

It's time to rethink your CRO.™

A background image showing a close-up of a multi-well microplate with a glass pipette tip positioned over one of the wells. The image is bathed in a green and blue light, creating a scientific and high-tech atmosphere.

## A Systems Integration Approach For Fully Electronic Regulated Bioanalysis

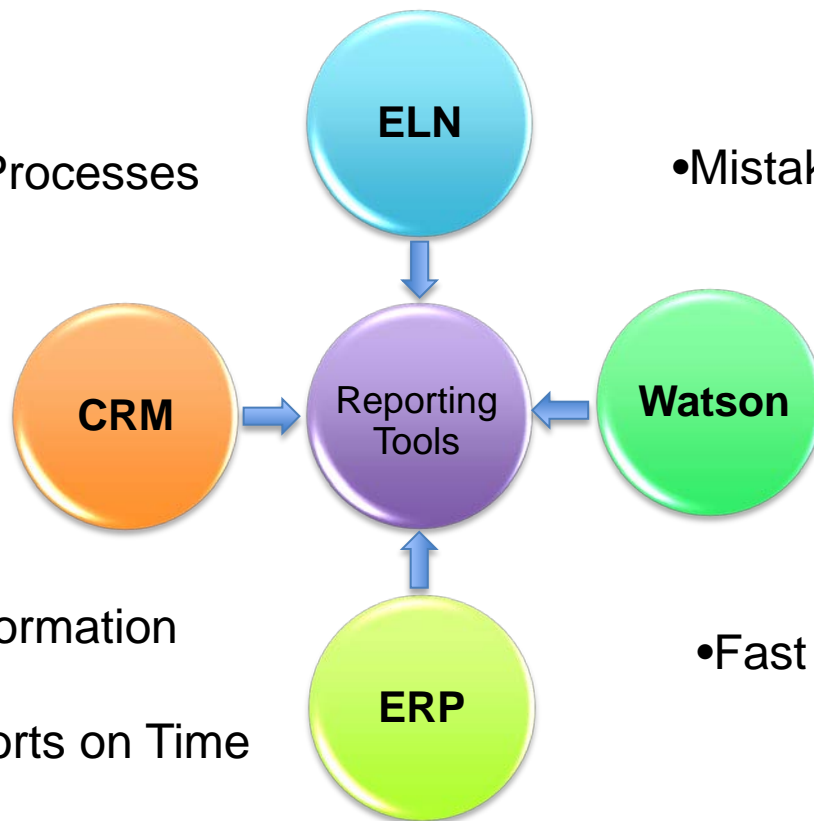
Brian D. Beato, PhD  
AIT Bioscience, LLC



## Requirements:

- Efficient Processes

- Mistake-Free Data



- Accessible Information

- Accurate Reports on Time

- Fast Project Turnaround

## Integrating LC-MS/MS Instrumentation and LIMS

- Tracks sample receipt and analyses
- ISR tracking and reporting within routine analytical runs
- TSQ Module™ provides seamless control of Waters UPLC® and Thermo TSQ Vantage™ MS/MS
- Compiles run data, MS/MS conditions, instrument control files all in one bundle for review and archive.



