



Human Pre-clinical Exposure Assessment

Objective: To develop a psychophysiological test battery for rapid preclinical assessment of newly developed reduced risk prototypes that may provide important feedback on exposure effects prior to more extended clinical studies.

Address:

- Legal issues & Institutional Review Board approval
- External Subject recruitment and management
- Cost
- Time
- future studies to include e.g., saliva analysis, cig. butt analysis, smoking time



Summary of results

- Smoking topography measured on 75 subjects smoking Marlboro Lights, Accord® Series JLI and Series K.
- Results for ML and JLI resembled those from extensive clinical study.
- There are slight but statistically significant increases in volume and flow rate for Accord® Series K.
- There was an overall preference and liking for Accord® Series K, which was perceived as being more similar to subjects' usual brand.

Take-aways

- It is possible to conduct a topography study using PI approved products in 5 weeks or less, if all of the infrastructure is in place (legal review, contracts, document templates, facilities).
- Cost

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 for 75 subjects.
- Comparison of 3 products/prototypes is feasible.

Knowledge gained:

- Smoking topography and sensory data on a prototype (Series K) relative to 2 products.

Benefit:

- We may be informed of potential problems during product development and prior to extensive clinical studies.
- Guidance for development of new products that minimize exposure to potentially harmful substances.

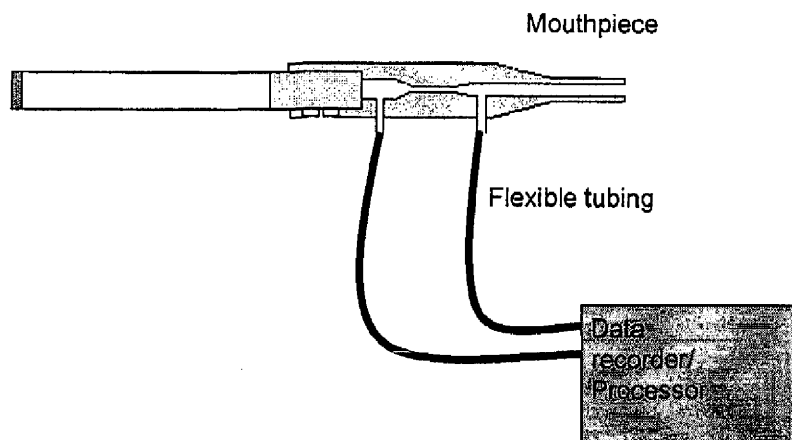


Next steps

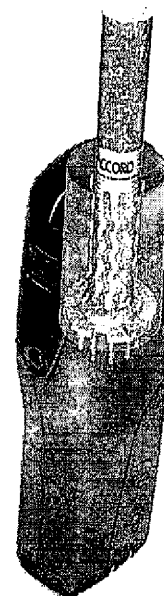
- Create and staff Behavioral Research Facility (COC can be used as an interim location).
- Establish infrastructure (including contractor) for recruiting and managing external subjects.
- Expand exposure marker capability:
 - Improve topography measurement device
 - Develop additional measures
 - saliva analysis
 - butt nicotine analysis
 - butt color
 - smoking time

Materials

- The CReSS[®] Micro Device
"Plowshare (PS)"

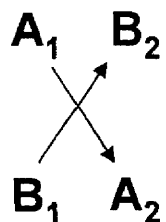


- The ACCORD[®] JLI Smoking System



Crossover Design

Group

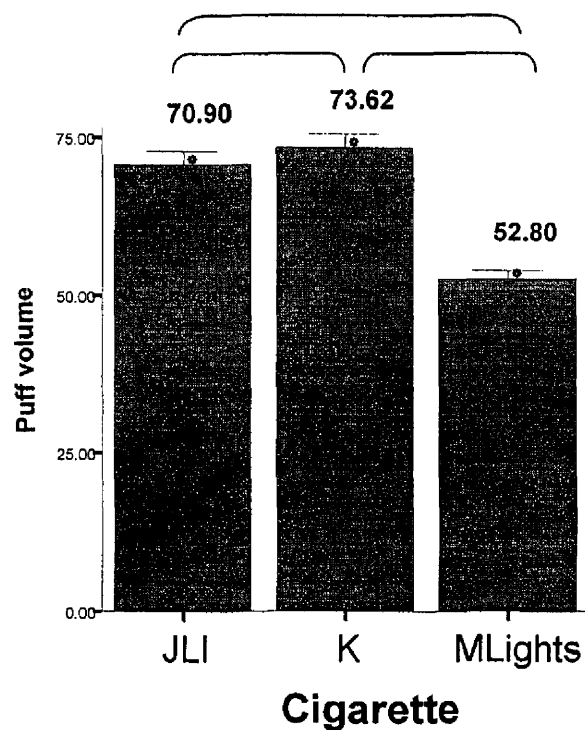


ML-PS	JLI	JLI-PS	6 x JLI-PS	ML-PS	JLI Sensory
ML-PS	K	K-PS	6 x K-PS	ML-PS	K Sensory

Training

PS = with Plowshare device attached

Results: Puff volume



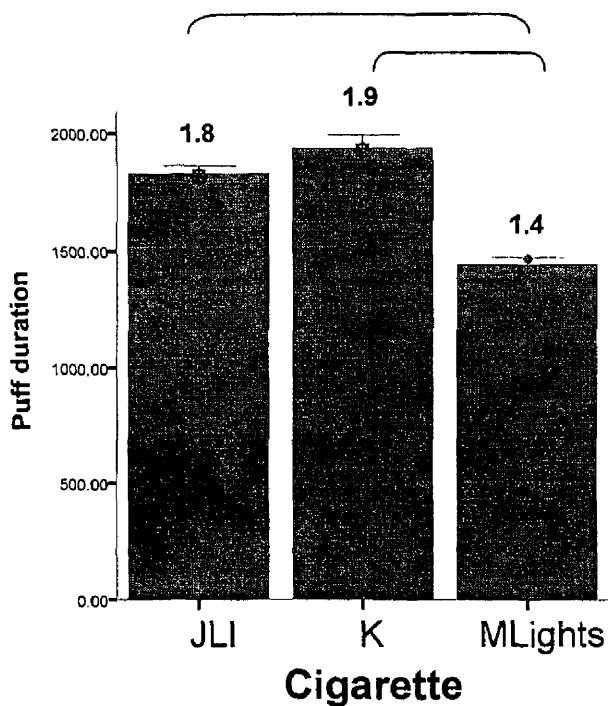
Medians (mL)

JLI	JLI	Marlboro Lights	Marlboro Lights
71	83 <i>Controlled</i> 72 <i>Uncontrolled</i>	54	47

Sensory
Research

Clinical
Research

Results: Puff duration



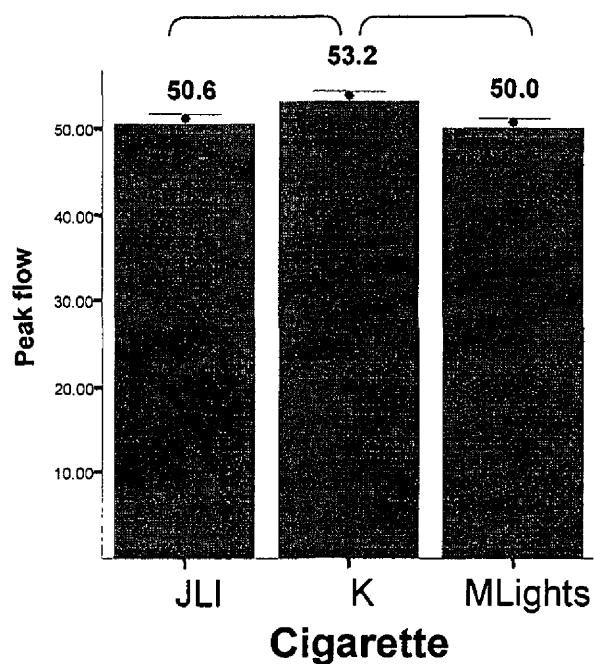
Medians (sec)

