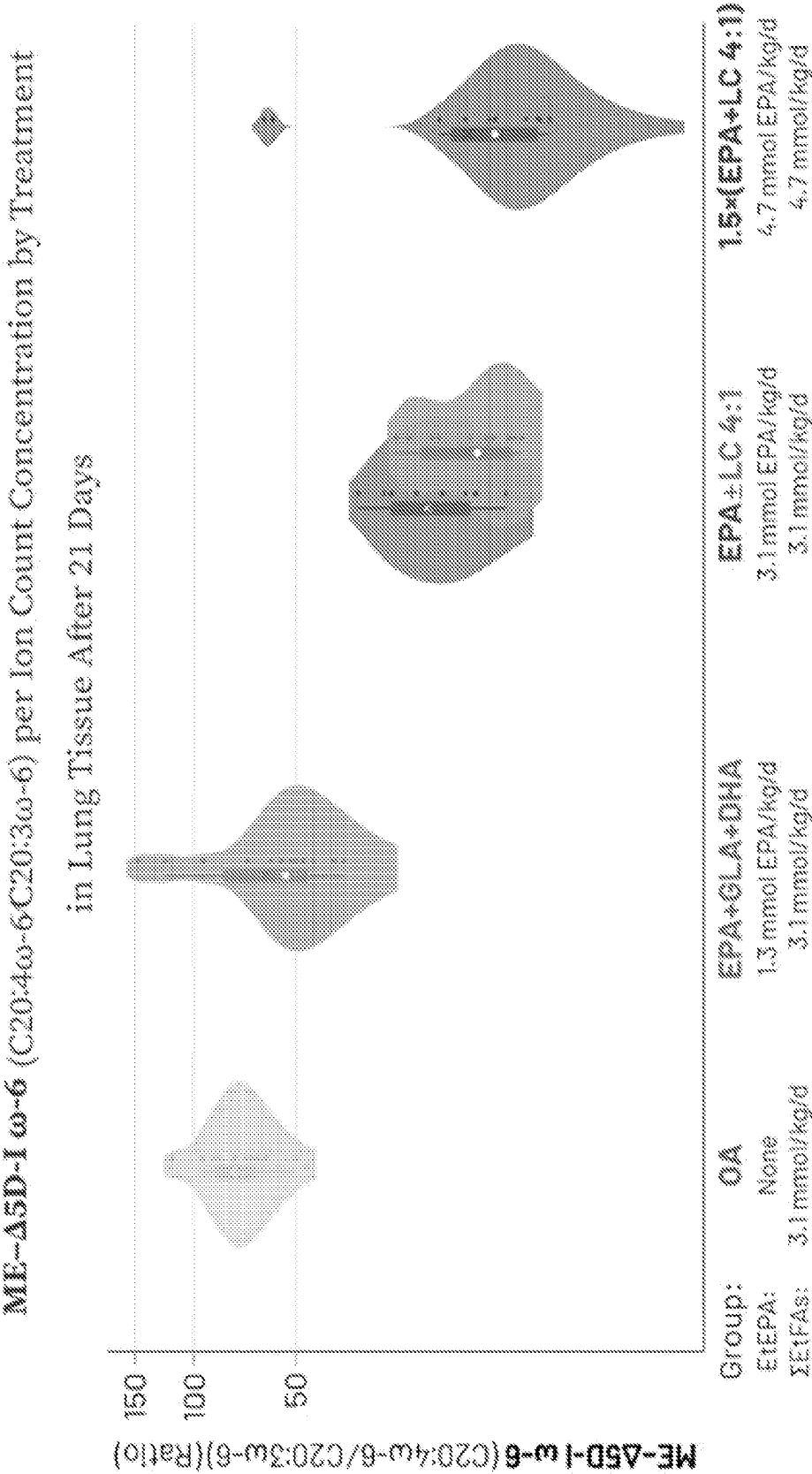


FIG. 31A

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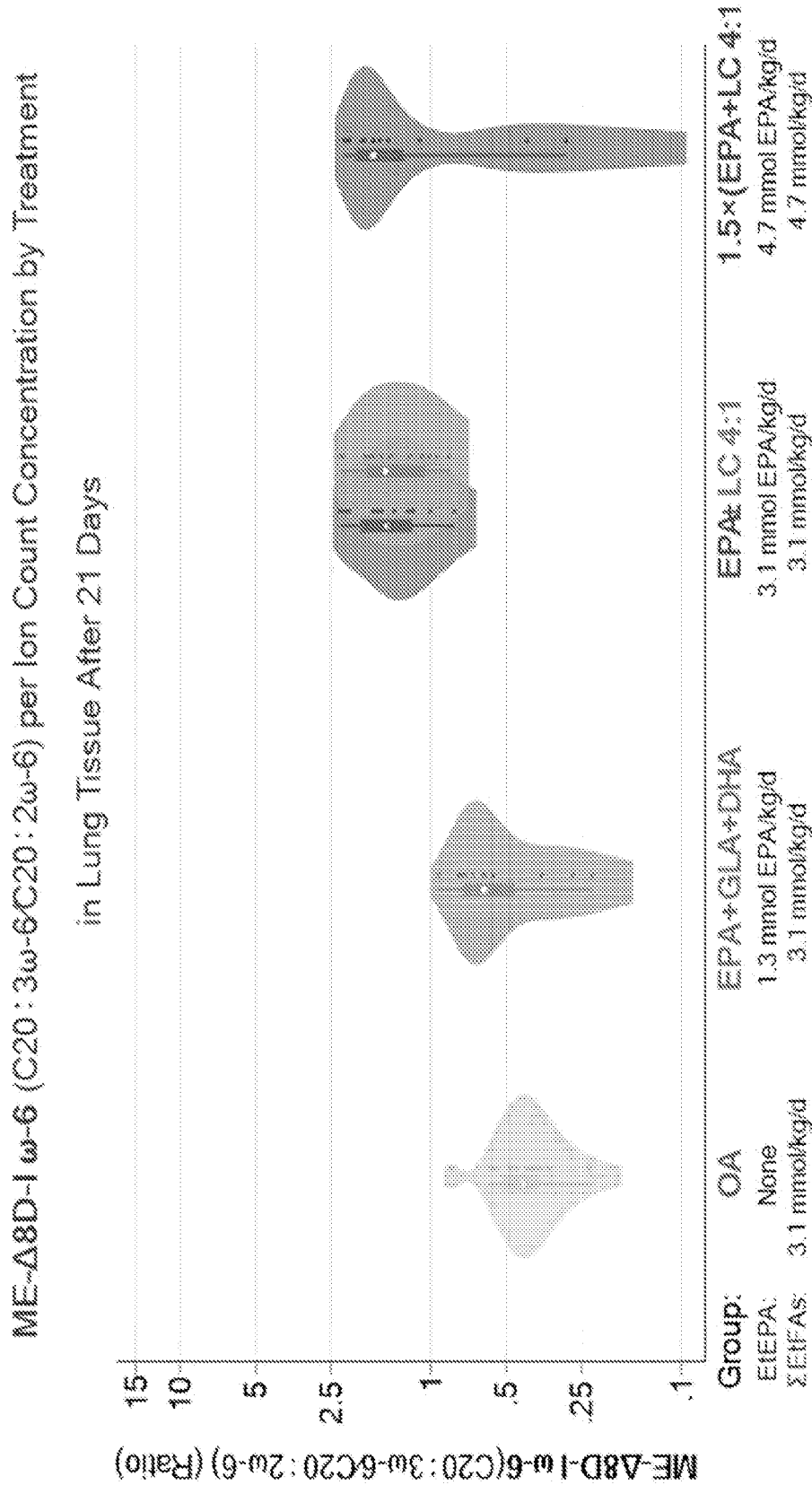


FIG. 31B

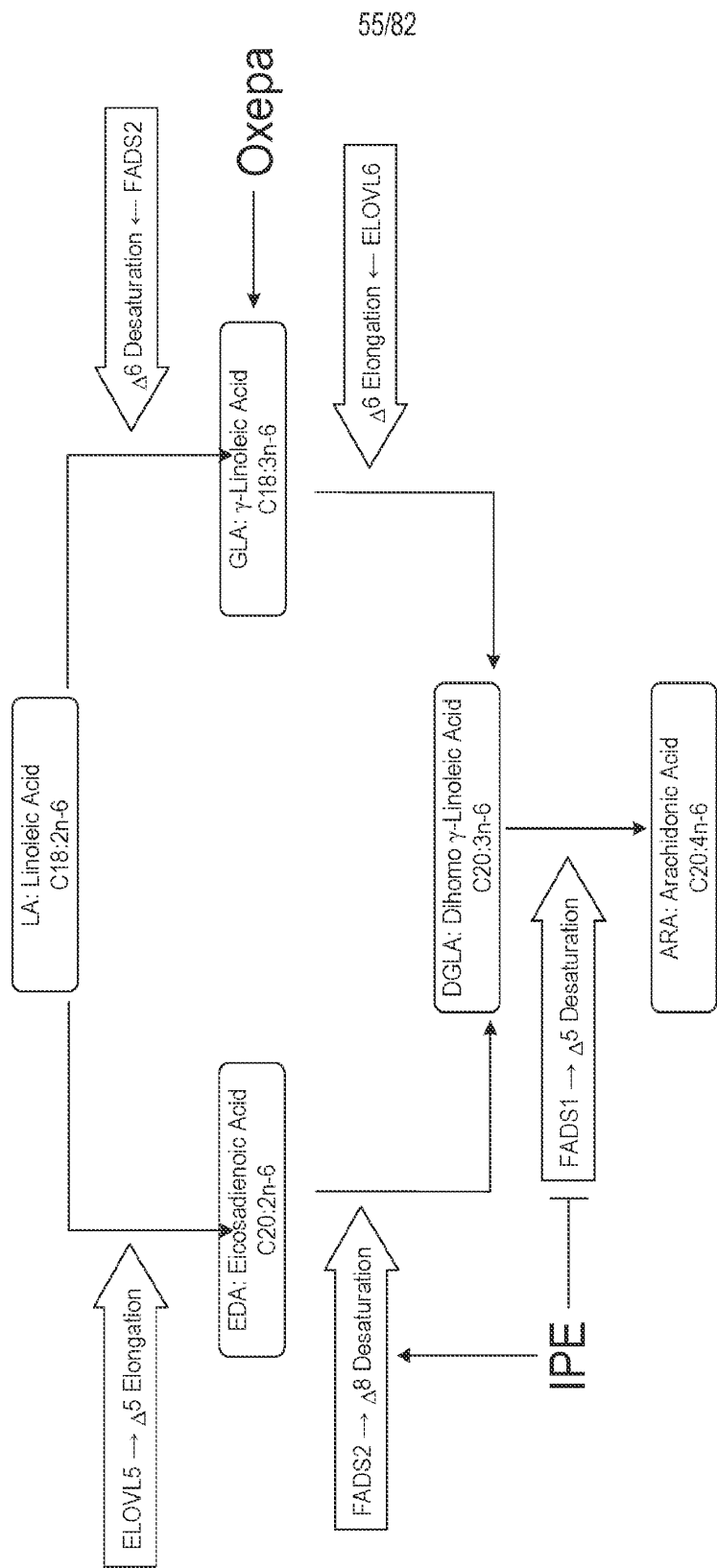
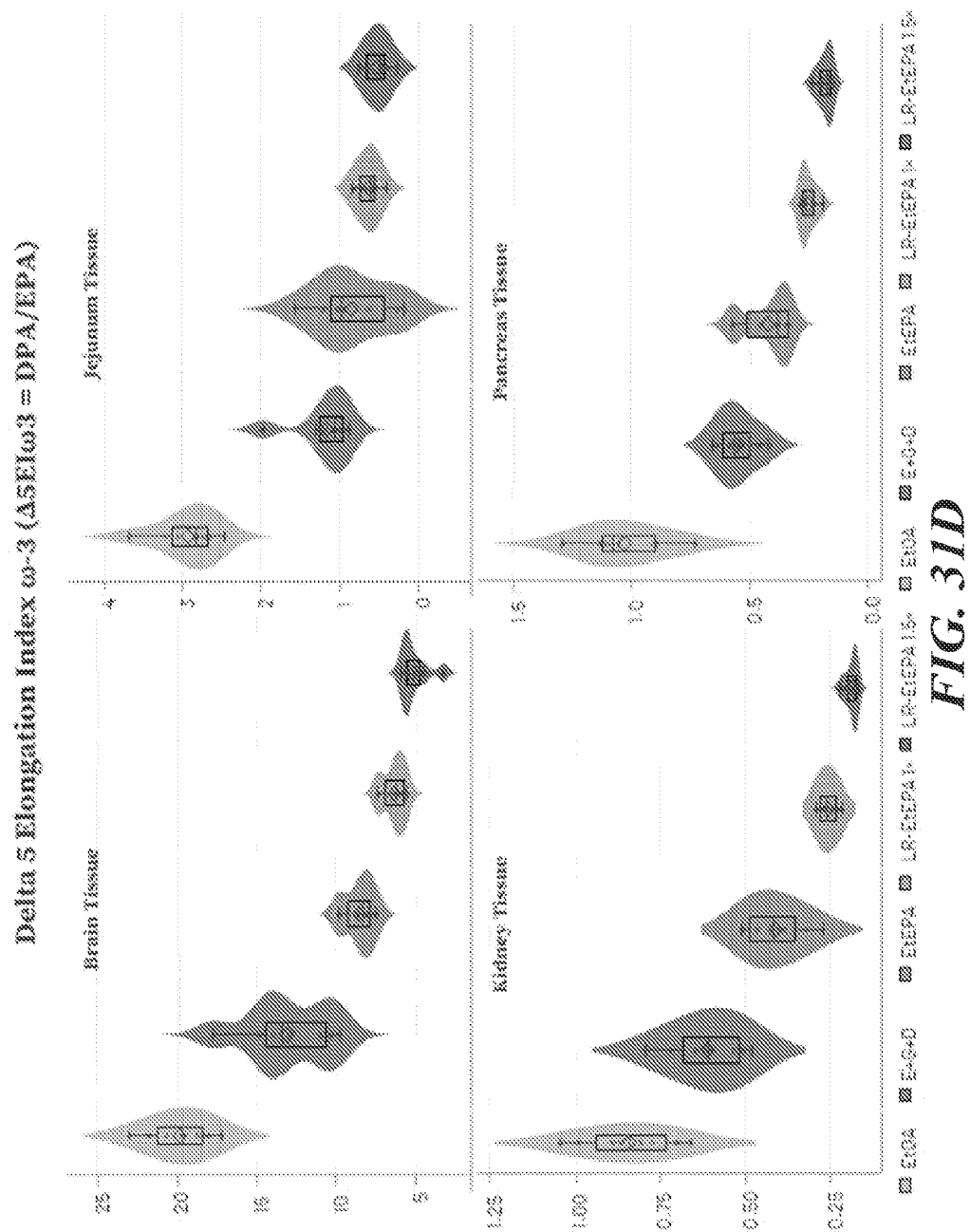