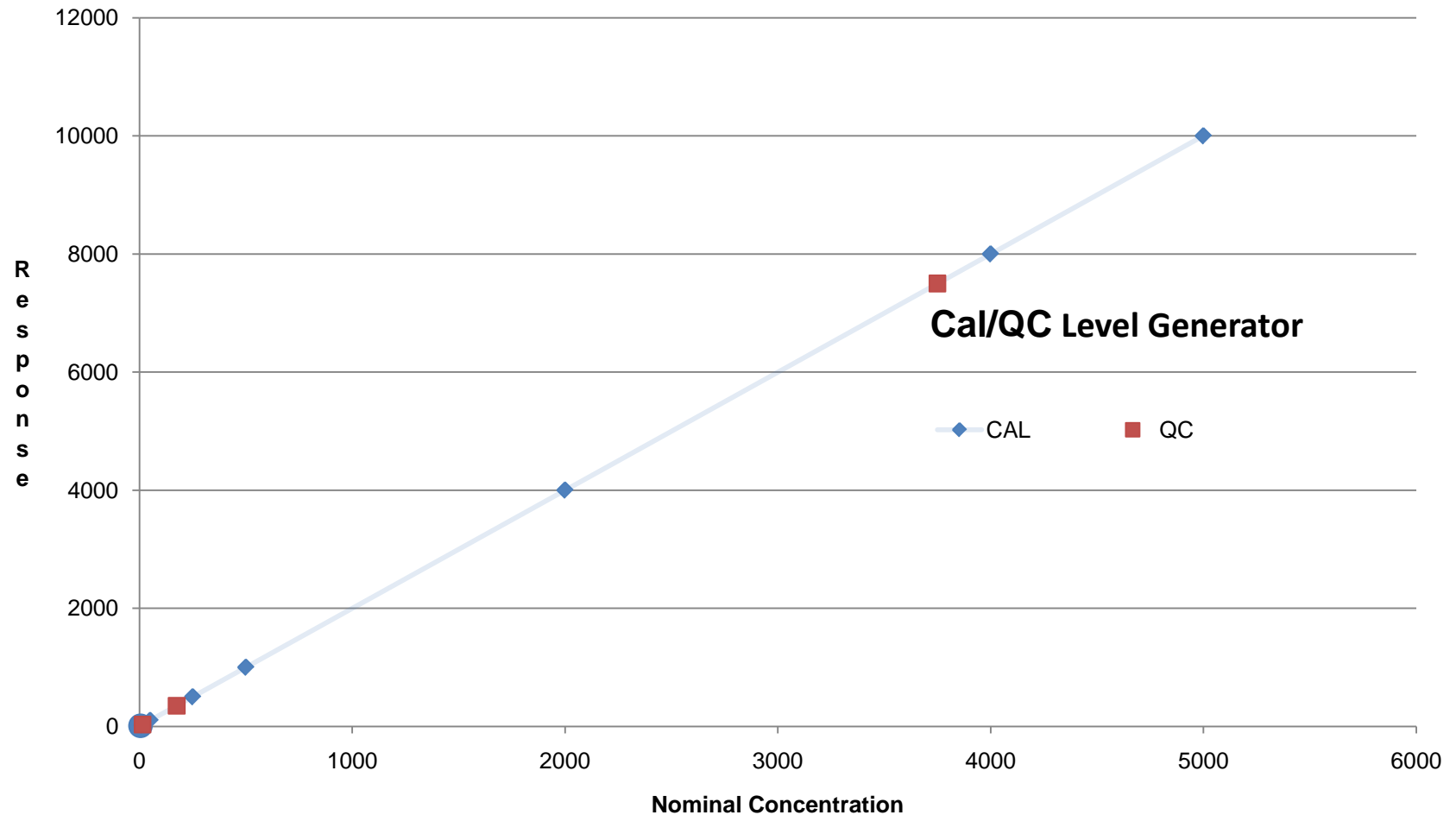


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## Watson 7.5 to Interface with Hamilton Star

- Barcodes on samples read by liquid handler
- Hamilton can aliquot, spike Calibrators, prepare QC pools, and even extract