JLI	JLI	Marlboro Lights	Marlboro Lights
1.8	2.7 <i>Controlled</i> 2.2 <i>Uncontrolled</i>	1.5	1.3

**Sensory
Research**

**Clinical
Research**

Results: Peak flow rate



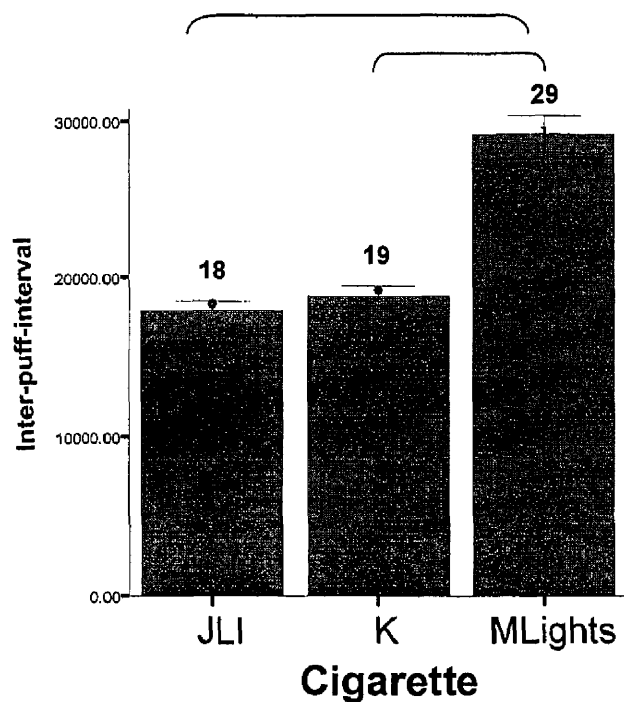
Medians (mL)

JLI	JLI	Marlboro Lights	Marlboro Lights
49	45 <i>Controlled</i> 46 <i>Uncontrolled</i>	50	54

Sensory
Research

Clinical
Research

Results: Inter-puff-interval



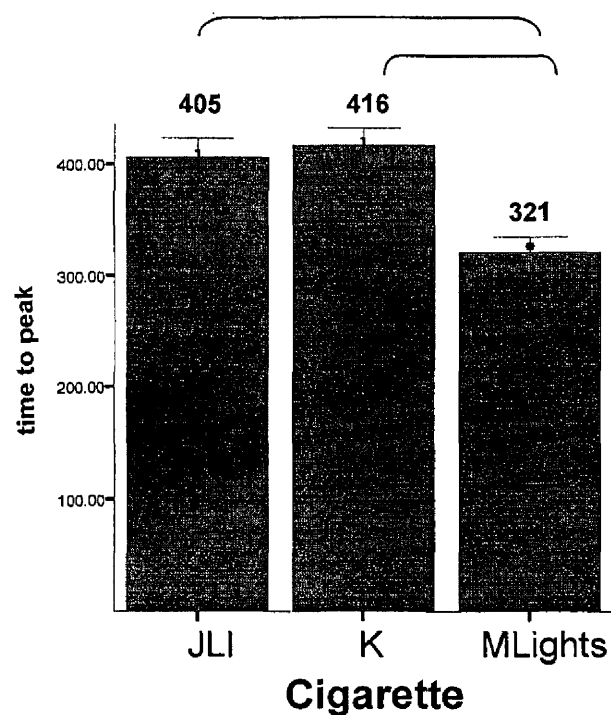
Medians (sec)

JLI	JLI	Marlboro Lights	Marlboro Lights
17	37 <i>Controlled</i> 25 <i>Uncontrolled</i>	27	21

**Sensory
Research**

**Clinical
Research**

Results: Time to peak flow

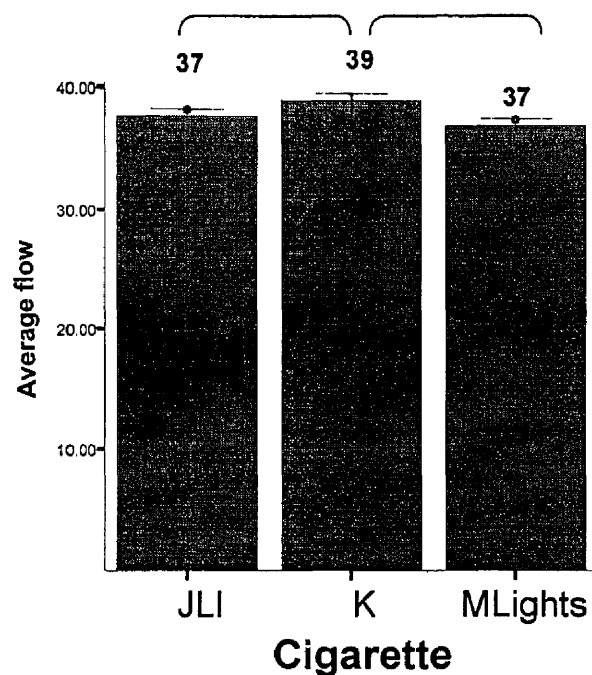


Medians (msec)