FIG. 31C



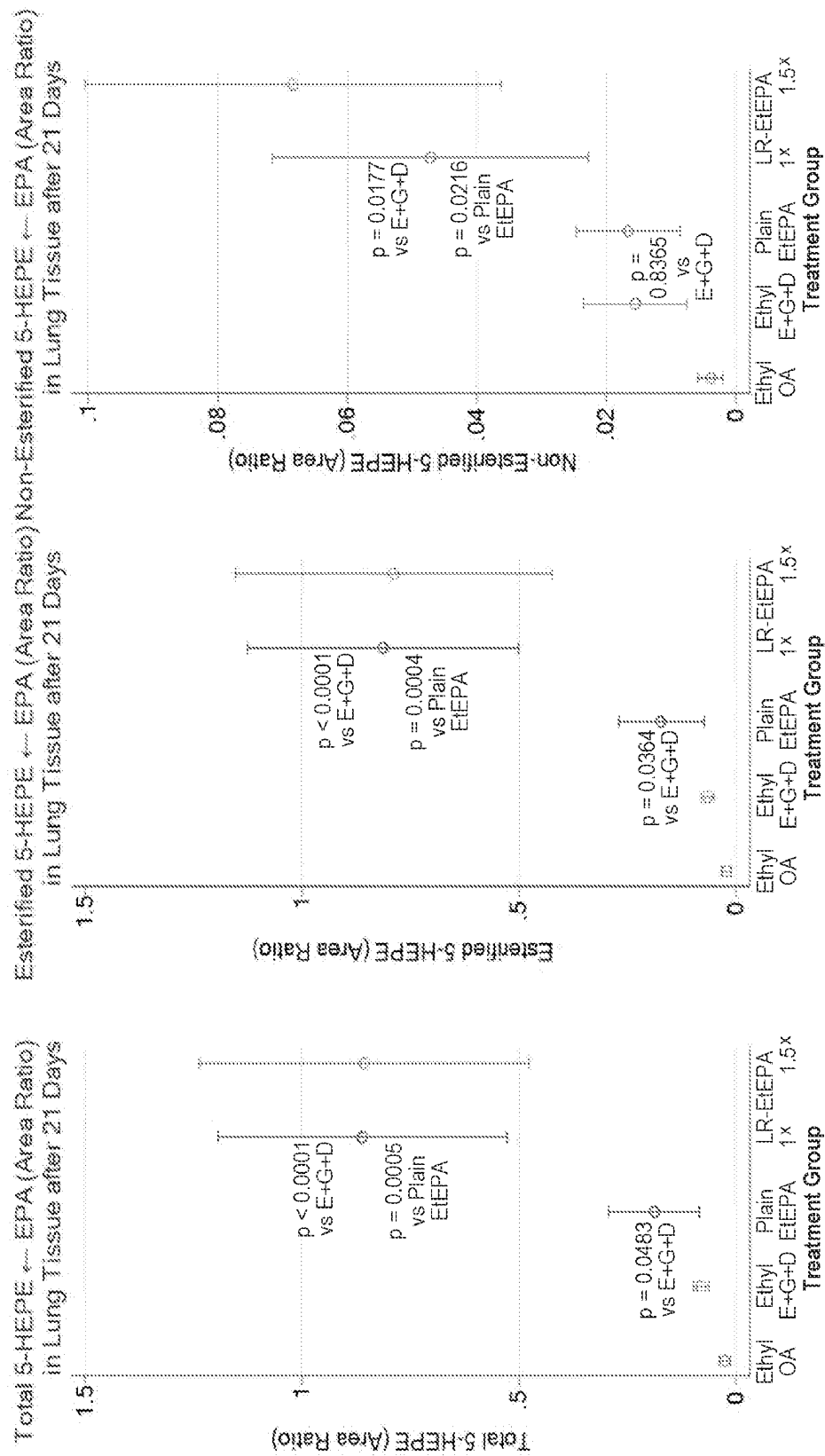


FIG. 32A

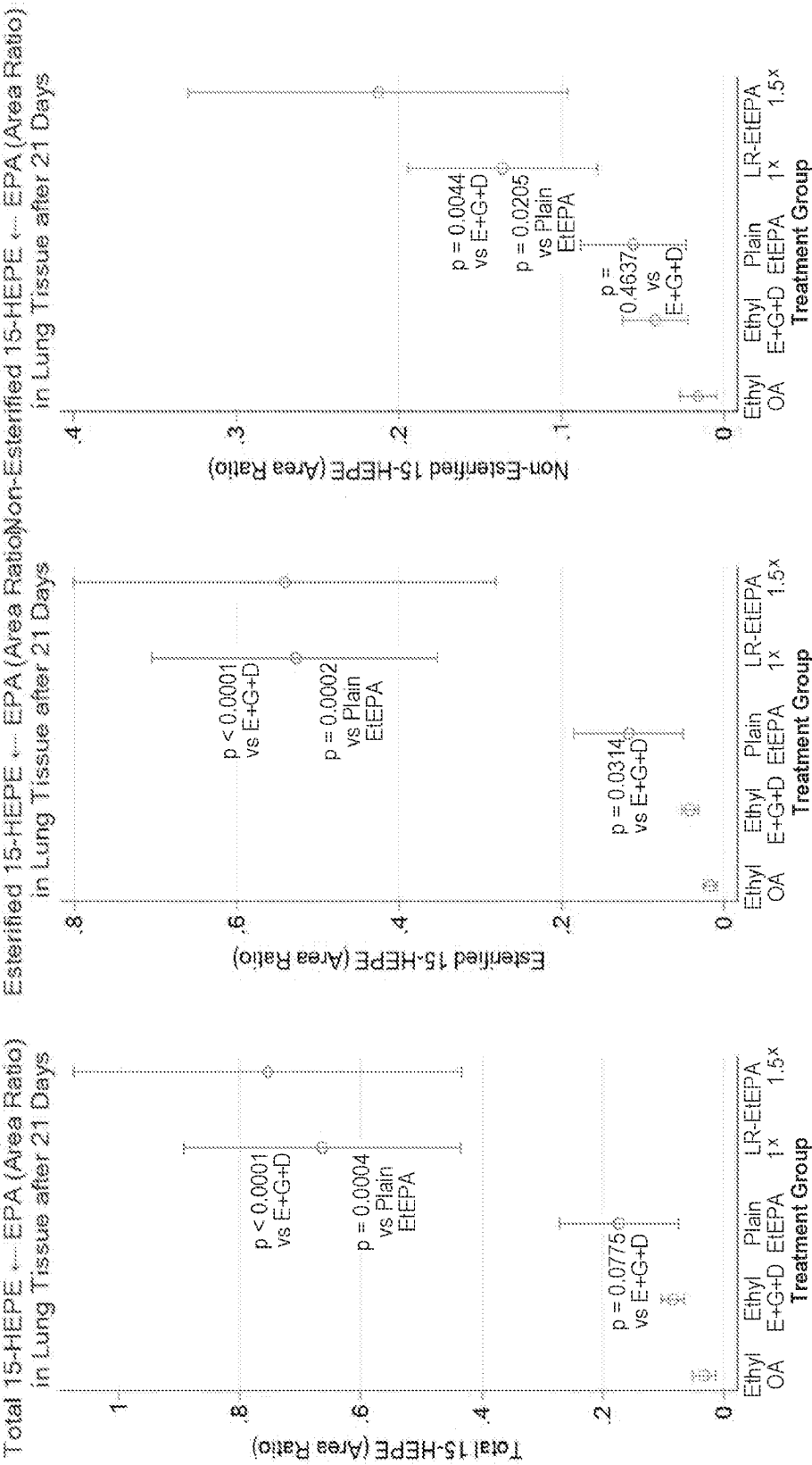


FIG. 32B

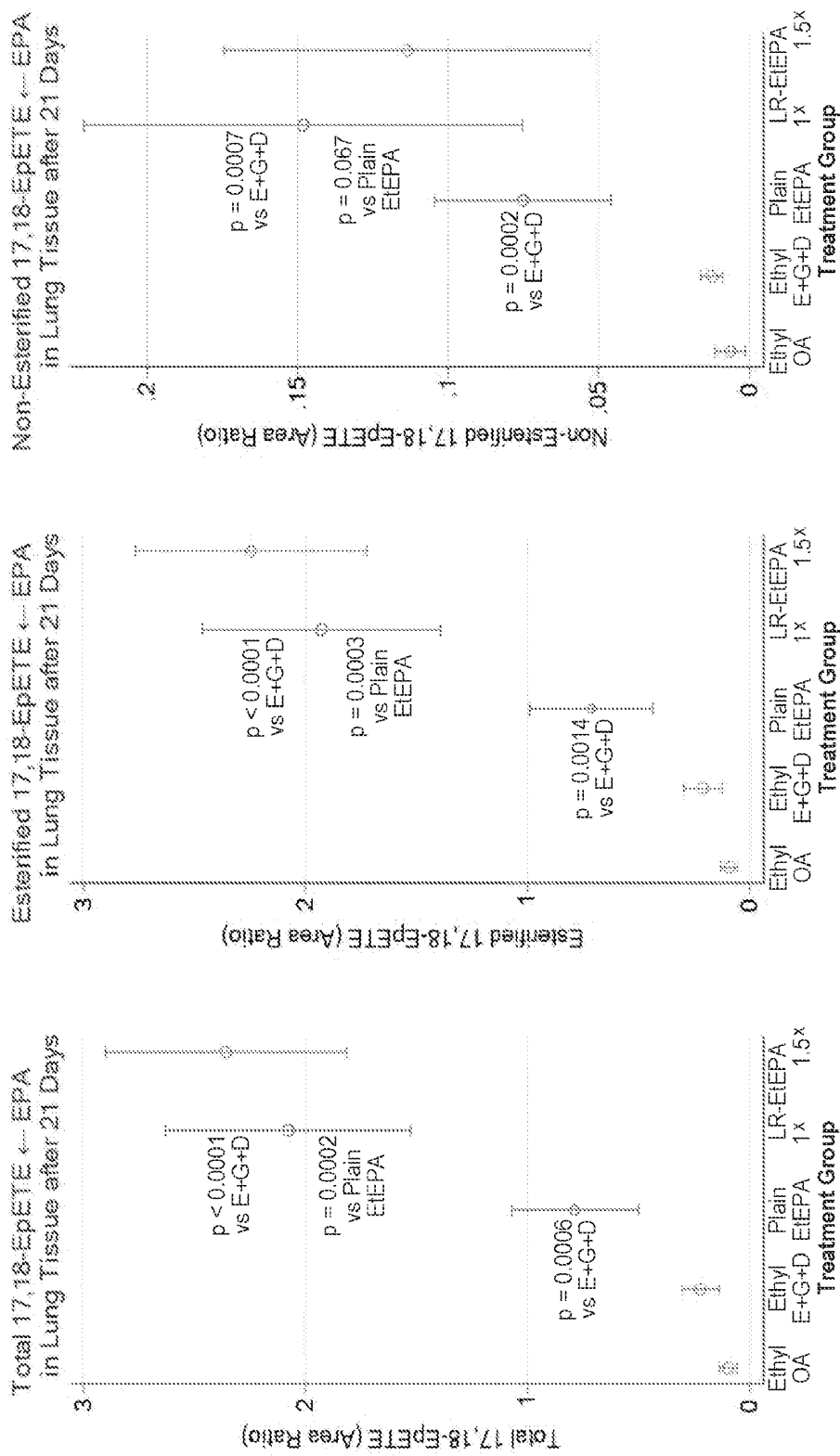


FIG. 32C