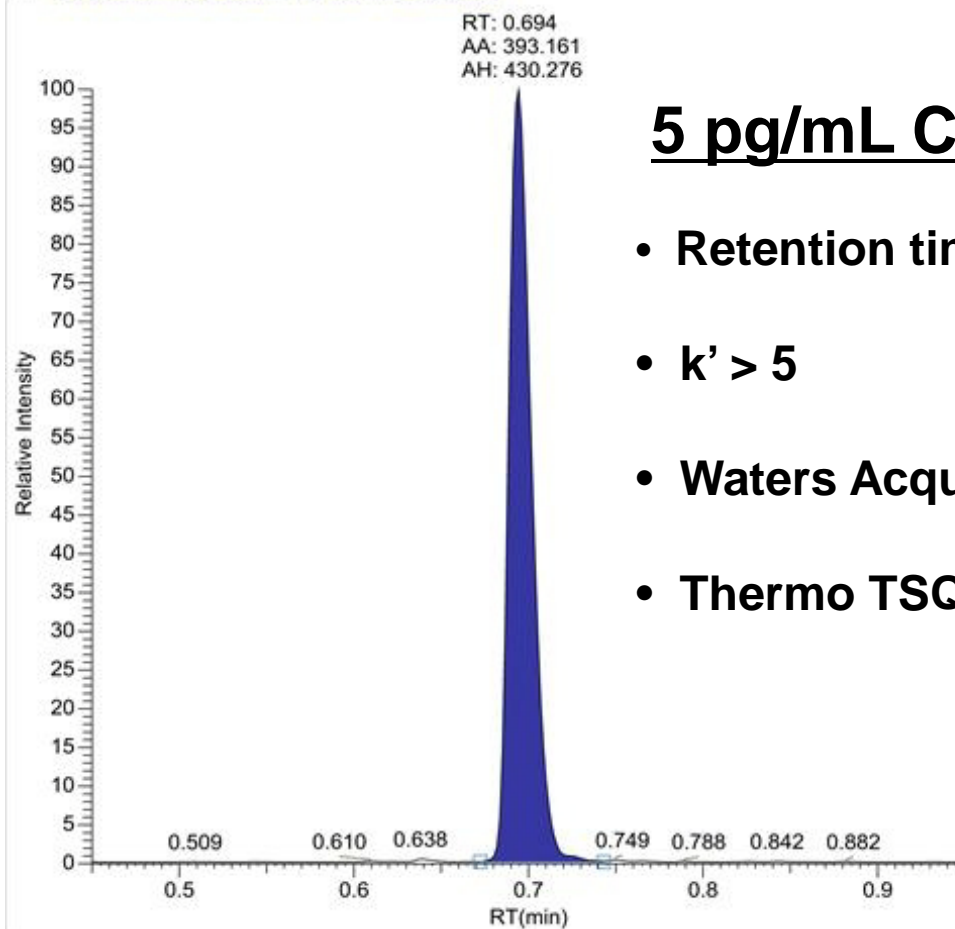
- Standardized methods require fewer analyst qualifications
- Simplified, consistent programming





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1234-0007 CS 5.00 1 Fentanyl  
m/z: 188.226 RT: 0.45 - 0.95 NL: 4.31E2  
F: + c ESI SRM ms2 337.177 [ 188.176-188.276]



## 5 pg/mL Calibration Std.

- Retention time = 42 seconds
- $k' > 5$
- Waters Acquity UPLC®
- Thermo TSQ Vantage™ MS/MS

# Fentanyl in Plasma, 5 – 5000 pg/mL

## Calibration Standards - Robotic Preparation

Summary Statistics	5.00 (pg/mL)	10.0 (pg/mL)	50.0 (pg/mL)	250 (pg/mL)	500 (pg/mL)	2000 (pg/mL)	4000 (pg/mL)	5000 (pg/mL)
First curve	4.70	10.5	50.2	248	483	1950	4020	5010
Last curve	5.09	10.3	51.4	247	502	1970	4020	5050
Intra-run Mean	4.90	10.4	50.8	248	493	1960	4020	5030
Intra-run % Bias	-2.0	4.0	1.6	-0.8	-1.4	-2.0	0.5	0.6
n	2	2	2	2	2	2	2	2

## Quality Control Samples – Manual Preparation

Summary Statistics	LLOQ (5.0 pg/mL)	Low (15.0 pg/mL)	Mid (375 pg/mL)	High (3750 pg/mL)
Intra-run Mean	4.63	14.0	357	3600
Intra-run SD	0.167	0.339	5.27	52.5
Intra-run %CV	3.6	2.4	1.5	1.5
Intra-run %Bias	-7.4	-6.7	-4.8	-4.0
n	18	18	18	18

- IDBS E-Workbook Suite with custom workflows
- Interfaces with Watson to perform automated, validated calculations and other functions
- Used in every aspect of R&D and regulated bioanalysis
- GLP, Part 11 compliant
- Prevents errors in real time

