FDA QUALIFIED KIDNEY TUBULAR INJURY SAFETY BIOMARKER PANEL

The FDA has approved the Qualification of the Safety Biomarker Panel to aid in the detection of kidney tubular injury in Phase I trials.

nexelis

disciplined agility

assay development ◦ specialty testing

The Safety Biomarker Panel includes creatinine-corrected biomarkers – Urinary KIM-1, NGAL, cystatin C, osteopontin, clusterin (ELISAs) & NAG (colorimetric)

The results from each biomarker are used to derive a composite measure, which determines the probability of kidney tubular injury for the cohort treated by the investigated drug. The panel, developed and validated at Pacific Biomarkers, is currently available. The ELISA-based biomarkers have been incorporated into a 5-plex, the AKI Array, using the Randox Biochip Array Technology (BAT).

AKI Array

- Clusterin
- Cystatin C
- KIM-1
- NGAL
- Osteopontin

Additional Kidney Injury Biomarkers

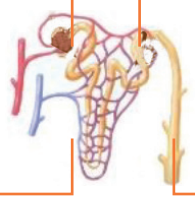
- a-GST
- BUN (S)
- Creatinine (U, S)
- Cystatin C (U, S)
- IL-18
- NAG
- RBP4
- Microalbumin
- Total Protein

We have assessed renal toxicity for 33 drug programs since 2010.

The AKI Array target standard curve ranges were established after analyzing the span of biomarker concentrations in urine from thousands of subjects with normal kidney function or potential AKI as determined by PBI's Gold Standard ELISA methods:

Proximal Tubules
- KIM-1
- Clusterin
- NGAL
- Osteopontin
- Cystatin C

Loop of Henle
- Osteopontin



Distal Tubules
- Osteopontin
- Clusterin
- NGAL

Collecting Duct
- Cystatin C

Urine AKI marker	units	n	ELISA LLOQ	Max Reported Value (w dilution)	% <LLOQ	Ideal Measurable Range	AKI Array Measurable Range	AKI Array LLOQ
KIM-1	pg/mL	2609	< 12	18.688	0.9%	40 - 4000 (<40 = 3.72%, >4000 = 7.63%)	31.2 - 4000	< 26
NGAL	ng/mL	3647	< 0.4	761.6	0.3%	1.0 - 100 (<1.0 = 2.33%, >100 = 4.66%)	0.8 - 100	< 0.5
Cystatin C	ng/mL	2499	< 1.3	694.6	2.1%	1.5 - 150 (<1.5 = 2.1%, >150 = 2.8%)	1.4 - 180	< 0.98
Osteopontin	ng/mL	2499	< 40	32.352	2.6%	80 - 8000 (<80 = 2.95%, >8000 = 3.27%)	62.5 - 8000	< 43
Clusterin	ng/mL	2676	< 10	1,860	2.5%	10 - 1000 (<10 = 2.5%, >1000 = 0.07%)	10.4 - 1000	< 5.4

OUR LEGACY

Over almost 30 years, Nexelis has maintained a "fit-for-purpose" assay development and validation philosophy.
This covers a range of ratification options, from feasibility to full validations using CAP, CLSI, or FDA bioanalytical guidelines that match the intended use.

Our validation procedures apply to novel biomarkers, proprietary technology transfers, and comprehensive bioanalytical services for biologics, where PK, ADA and immunogenicity assays are required.

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