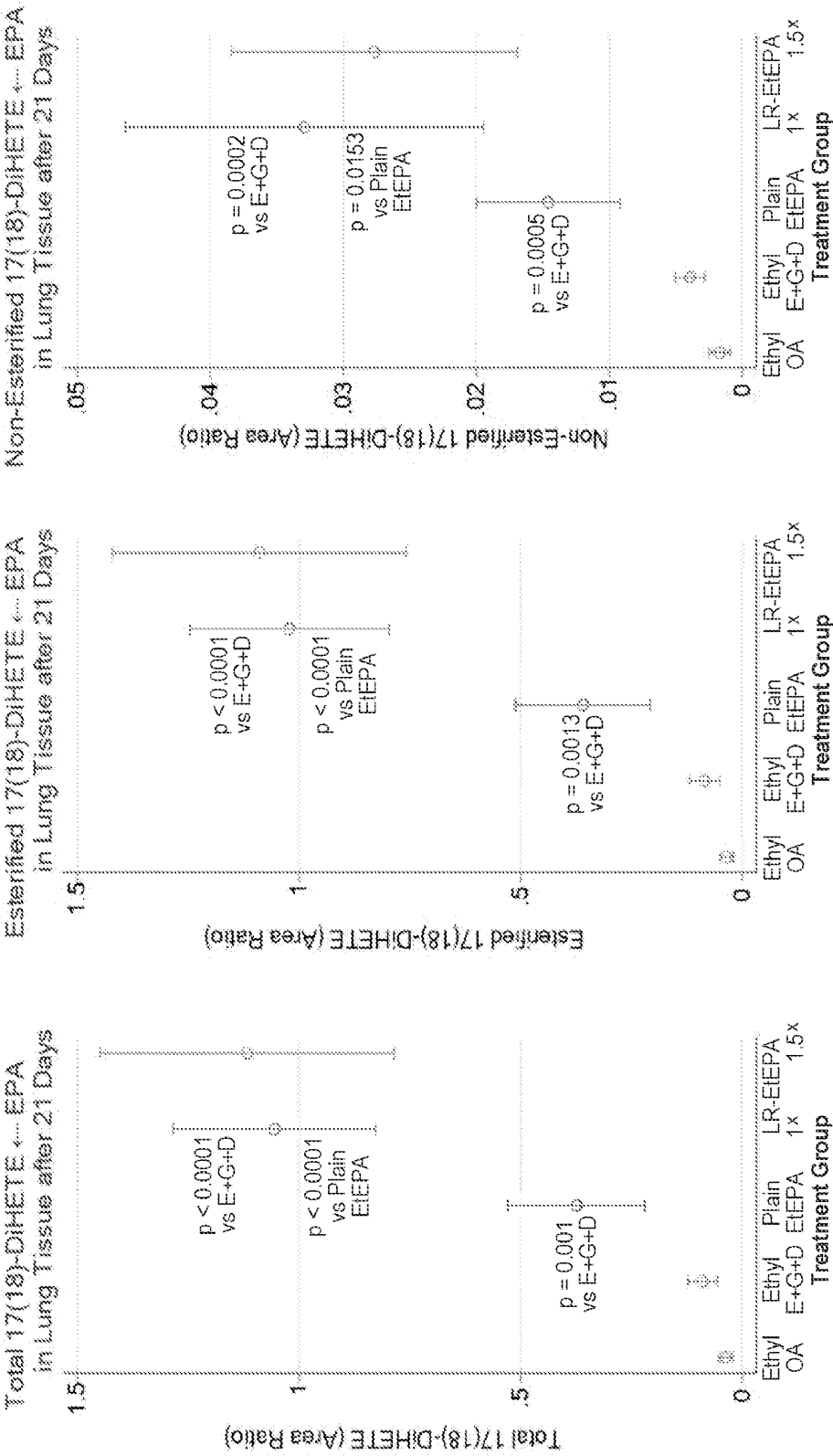


FIG. 32D

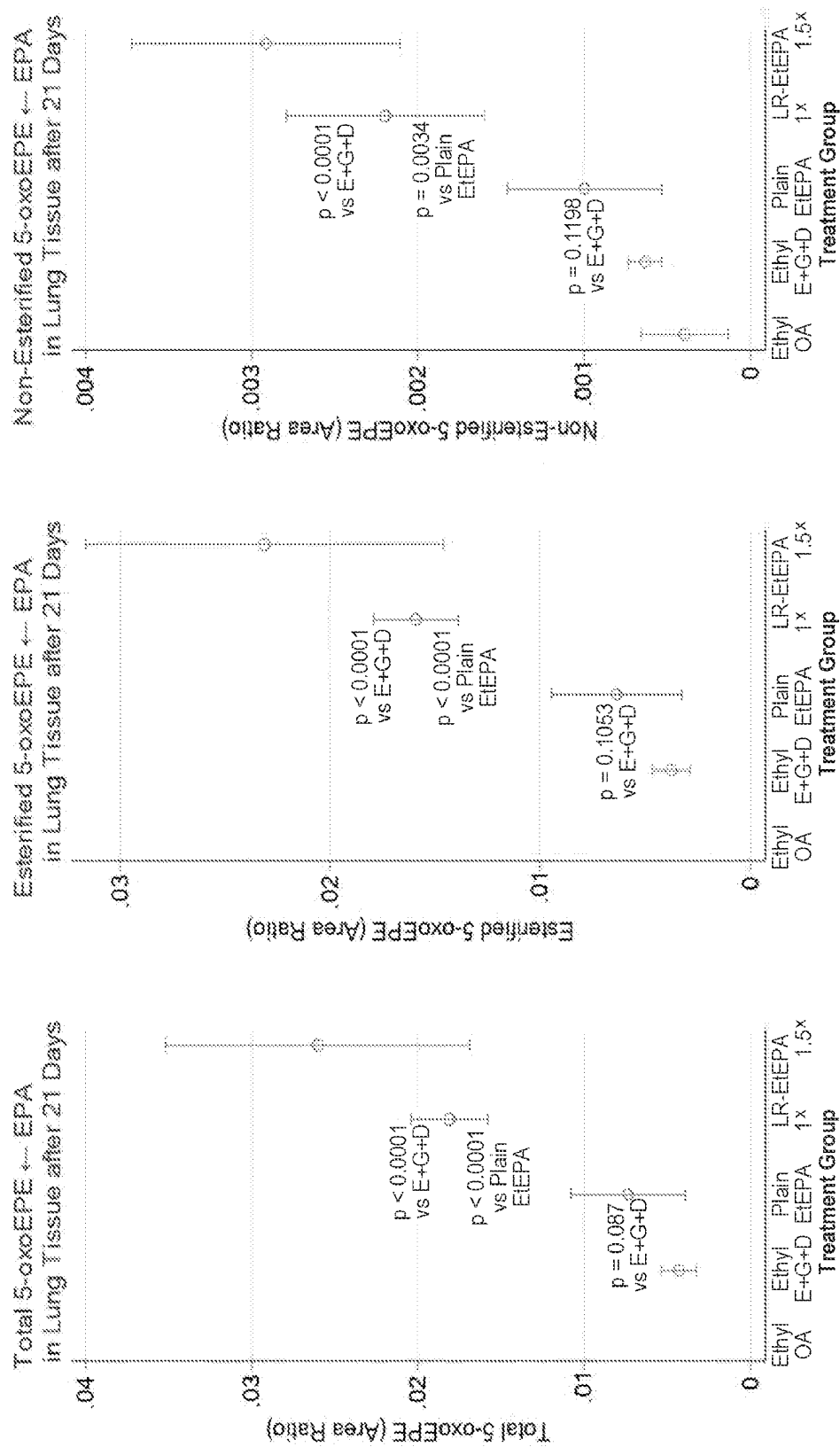


FIG. 32E

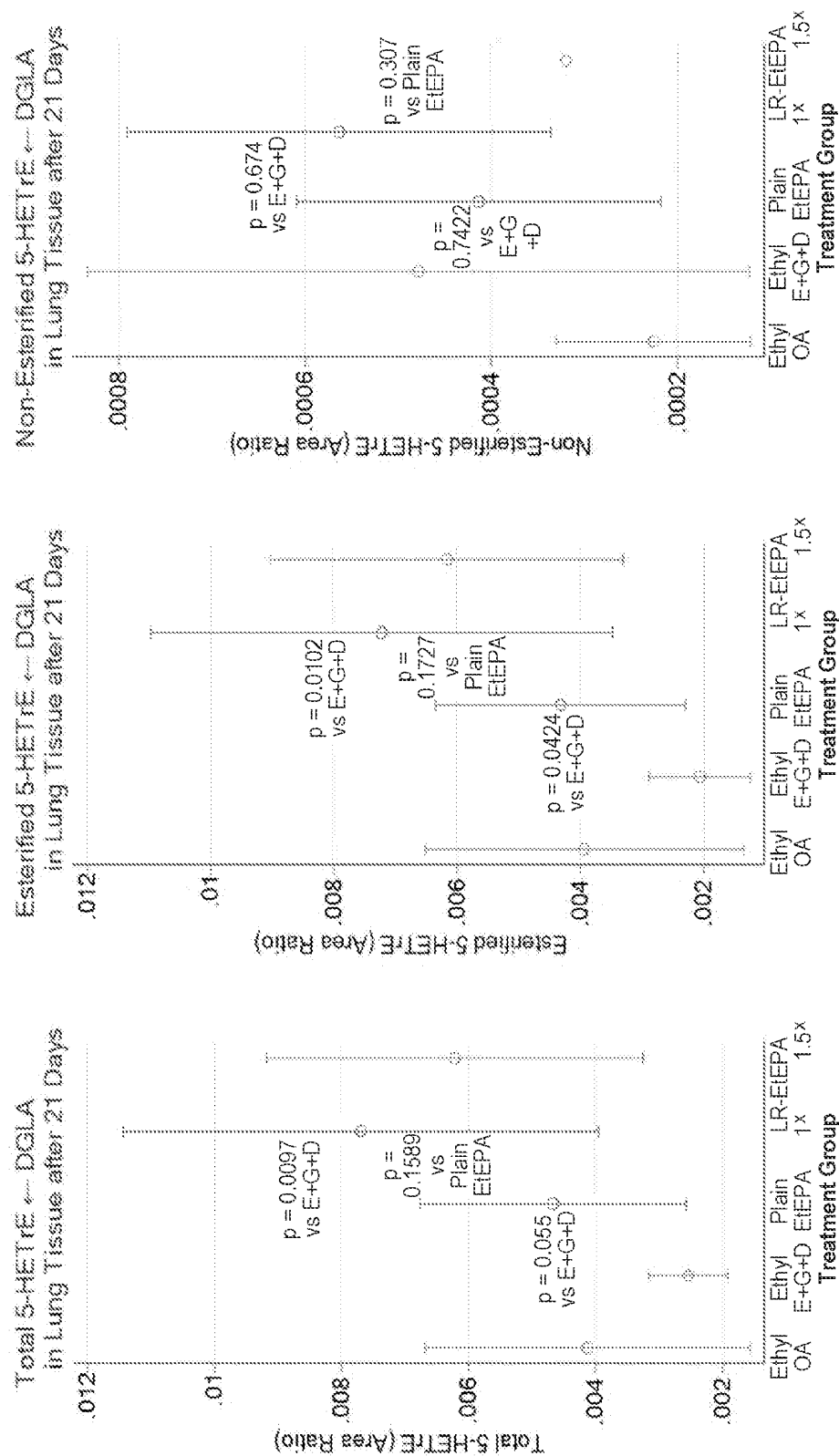


FIG. 32F