Title: Structures &amp; MW

Version Type: DRAFT

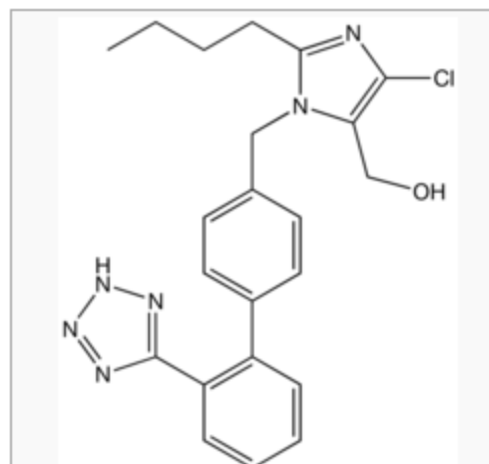
Version Number: 2



(v0) Structure &amp; Info: Losartan.pdf



### Losartan



#### Systematic (IUPAC) name

(2-butyl-4-chloro-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-imidazol-5-yl)methanol

#### Identifiers

CAS number	114798-26-4
ATC code	C09CA01
PubChem	3961
IUPHAR ligand ID	590
DrugBank	APRD00052

#### Chemical data

Formula	$C_{27}H_{23}ClN_8O$
Mol. mass	422.91

(v1) Structure &amp; Info: Losartan Carboxylic Acid.jpg



Title: Related Literature

Version Type: DRAFT

Version Number: 4

 **(v3) Full Article:** J. Pharm. Biomed. Anal. 49(2009) 862\_867   File: J. Pharm. Biomed. Anal. 49(2009) 862\_867 **(v1) Full Article:** Bucolome (inhibitor) for Losartan Drug Met Pharm 2008.pdf   **(v1) Full Article:** J Pharm Sci Losartan in Rat Plasma LCMSMS 2009.pdf   **(v1) Poster:** CEDRA Irbesartan Poster.pdf   **(v1) Abstract:** J Chrom B Abstract Losartan 1999.pdf   **(v1) Abstract:** J Sep Sci Abstract 2009 LOS & LCA.pdf   **(v1) Abstract:** J Pharm Biome Anal Abstract 2009 LOS & LCA.pdf   **(v1) Abstract:** MDS Abstract LOS & LCA.pdf   **(v1) Abstract:** Anapharm Abstract LOS & LCA.pdf   **(v1) Abstract:** LOS & LCA Clin R&R. Affairs Abstract 2008.pdf  

Title: MS-MS Tuning & UPLC Gradient

Version Type: DRAFT

Version Number: 2



**(v0) FINAL:** TSQ #1 BAM.0013 MS-MS Parameters.pdf

Scan Editor | Syringe Pump | Divert Valve | Method Summary

Calibration Correction Method

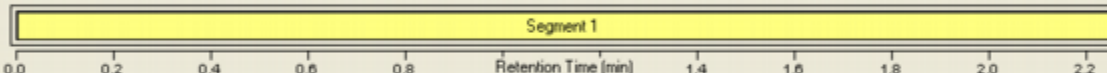
Run Settings

MS Acquire Time (min): 2.25

Segments: 1

Current Segment: 1

To display a chromatogram here, use Quantum/Open Raw File...



Segment 1 Settings

Segment Time (min): 2.25

Tune Method: C:\calbur\methods\BAM.0013\TSQ1\_BAM0013\_001.TSQTune

Scan Events: 1

Chrom Filter Peak Width (s): 3.0

Collision Gas Pressure (mTorr): 1.5

Current Scan Event: 1

Scan Event 1

Scan Event 1

Scan Type: SRM

Polarity:

Positive  Negative

Data Type:

Centroid  Profile

Declustering Voltage:

QCV (V): 10

Same value for all SRMs

Scan Width (m/z): 0.010

Scan Time (s): 0.050

Coll. Energy (V): 10

Peak Width

Q1 (FWHM): 0.70

Q3 (FWHM): 0.70

Use Tuned S-Lens Value

	Parent Mass	Product Mass	Collision E	S-Lens
1	423.145	207.086	21	86
2	432.145	207.086	21	89
3	437.137	235.049	17	89
4	446.137	235.049	17	89
*	446.137	235.049	17	89