JLI	Marlboro Lights
372	296

**Sensory
Research**

Results: Average flow rate

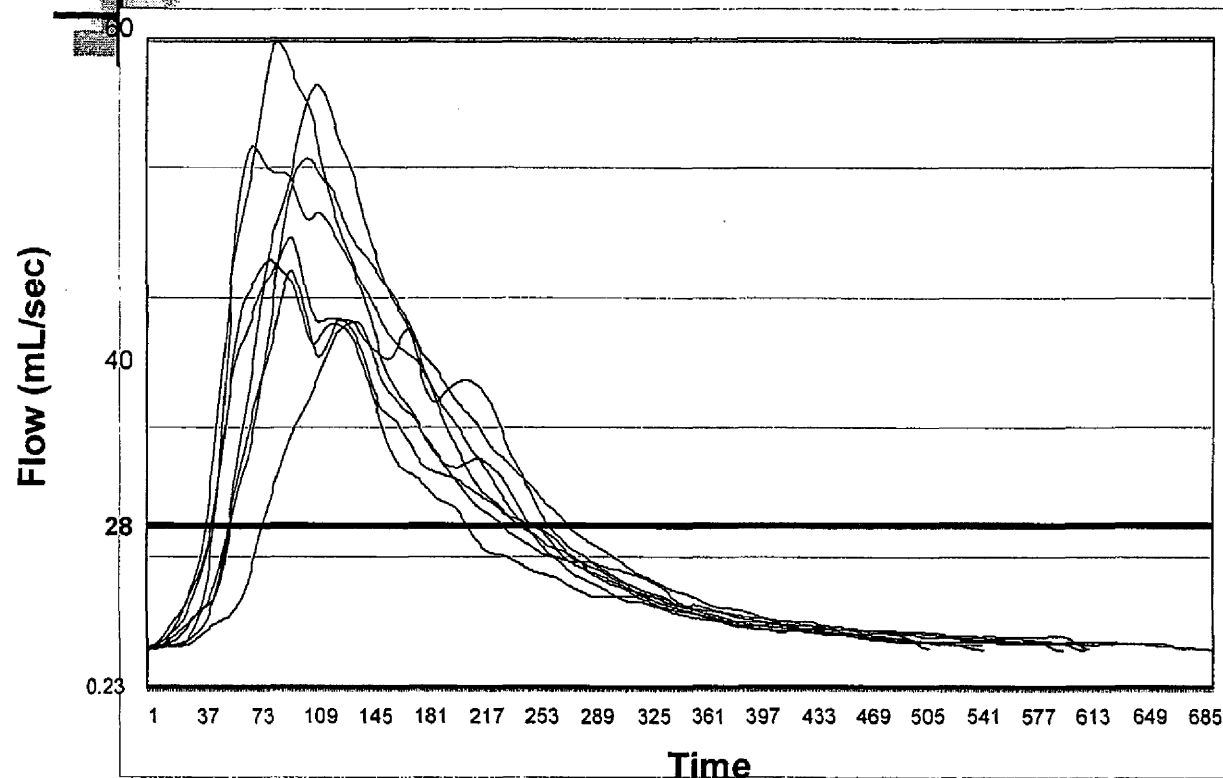


Medians (mL)

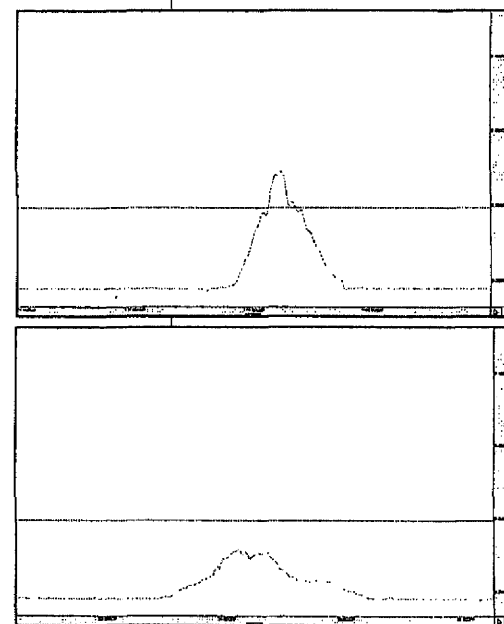
JLI	Marlboro Lights
37	36

**Sensory
Research**

Puffs from a single cigarette



Extreme examples



Puff Volume (mL)	Calculated Puff Vol. (mL)	Puff duration (sec)	Calculated Puff Dur. (sec)	Peak Flow (mL/sec)	Calculated Peak Flow (mL/sec)
57	40	3	1	50	53

Results Sensory ratings

Trade Secret Information Redacted

— - JUL

— K

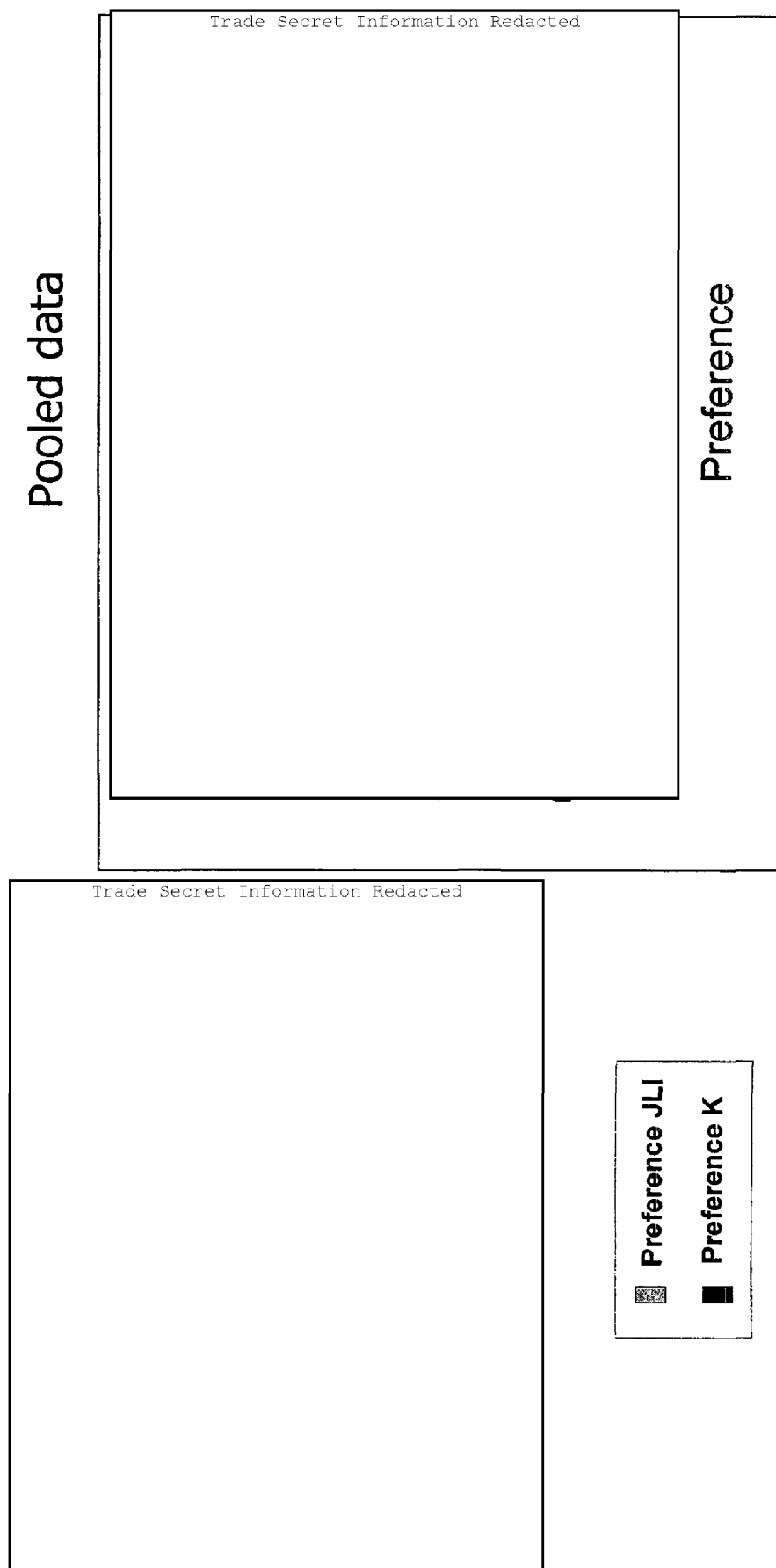
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Results Sensory preference ratings