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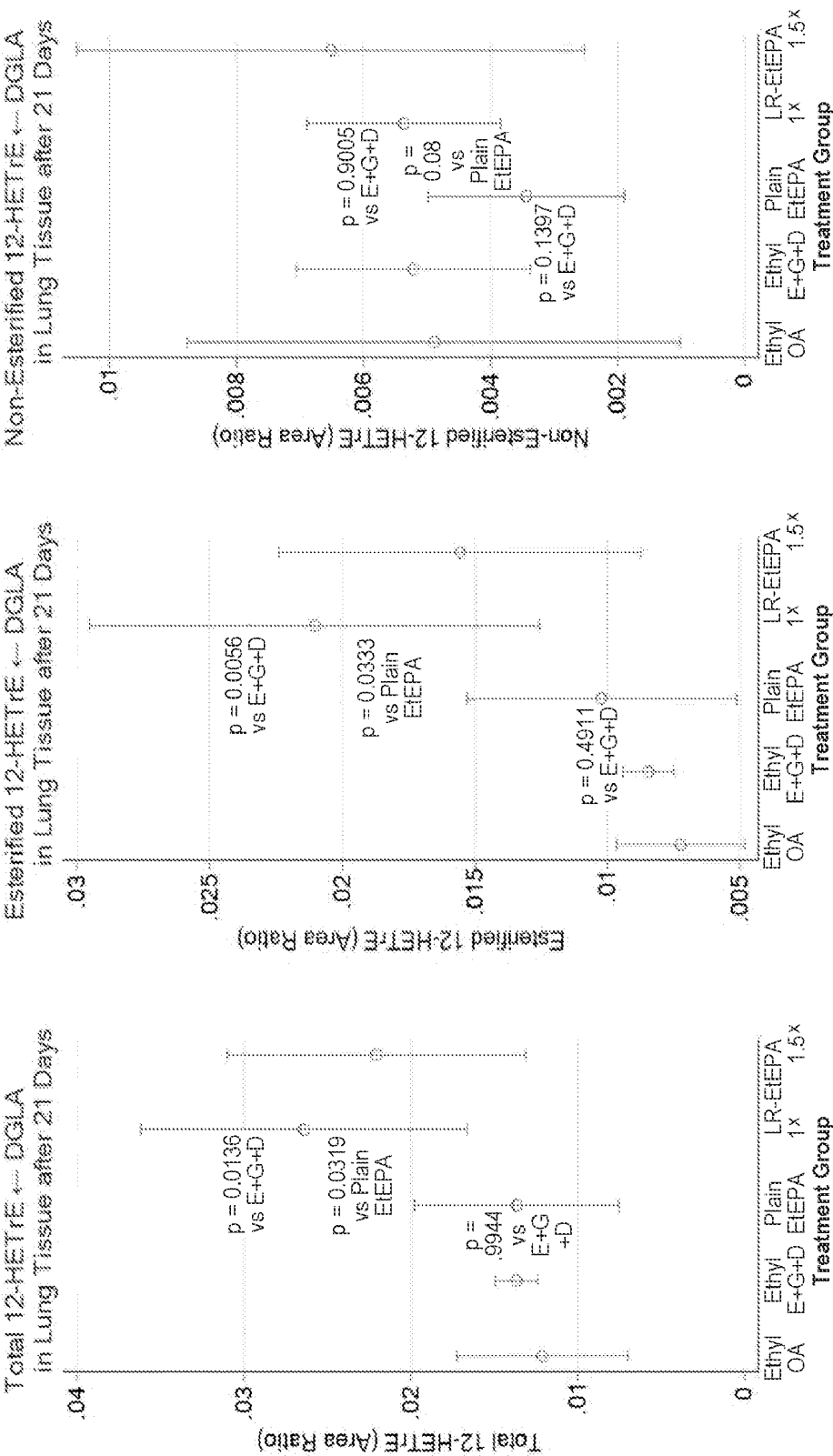


FIG. 32G

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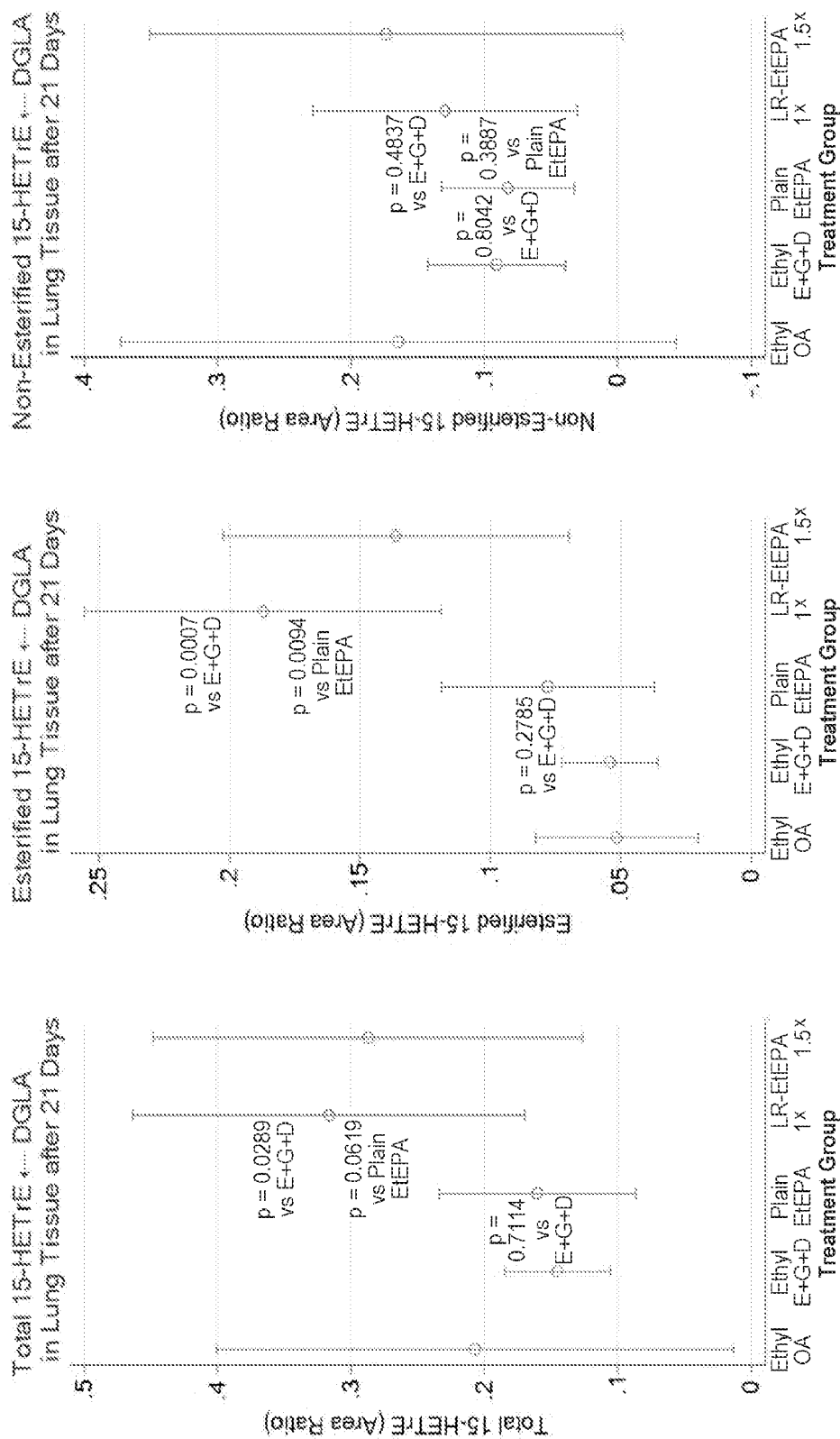