Micro Scans:

1

Copy ScanEvent

Paste ScanEvent

Help

Tune

**(v1) FINAL:** TSQ #1 BAM.0013 UPLC Gradient.jpg



**(v1) FINAL:** TSQ #1 BAM.0013 UPLC Parameters.jpg



**(v1) Chrom Peaks:** Losartan LLOQ system check.jpg





# Tablet PC

-Wireless client for Watson, ELN, and other applications, just like a laptop.

-Barcode  
Scanner

-Camera

-RFID Reader

-Stand-alone  
or docking

pick list.

b) Enter an "Expiration Date"

**4. Check the Status table "Is Form complete?" & "Passed All Field Checks?" fields to see if the mandatory fields are completed and field validation checks have been passed**

a) Red indicates missing data or validation errors. Green indicates all fields are completed.

b) Enter an user entered issues in the comment field

c) Review any issues on the Issue Tracking table and enter comments as appropriate.

d) A valid Stock Solution Prep ID will only be generated if all Mandatory Fields have been completed, all field checks have passed or the user has entered comments to address these issues.

**5. Enter a label value into the Label Generator table.**

**6. Enter the Procedure steps into the Procedure table, as required.**

**7. Rename the Experiment**

a) Copy the Stock Solution prep ID (in the Status Table) by right-clicking over the field and selecting Copy

b) Close the spreadsheet.

c) Open up the Reports Properties menu option

Normal Edit HTML

	Entry	Field Status
Date	5-Oct-2009	
Lot Number		
CoA		
CoA Reference		
Material Name		
Material_Type		
Exhausted Status		
Potency Value		
Specificity Value		
Protein_Content A280 (mg/mL)		
Production Date		
Expiration Date		
Target Mass		
Target Mass Unit	mg	
Select Balance		
Balance Model		
Balance Weight Range High		
Balance Weight Range Low		
Weight Range Units	mg	
Balance Check Reference	Balance Check Hyperlink	
Reagent Prep Generic Name		
Diluent Prep Reference		

Solvents	
Component	Solvent 1
Grade	
Vendor	
Lot Number	

Preparation	
	Entry
Weighed Mass	
Weighed Mass UOM	mg
Preparation Container	
Container Volume (mL)	
Concentration	
Large Molecule Concentration	
Concentration UOM	mg/mL

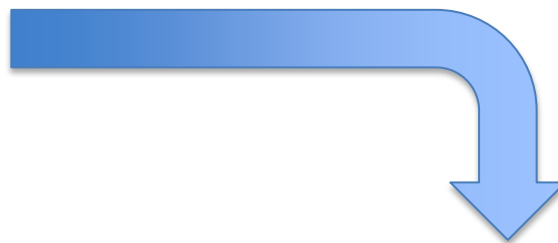
Storage	
	Entry
Storage Conditions	
Environmental Unit	
Environmental Unit Type	
Temperature (°C)	
Site	
Storage Container	
Prepared By	
Date	5-Oct-2009
Preparation Time	
Expiration Date	

Label Generator	
	Label Fields
labelType	Reagent:
labelValue	
reference	
preparationDate	10/5/2009
expirationDate	
storeRoomTemp	
storeRefrigerated	
storeFrozen	
scientist	
templateName	bioanalysis_reagent

Status	
<b>Stock Solution Prep ID</b>	
All Mandatory Fields Complete?	No
Passed All Field Checks?	Yes
User Entered Issue Comment	
Project_ID	JC project
Measurement Entry Witness	