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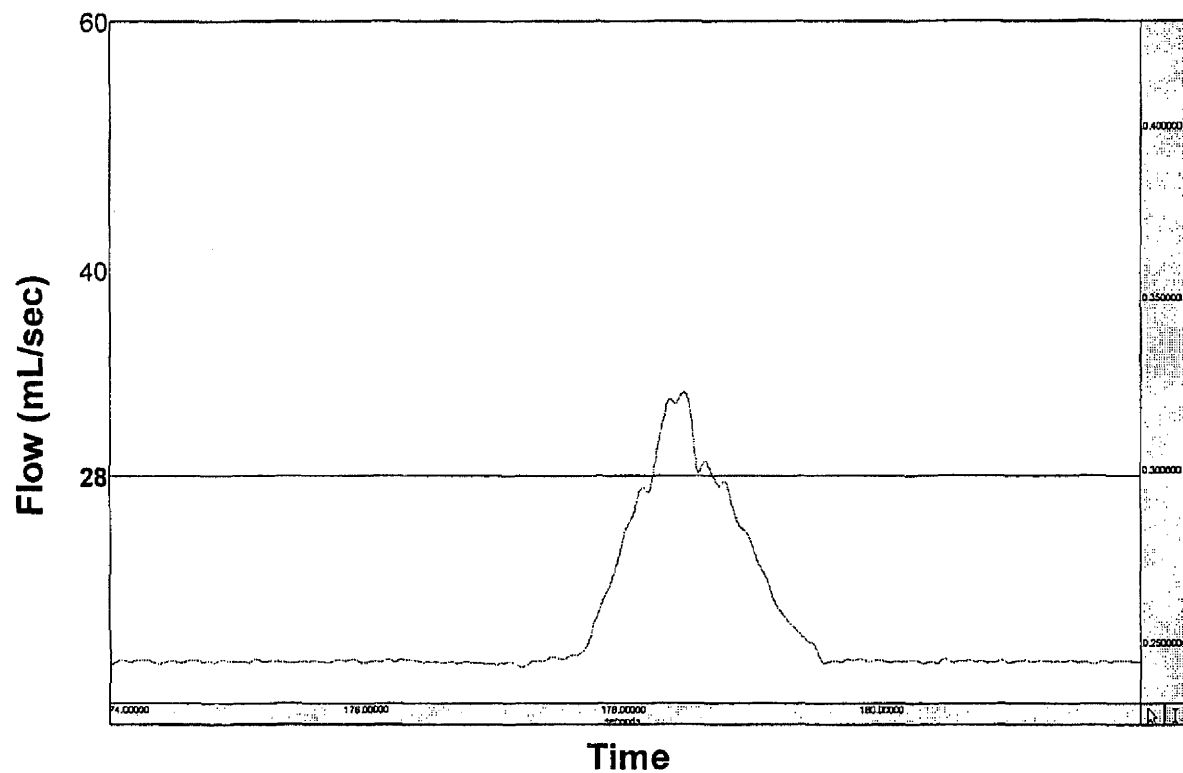
Neal Nunnally

John Hearn

Bill Griffin

Legal, Finance and Purchasing

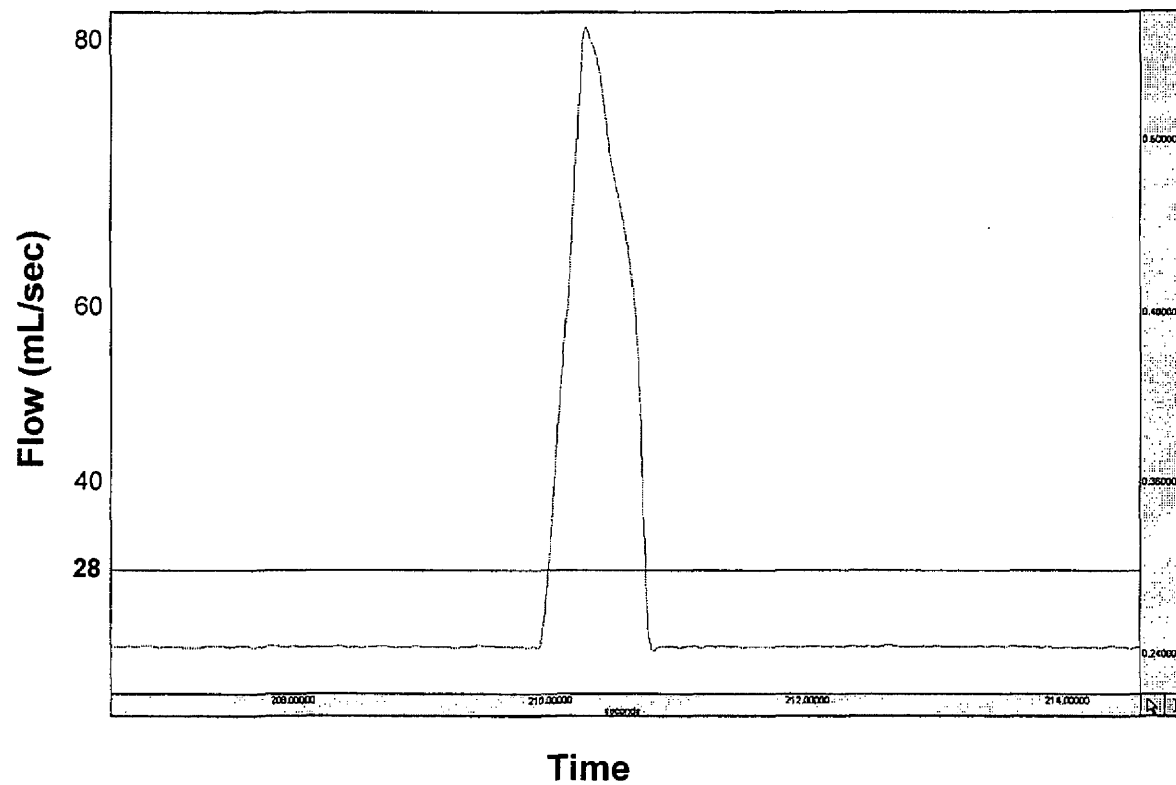
PD&E and AMA



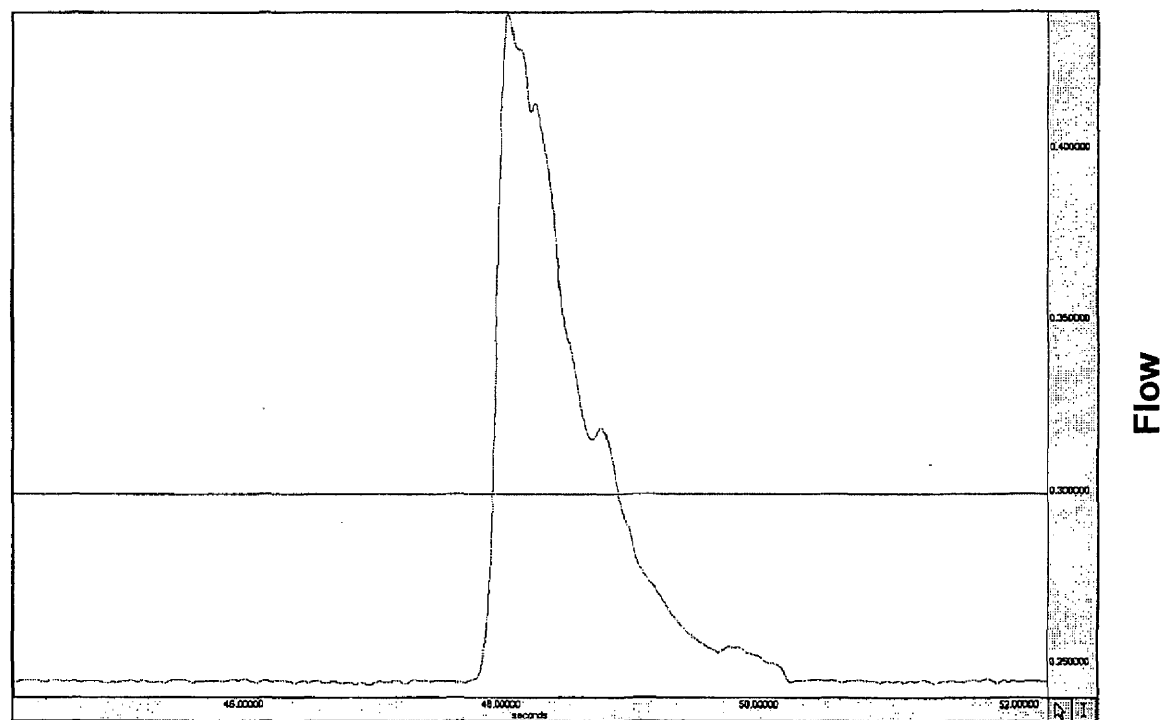
Puff Volume (mL)	Calculated Puff Vol. (mL)	Puff duration (sec)	Calculated Puff Dur. (sec)	Peak Flow (mL/sec)	Calculated Peak Flow (mL/sec)
45	27	1.9	0.7	39	43