FIG. 32H

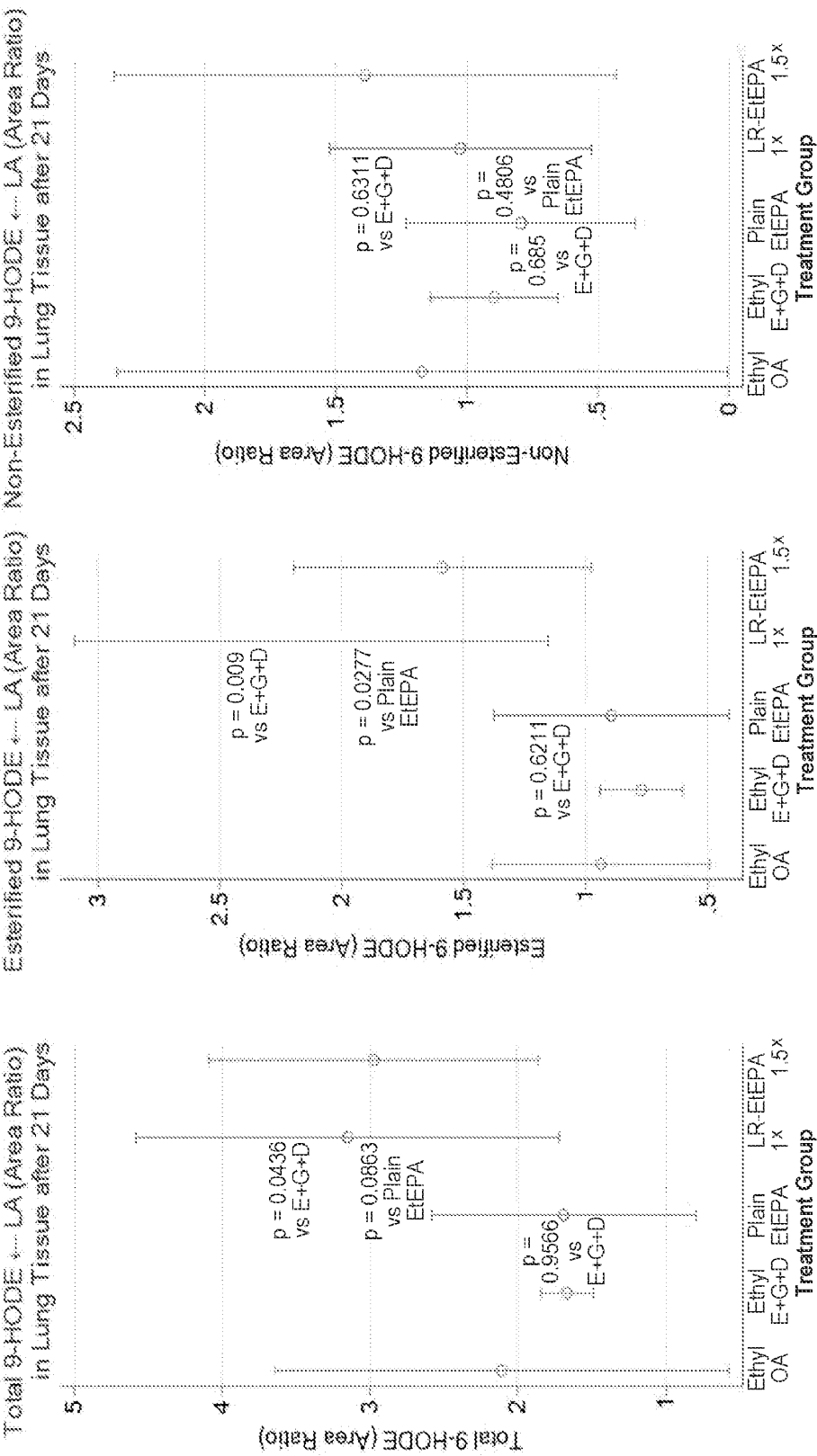


FIG. 32I

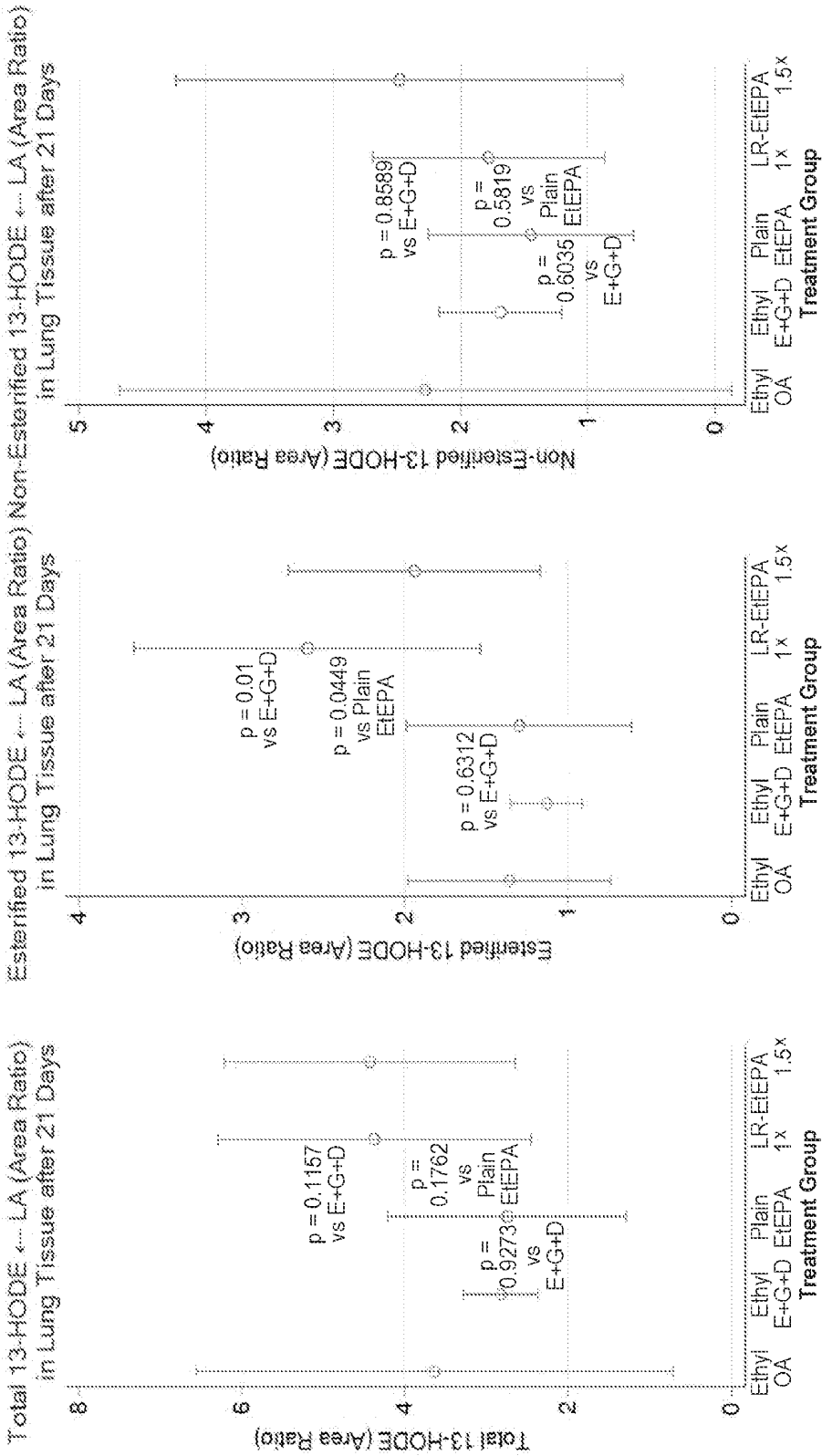


FIG. 32J

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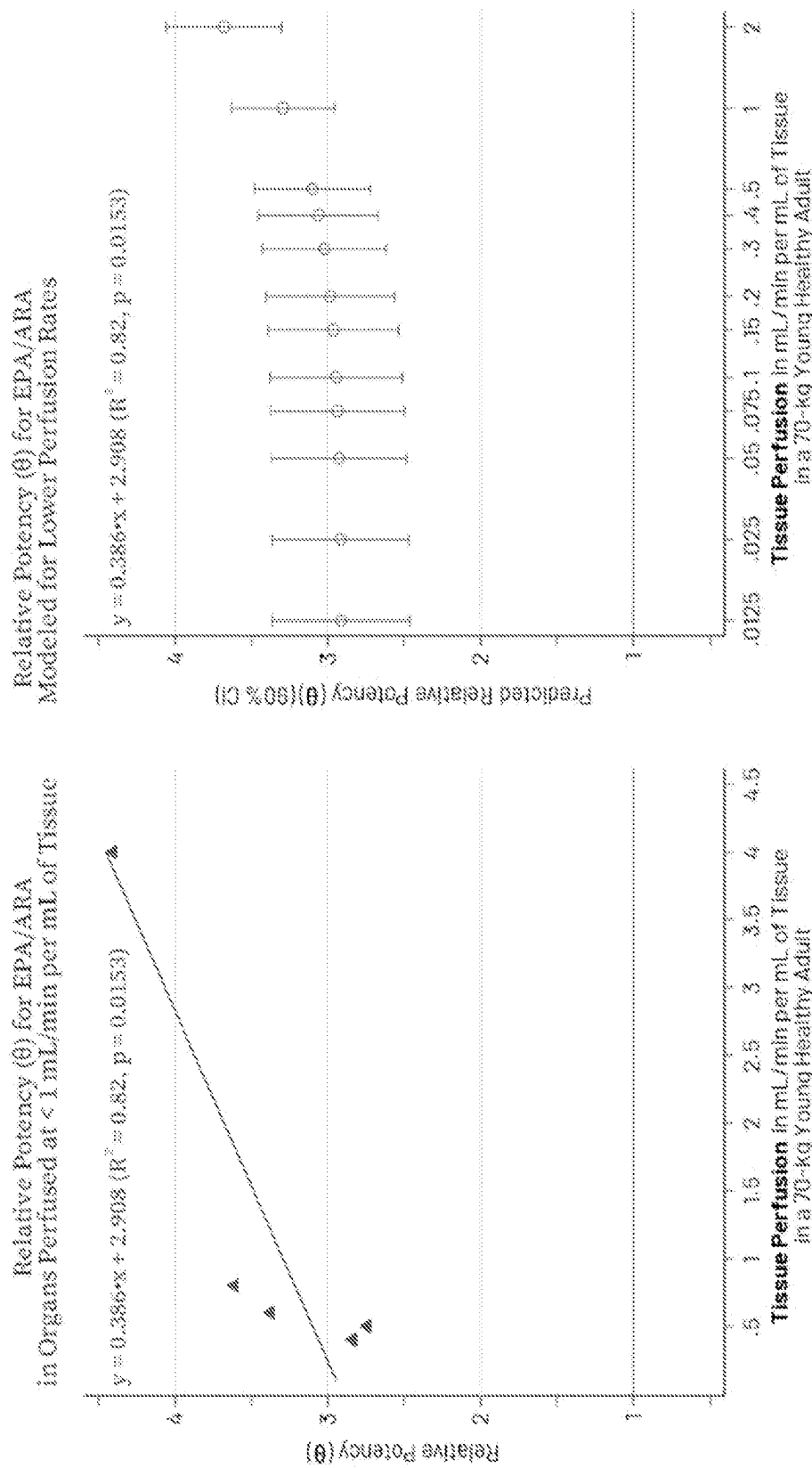


FIG. 33

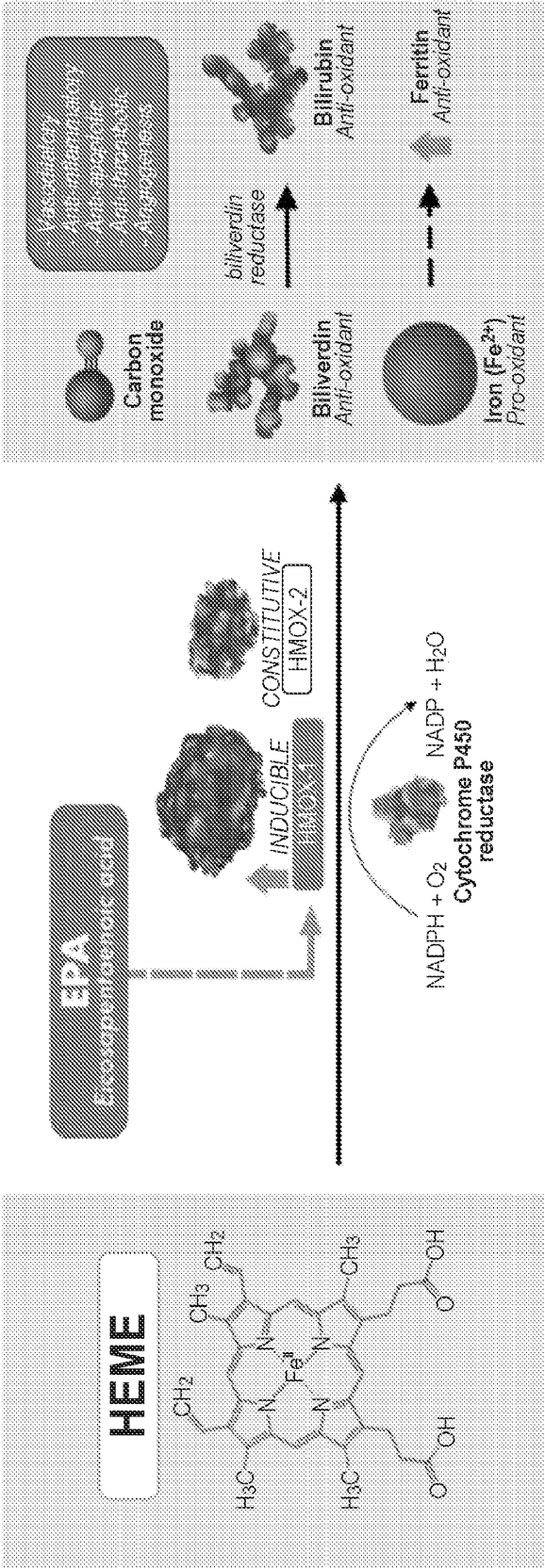


FIG. 34A

Significantly Modulated Proteins with EPA Treatment Relative to IL-6-Alone in Brain ECs