# ELN Workflow for weighing out standards

Wireless upload of data to ELN



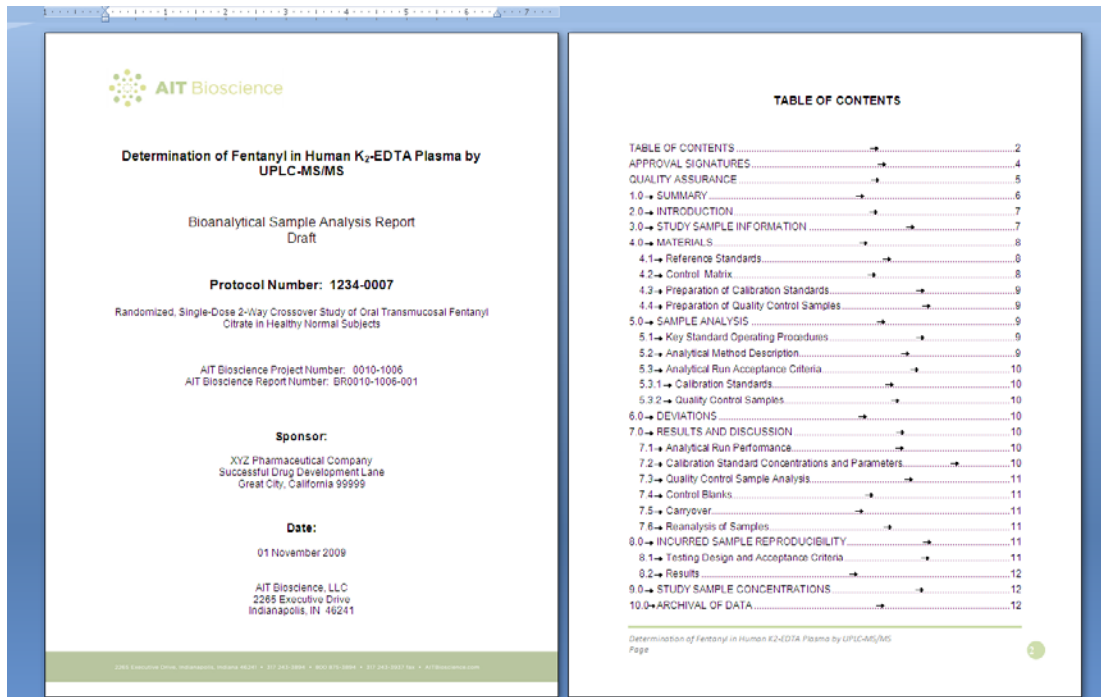
No transcription errors



## Use QC/QA Resources Up Front Instead of After the Fact

- All ELN templates are validated and controlled.
- Errors are prevented by correcting in real time.
- ‘Audit by Exception’ greatly reduces QC review time.
- Less rework & review means faster turnaround.

- Generated by pulling data directly from Watson, CRM, and ELN
- Saves time
- Reduces errors
- Currently evaluating Thermo's 'Designer' and Up to Data's 'iStudyReporter'



The screenshot displays two pages from an automated report. The left page is the title page, and the right page is the table of contents.

**Title Page:**

AIT Bioscience

**Determination of Fentanyl in Human K<sub>2</sub>-EDTA Plasma by UPLC-MS/MS**

Bioanalytical Sample Analysis Report  
Draft

**Protocol Number: 1234-0007**

Randomized, Single-Dose 2-Way Crossover Study of Oral Transmucosal Fentanyl Citrate in Healthy Normal Subjects

AIT Bioscience Project Number: 0010-1006  
AIT Bioscience Report Number: BR0010-1006-001

**Sponsor:**  
XYZ Pharmaceutical Company  
Successful Drug Development Lane  
Great City, California 99999

**Date:**  
01 November 2009

AIT Bioscience, LLC  
2265 Executive Drive  
Indianapolis, IN 46241

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Determination of Fentanyl in Human K<sub>2</sub>-EDTA Plasma by UPLC-MS/MS  
Page 1

- Access to Project Status (E-mail and/or Portal)
  - Samples received
  - Samples analyzed
  - Passing and failing batches
  - Study milestones and metrics
- Status Reports Updated Automatically
  - Pulls data from Watson LIMS and Enterprise Resource Planning (ERP) Databases
  - Maintains blinding



**AIT** Bioscience

**Our Laboratory: Paperless**

**Our Lavatory: Not so much**

It's time to rethink your CRO.™



Questions?

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