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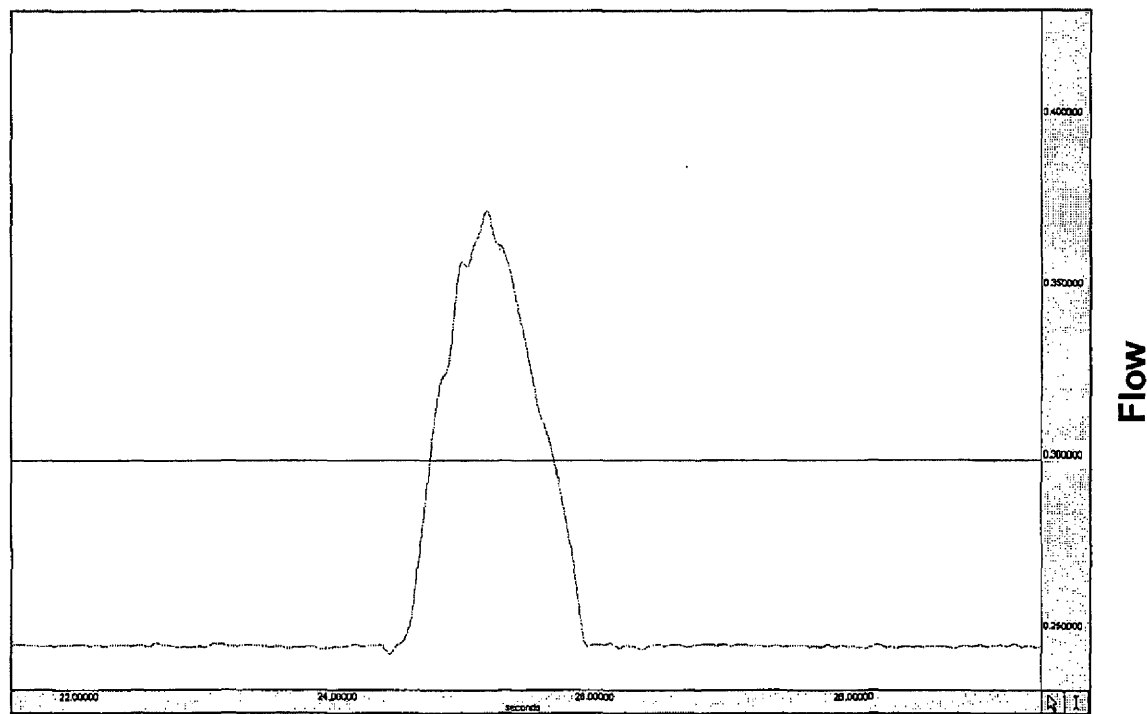
Vol. (mL)	Puff Vol. (mL)	delta T (sec)	Puff Dur. (sec)	Peak Flow (mL/sec)	Peak Flow (mL/sec)
73	48	.9	.8	81	81



Puff Volume (mL)	Calculated Puff Vol. (mL)	Time Puff duration (sec)	Calculated Puff Dur. (sec)	Peak Flow (mL/sec)	Calculated Peak Flow (mL/sec)
59	43	2.5	1.0	53	56

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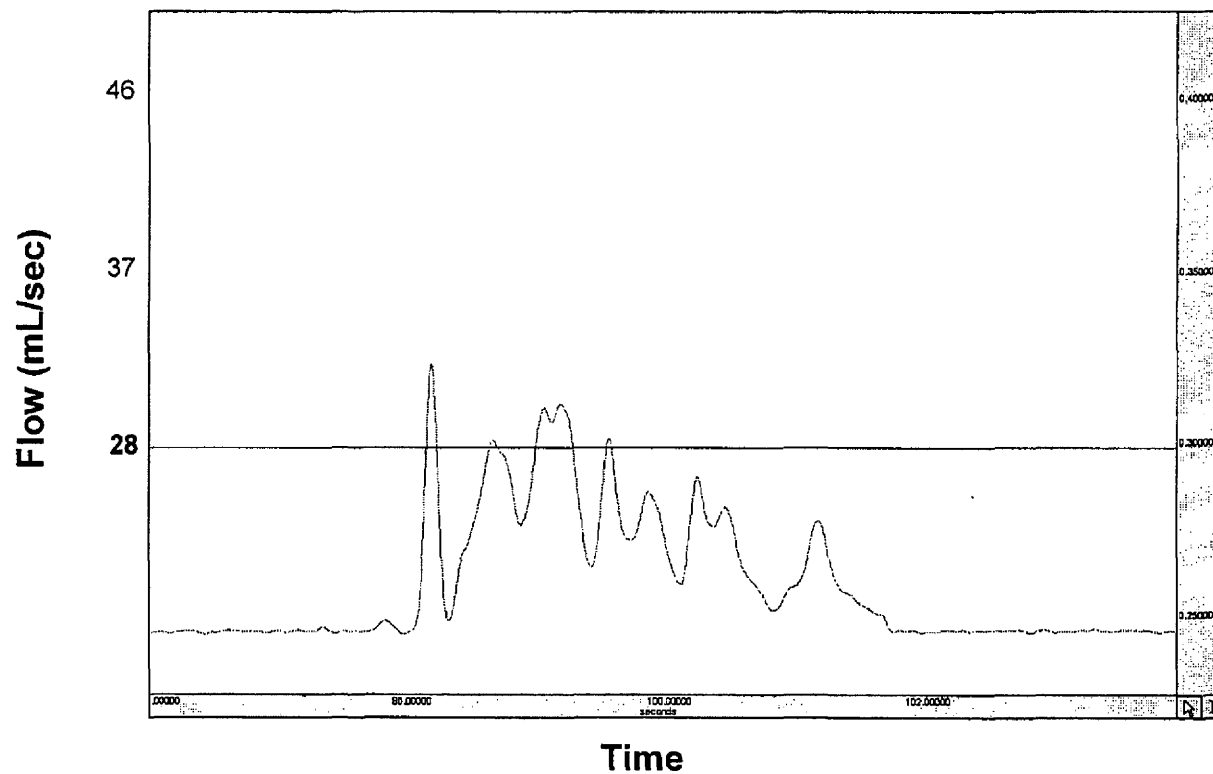
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Puff Volume (mL)	Calculated Puff Vol. (mL)	Time Puff duration (sec)	Calculated Puff Dur. (sec)	Peak Flow (mL/sec)	Calculated Peak Flow (mL/sec)
51	39	1.6	1.0	42	47