Protein	Effect with EPA vs IL-6	FC (p-value)
Heme Oxygenase-1	Increase	1.5 (4.70 × 10 ⁻¹⁶)
Fatty Acid Desaturase 2	Decrease	2.6 (1.28 × 10 ⁻¹⁵³)
Fatty Acid Desaturase 1	Decrease	1.4 (1.18 × 10 ⁻⁸)
Prothrombin	Decrease	1.3 (2.10 × 10 ⁻²⁴)

Significantly Modulated Proteins with EPA Treatment Relative to IL-6-Alone in Vascular ECs

Protein	Effect with EPA vs IL-6	FC (p-value)
Heme Oxygenase-1	Increase	2.2 (7.9 × 10 ⁻¹⁶)
Ferritin light chain	Increase	1.2 (4.0 × 10 ⁻³)
Ferritin heavy chain	Increase	1.4 (0.0002)
Protein Kinase LYN	Increase	1.2 (0.003)
Fatty Acid Desaturase 2	Decrease	1.6 (1.3 × 10 ⁻¹¹)

Significantly Modulated Proteins with EPA Treatment Relative to IL-6-Alone in Pulmonary ECs (all post IL-6 treatment)

Protein	Effect with EPA vs IL-6	FC (p-value)
Heme Oxygenase-1	Increase	1.9 (2.8 × 10 ⁻³²)

FIG. 34B

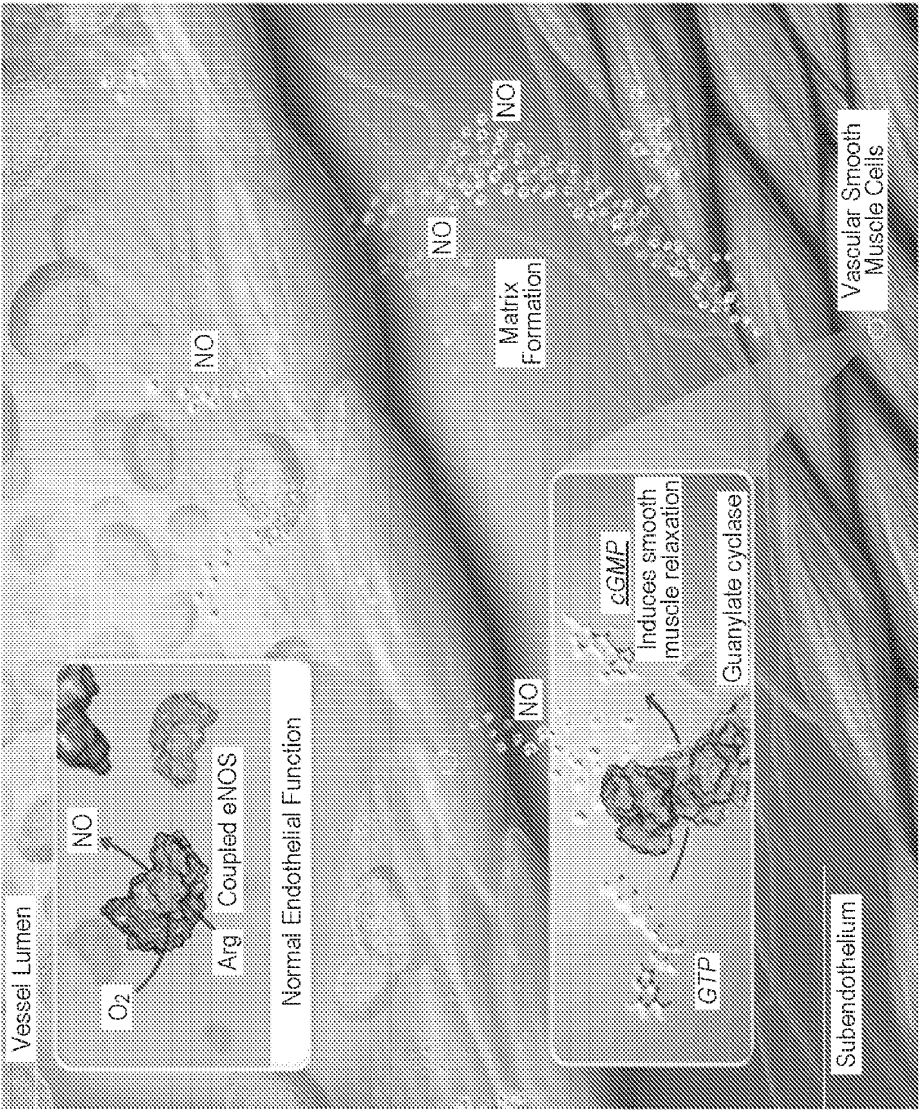


FIG. 34C

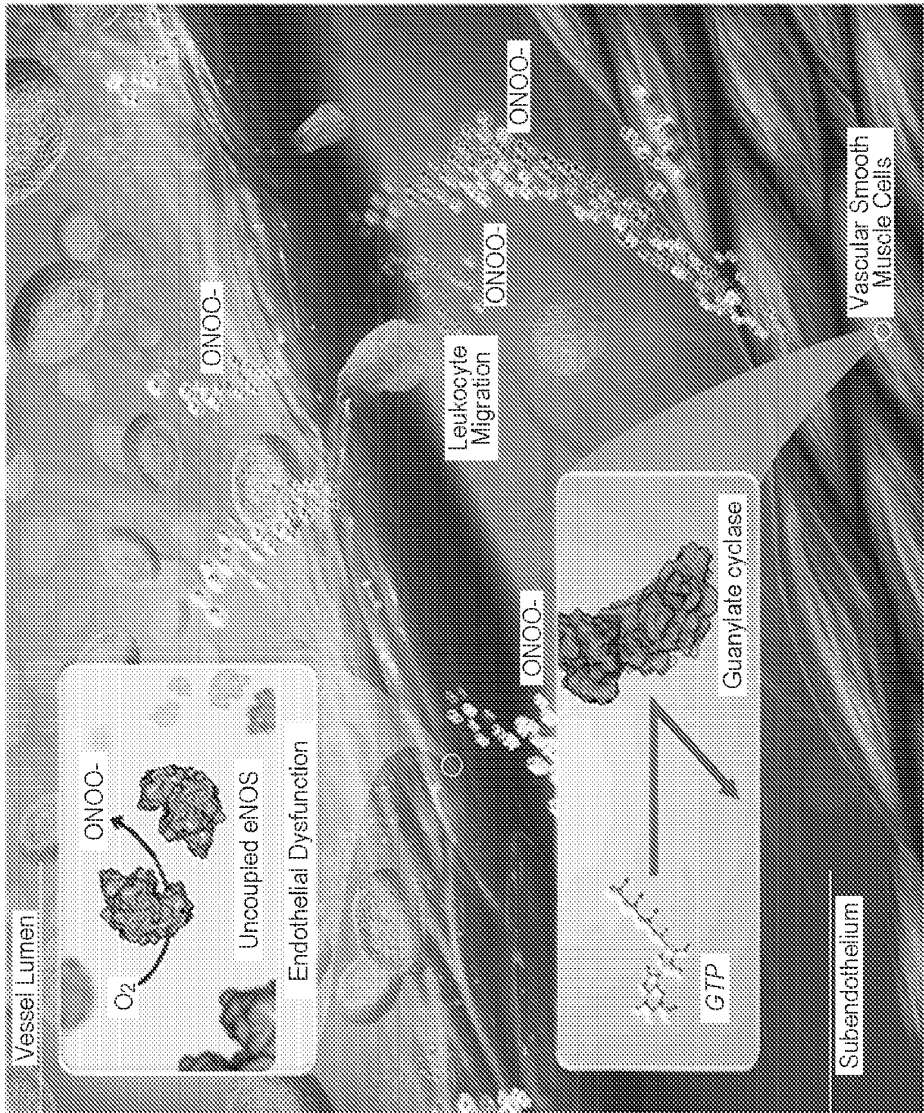


FIG. 34D

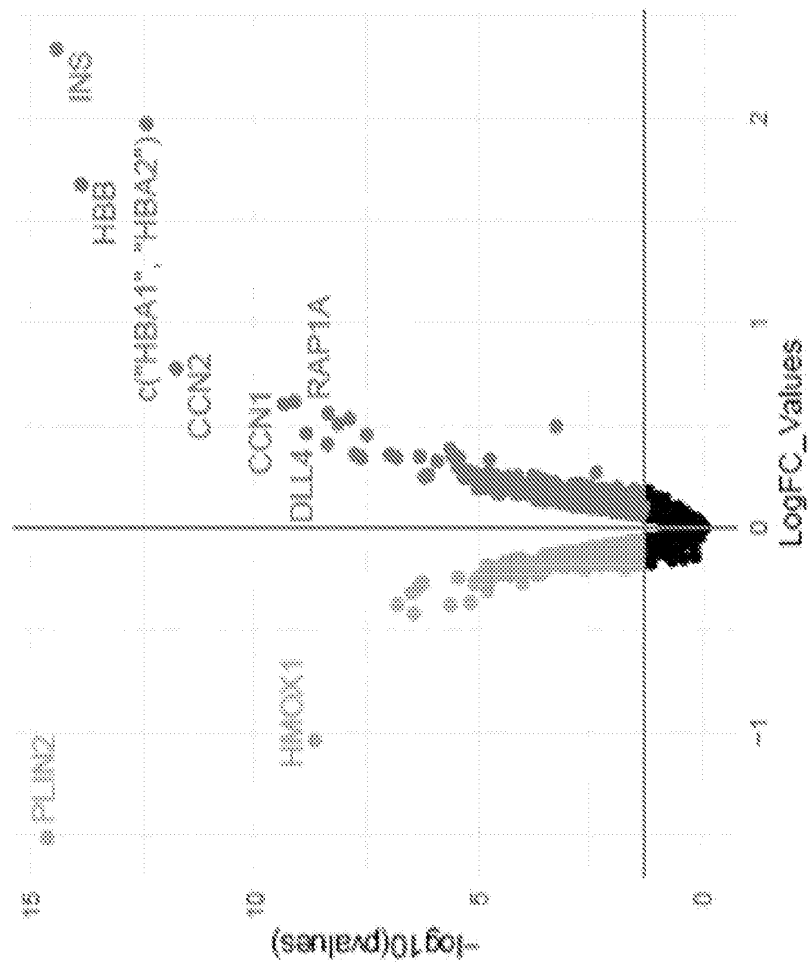


FIG. 35

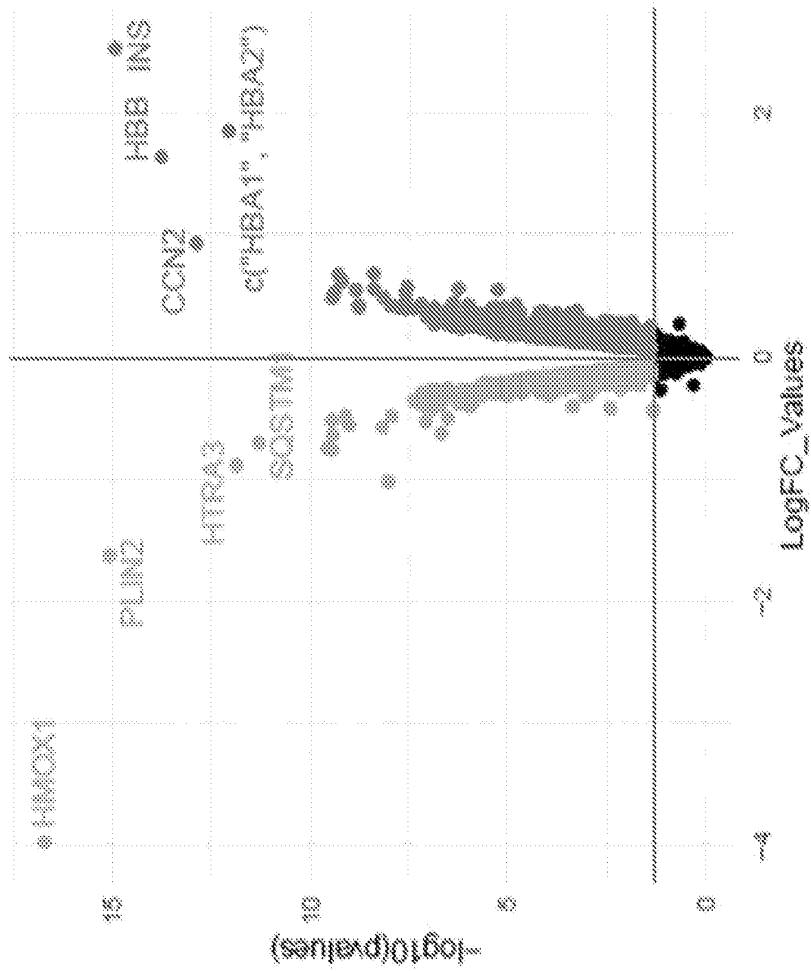


FIG. 36

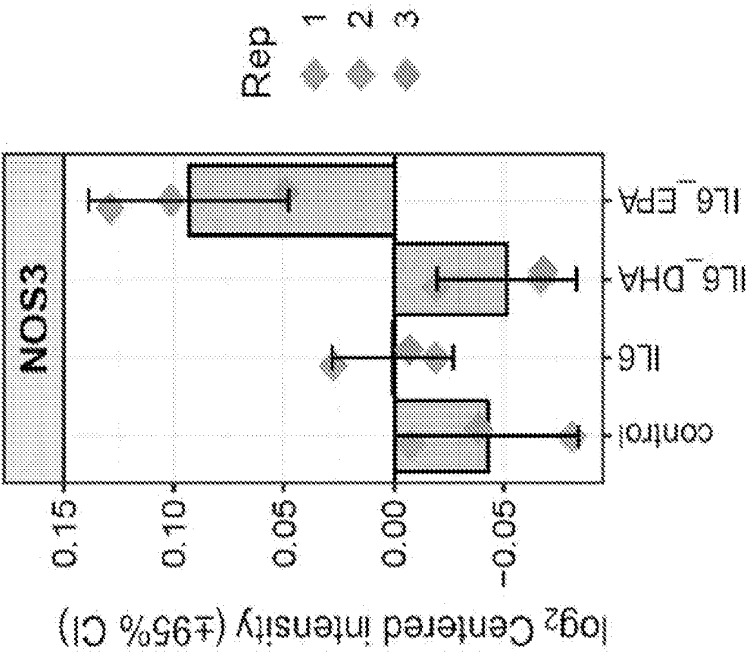
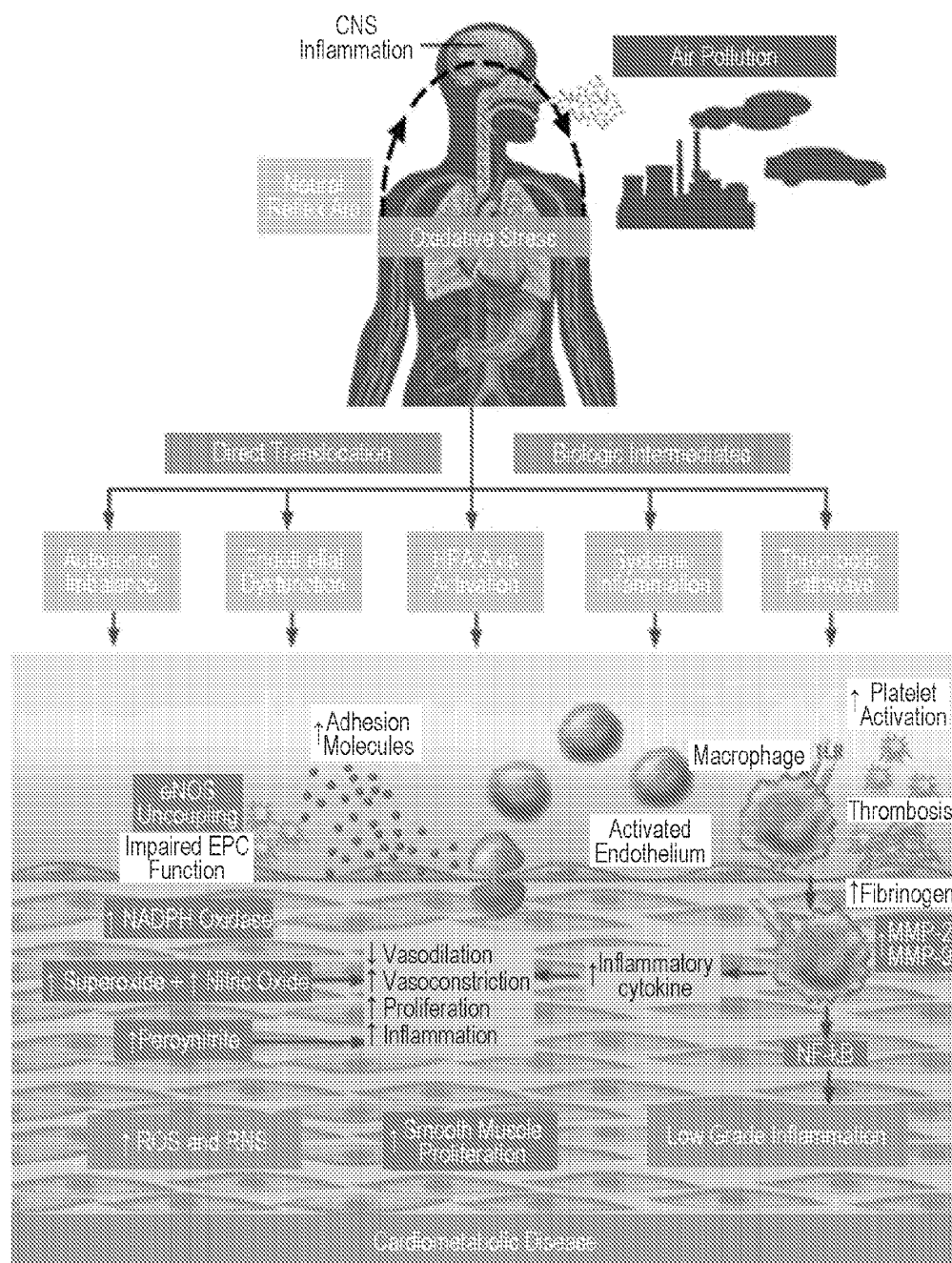