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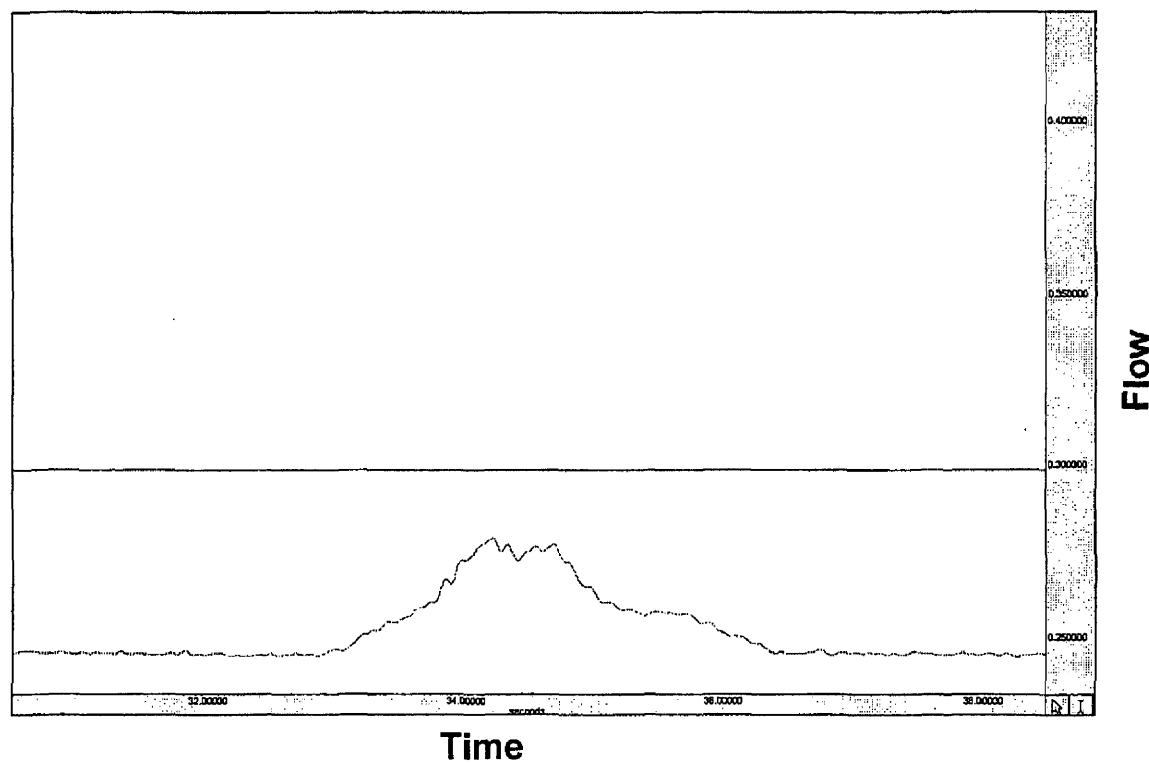
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Puff Volume (mL)	Calculated Puff Vol. (mL)	Puff duration (sec)	Calculated Puff Dur. (sec)	Peak Flow (mL/sec)	Calculated Peak Flow (mL/sec)
52	20	3.8	0.6	32	38

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Flow

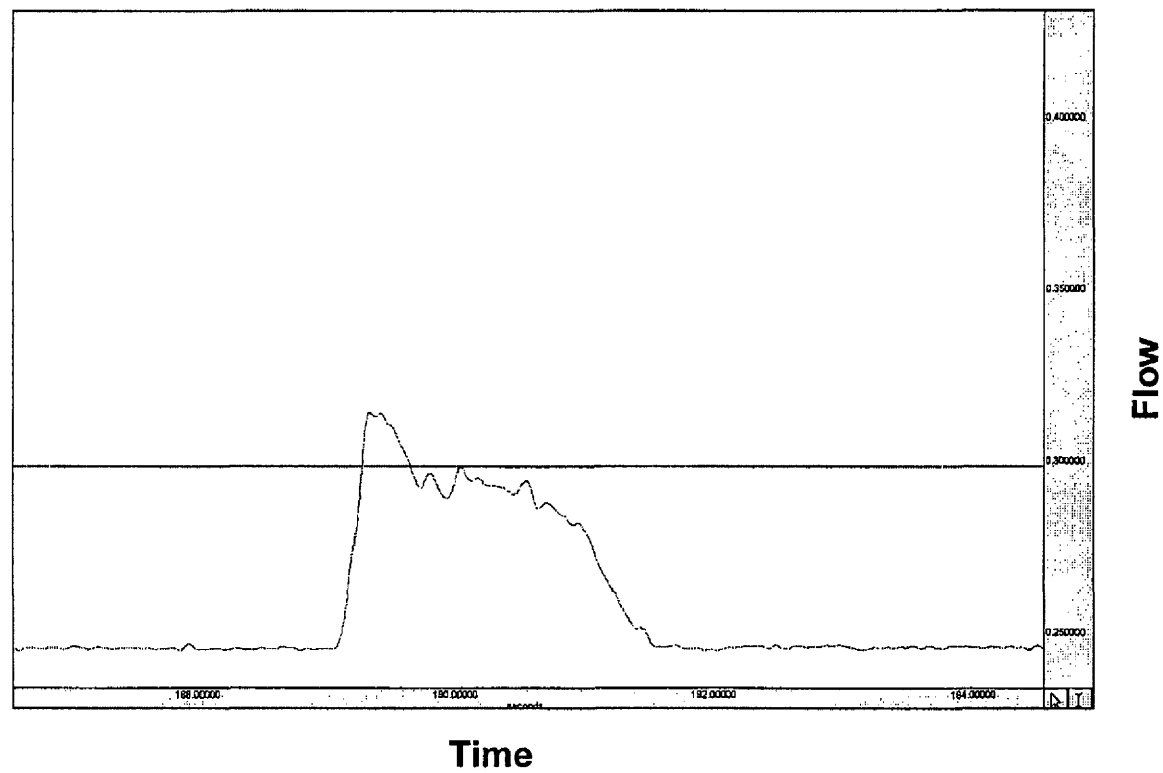
Time

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Flow

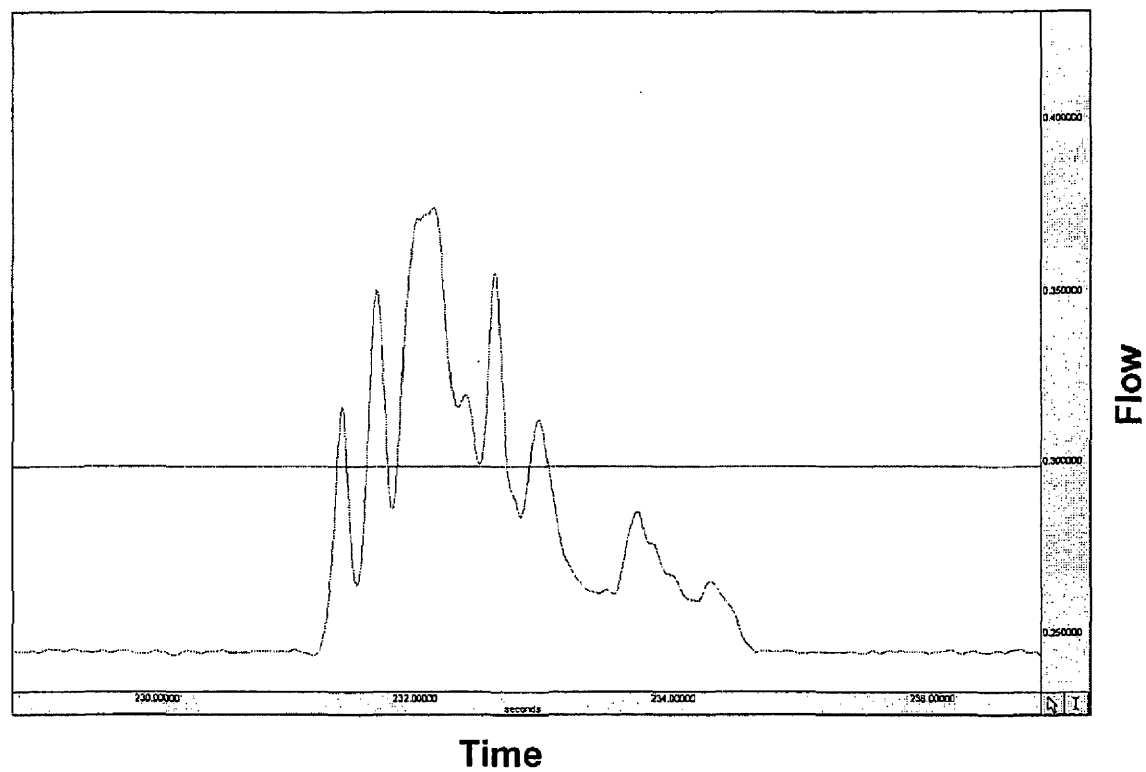
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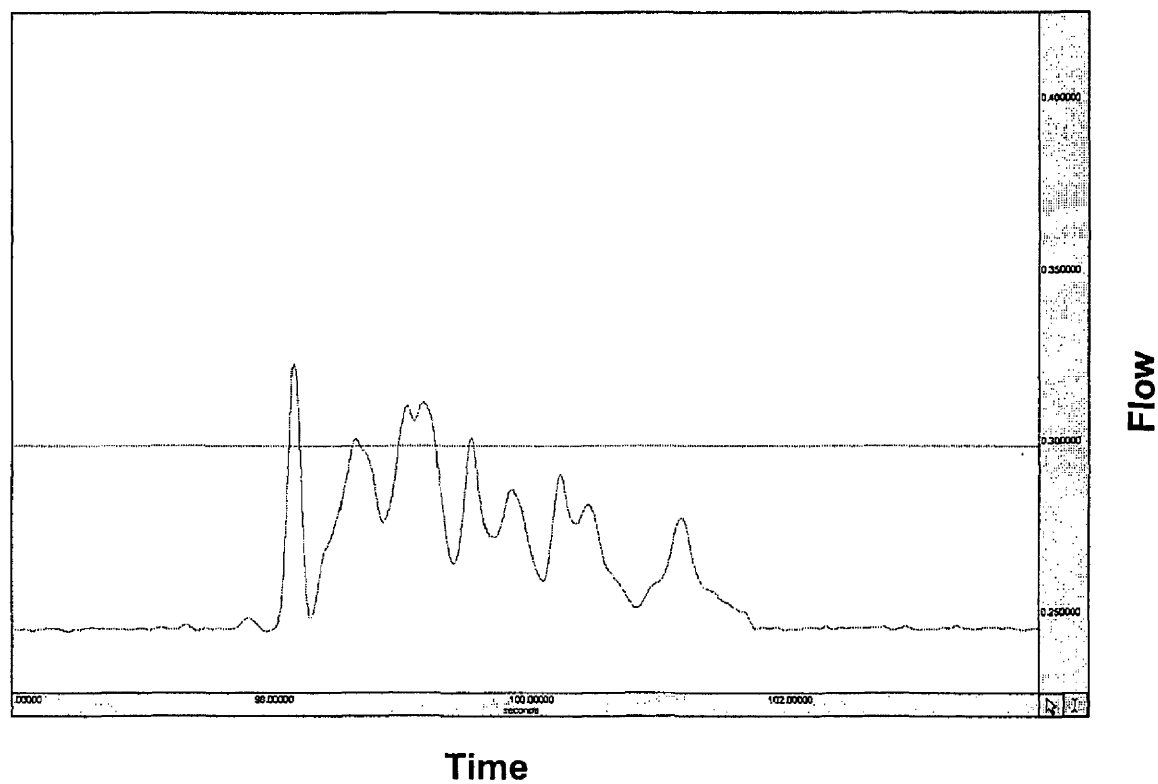
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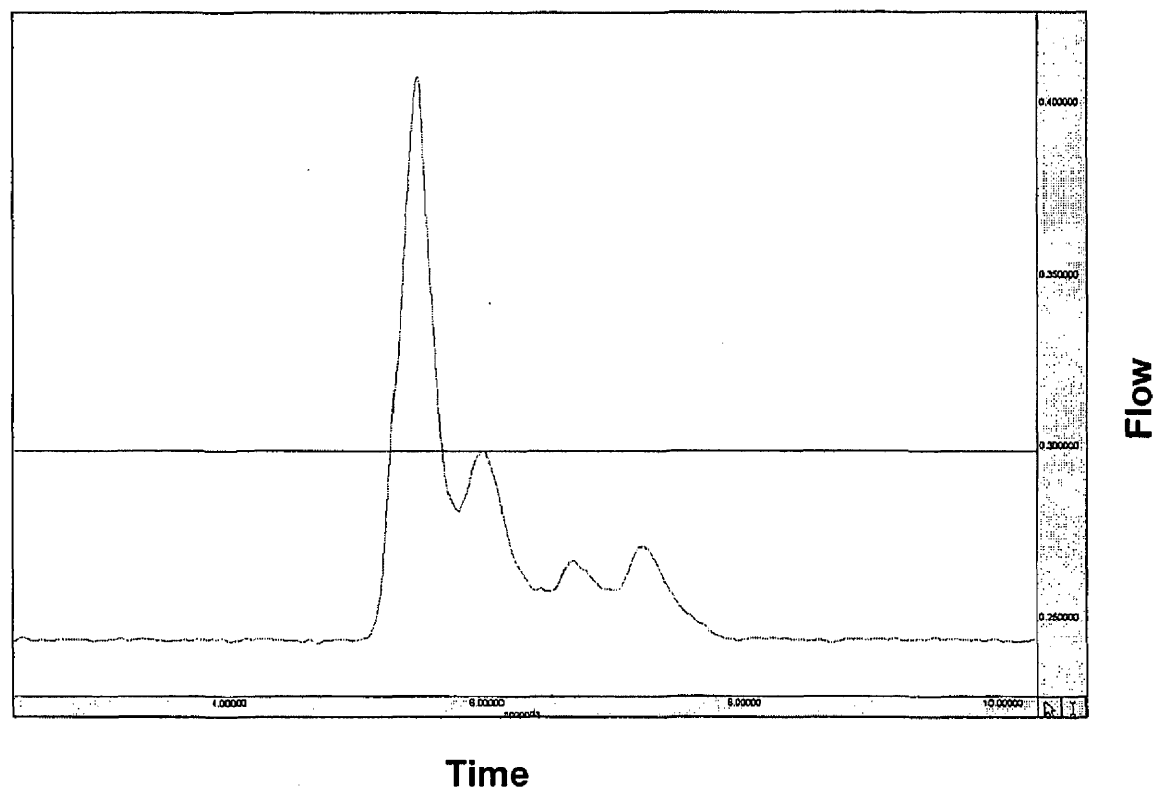