FIG. 37

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**FIG. 38**

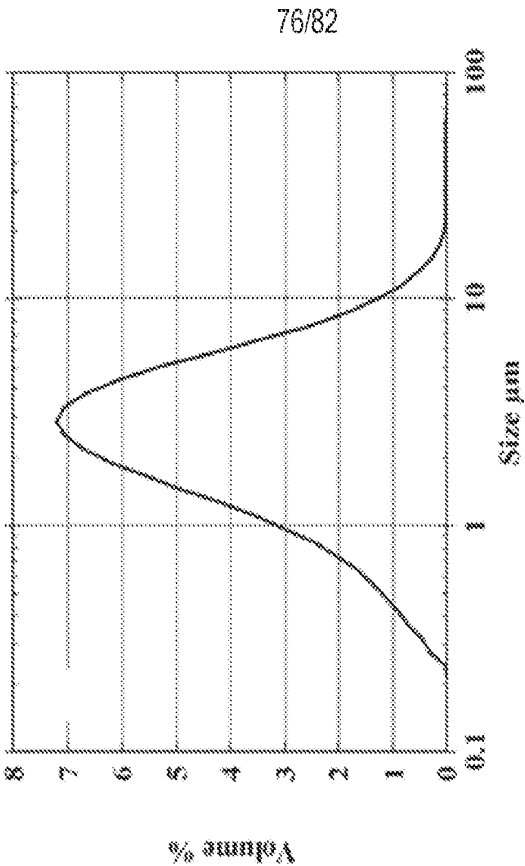


FIG. 39B

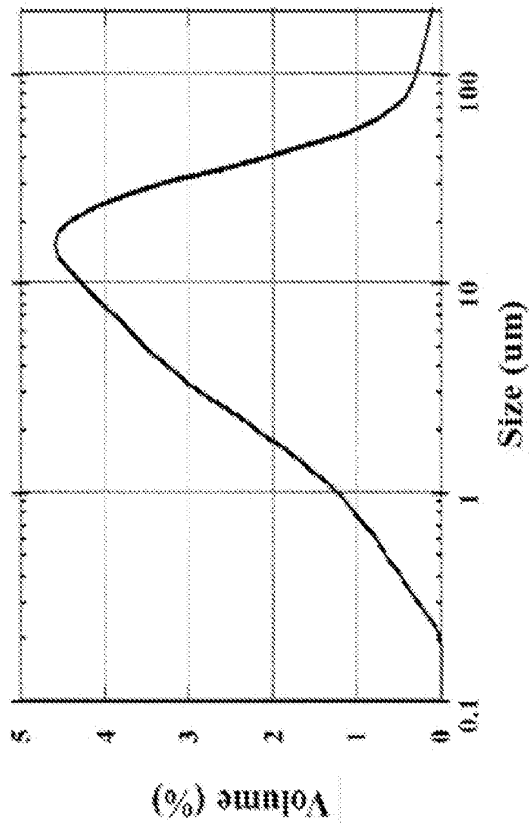


FIG. 39A

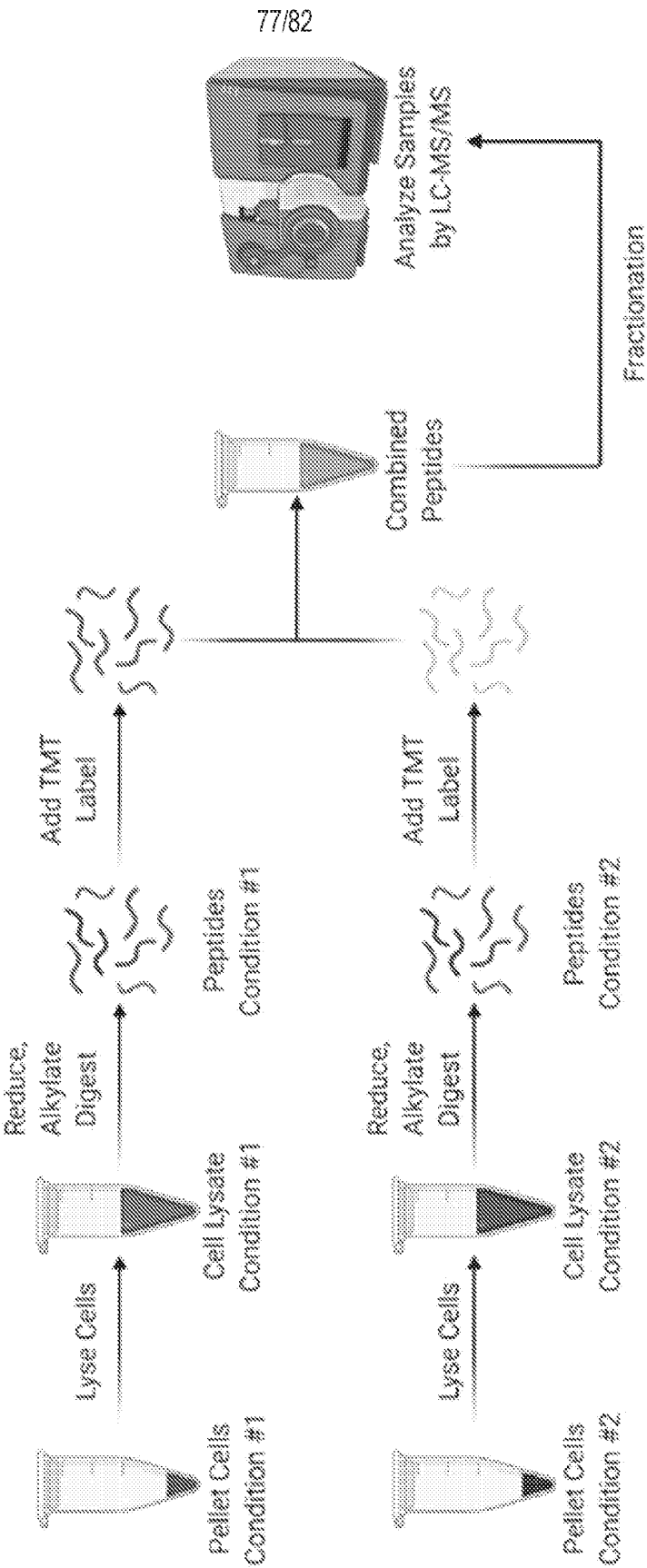


FIG. 40

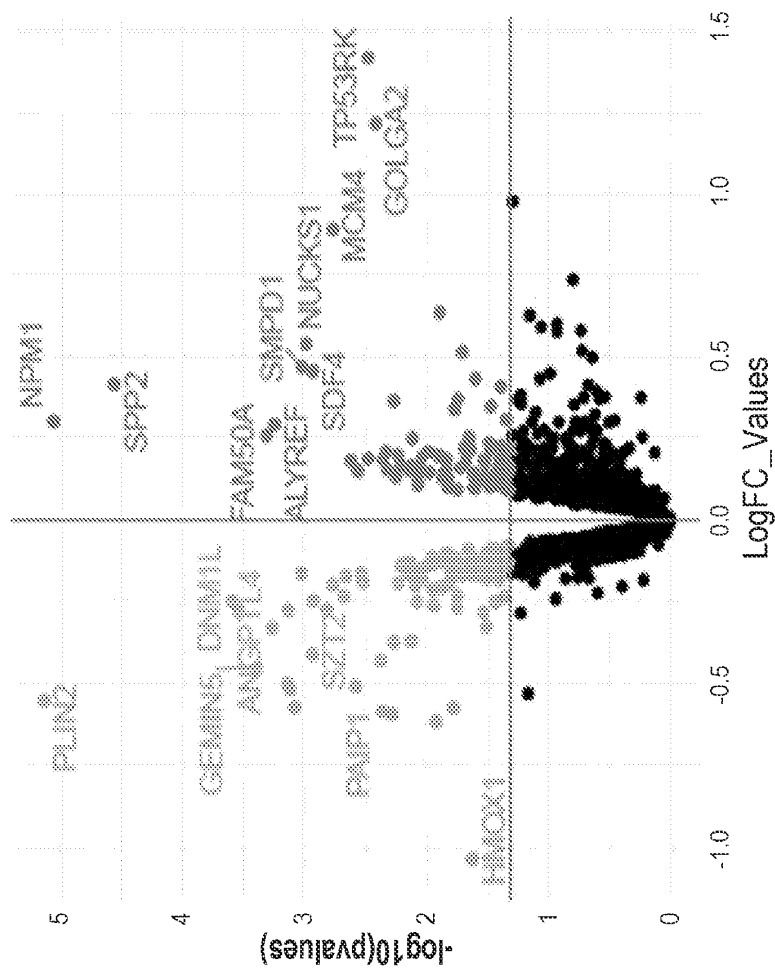


FIG. 41A

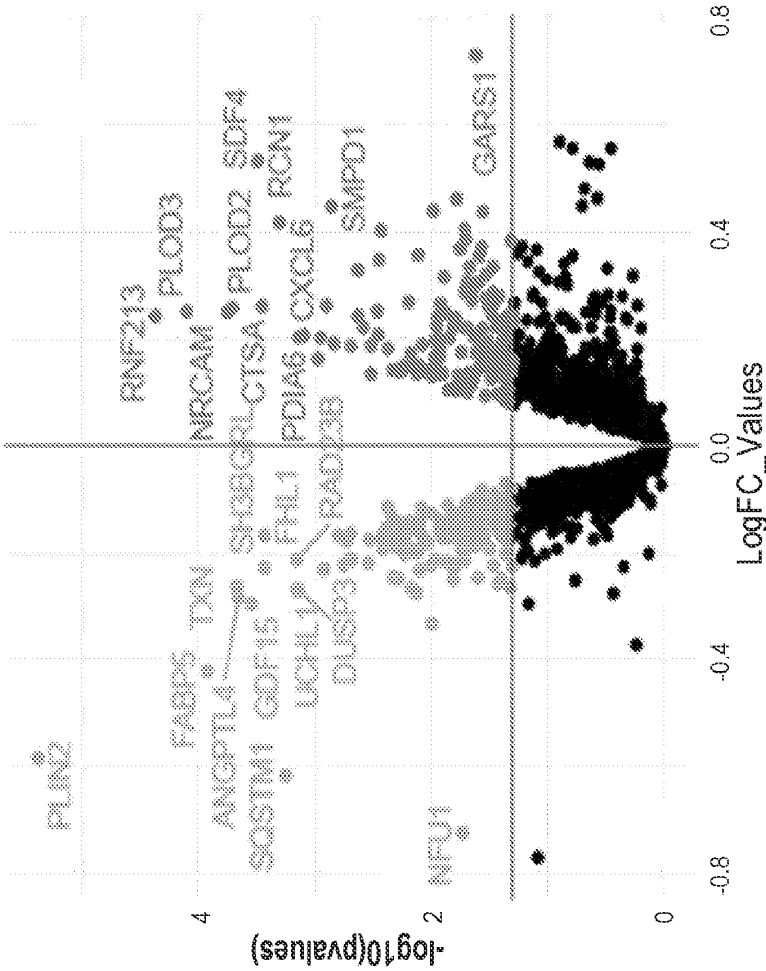


FIG. 41B

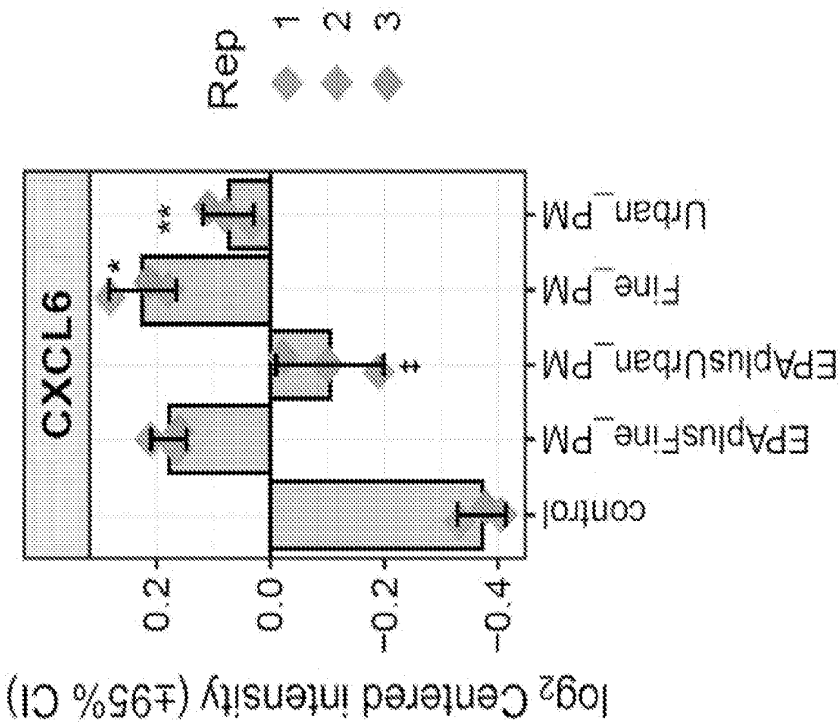


FIG. 42A

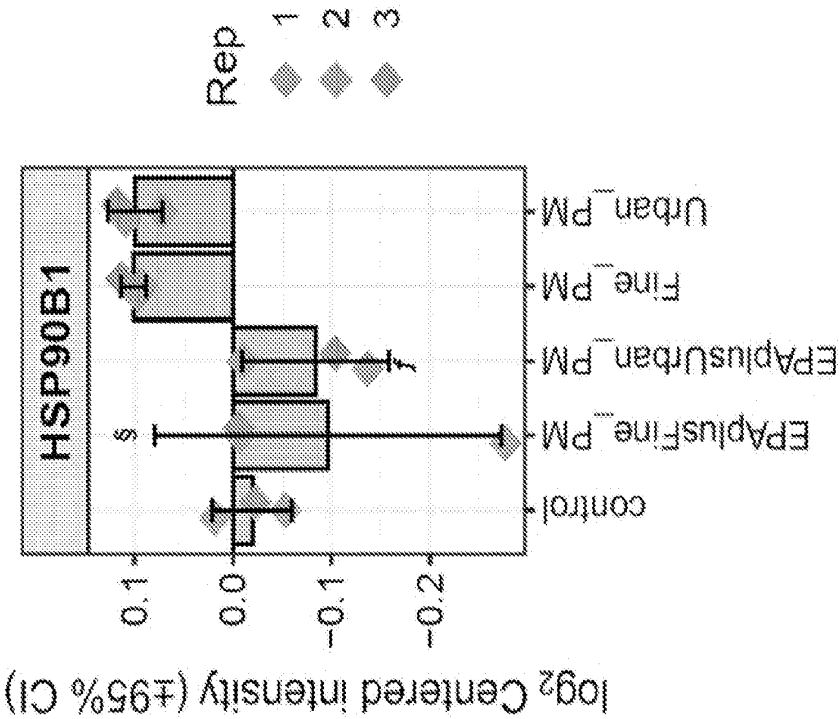


FIG. 42B

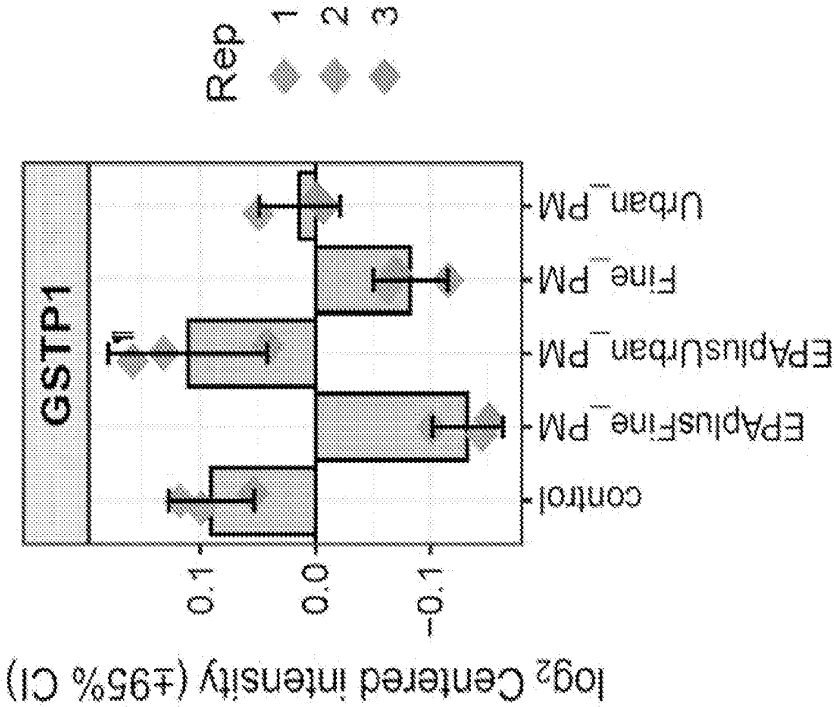


FIG. 42C