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Flow

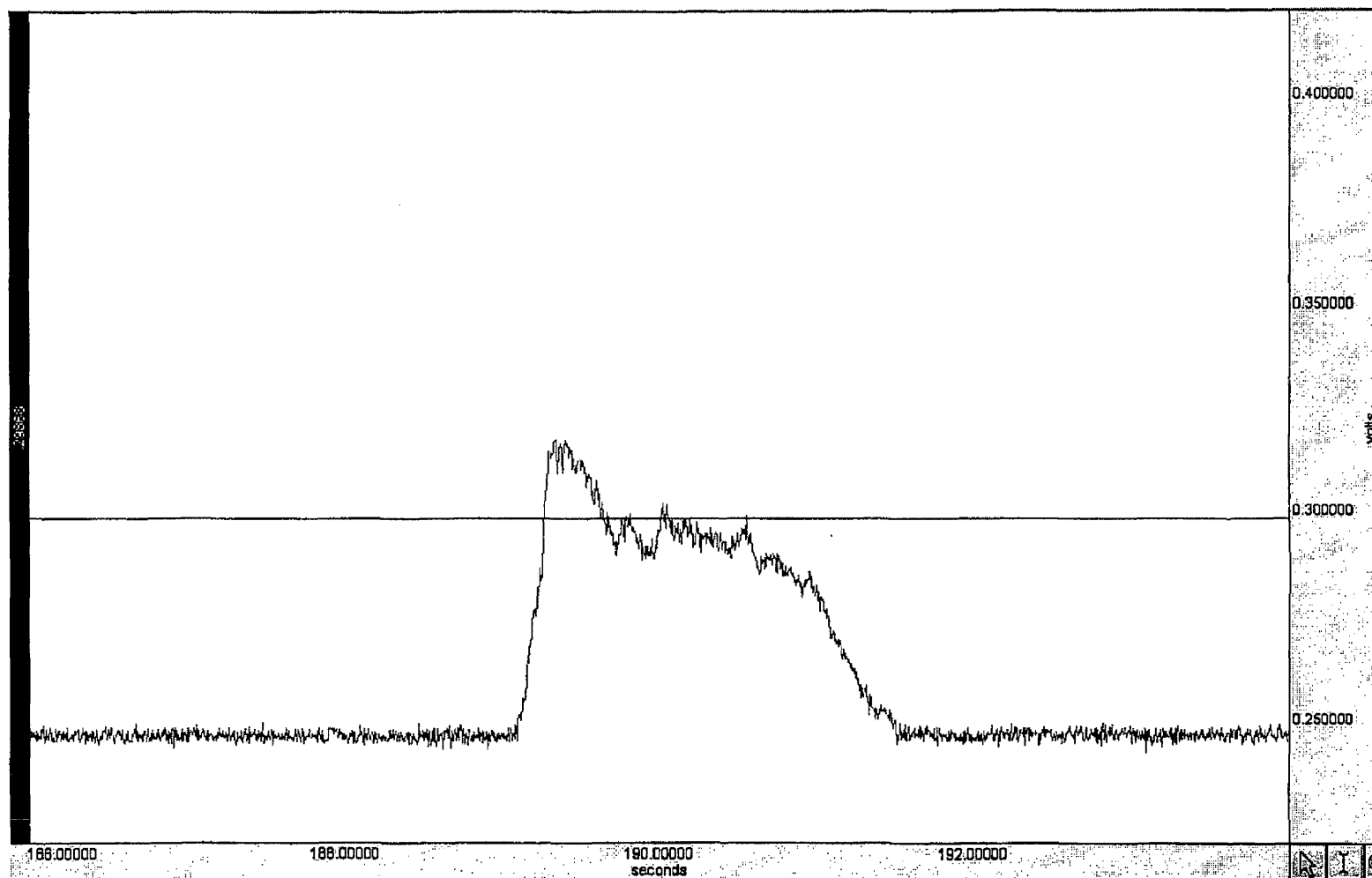
Time

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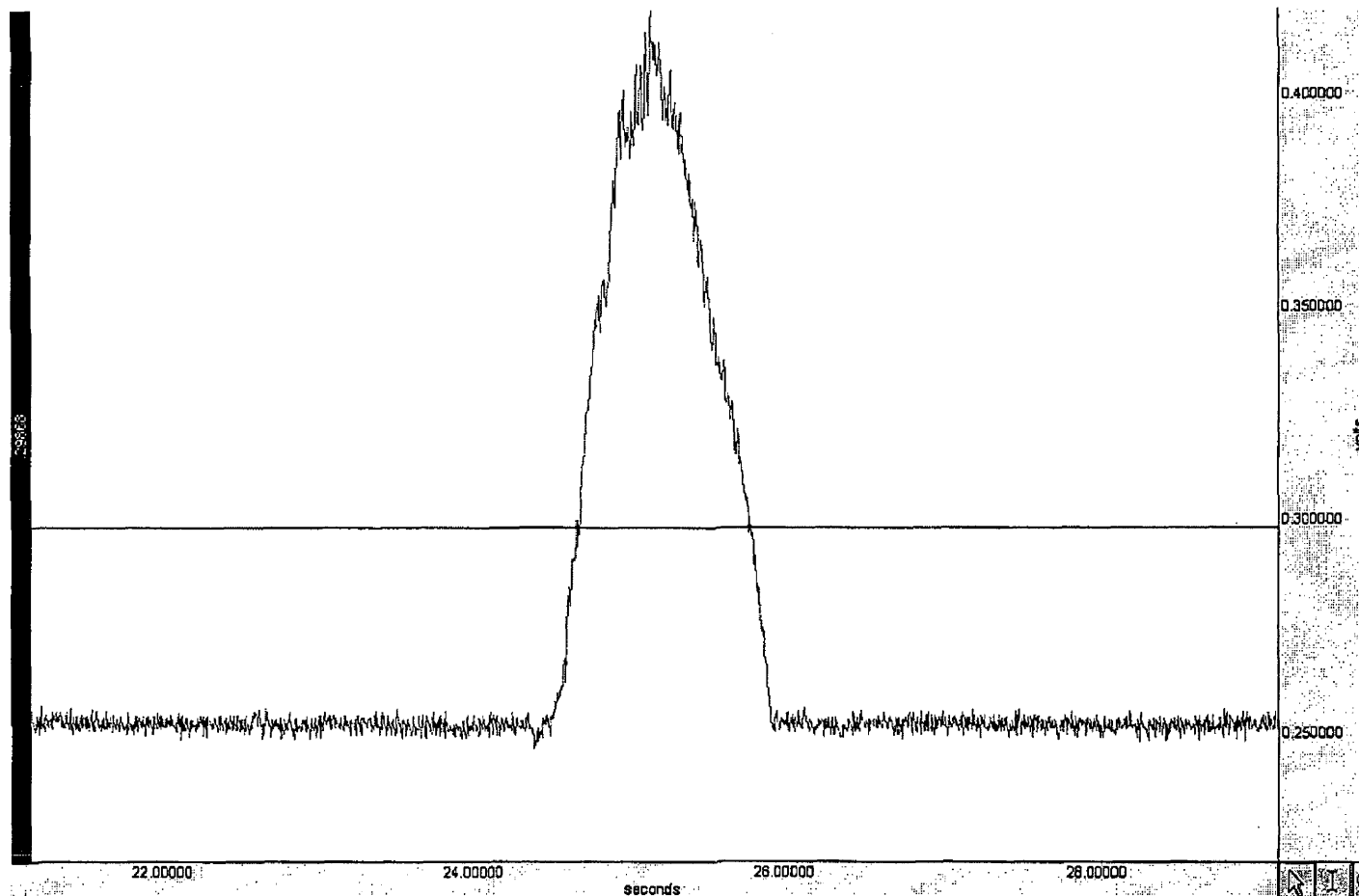


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