



Non-GLP Validation of Multi-Analyte Method for Active Ingredients



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Overview

The goal of this experiment was to validate:

- The CIPAC multi-analyte method in comparison to registered GLP methods
 - The CIPAC multi-analyte column has already been validated for the analysis of Chlorantraniliprole.
- To achieve this, eight of FMC active ingredients were analyzed:

Chlorantraniliprole	Azimsulfuron
Bifenthrin	Chlorsulfuron
Cyantraniliprole	Flutriafol
Indoxacarb	Triflusulfuron

Experimental Design

To Prove Equivalency



Design of experiment to prove equivalency between GLP Enforcement Method and Multi-Analyte Method

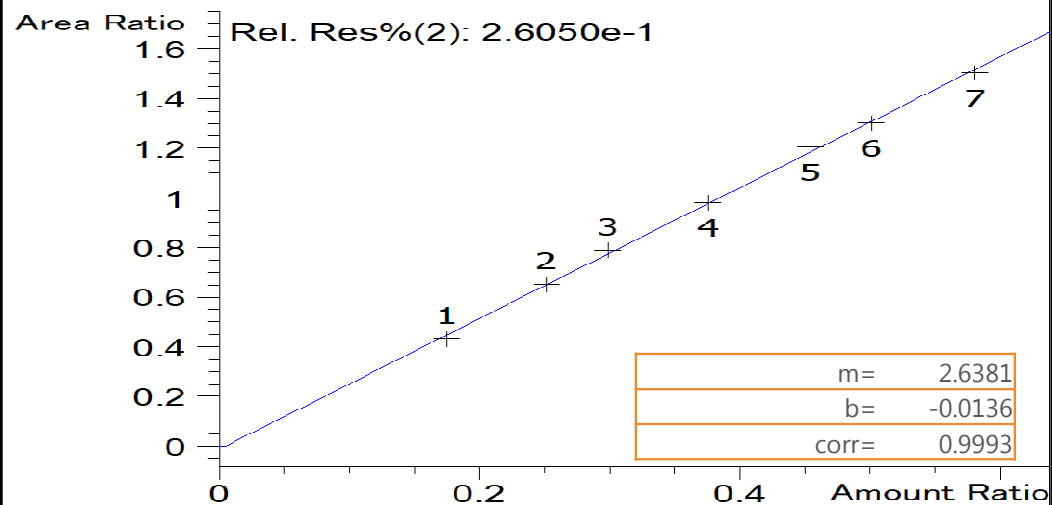
- Linearity
 - 7 point calibration curve desired correlation of 0.99 or greater.
- Accuracy
 - Duplicate samples prepared at 3 separate concentrations.
 - 75%, 100% and 125% of the concentration of the GLP sample solution.
- Precision
 - 8 individual samples for method precision.
 - 1 sample run 8x's to ensure instrument precision.
- Specificity
 - Qualitative analysis for impurity interference for all samples.
 - Concern for any impurity at 3% or greater of the overall sample composition.

Linearity

Data and Examples

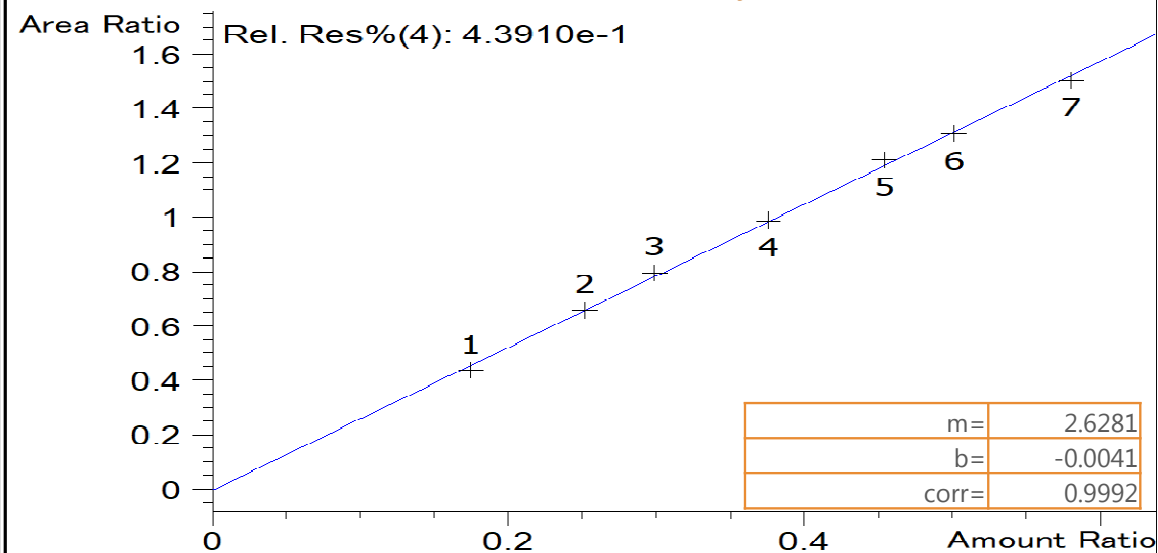


Azimsulfuron GLP Method



No difference in Linearity

Azimsulfuron Multi-Analyte Method



FMC

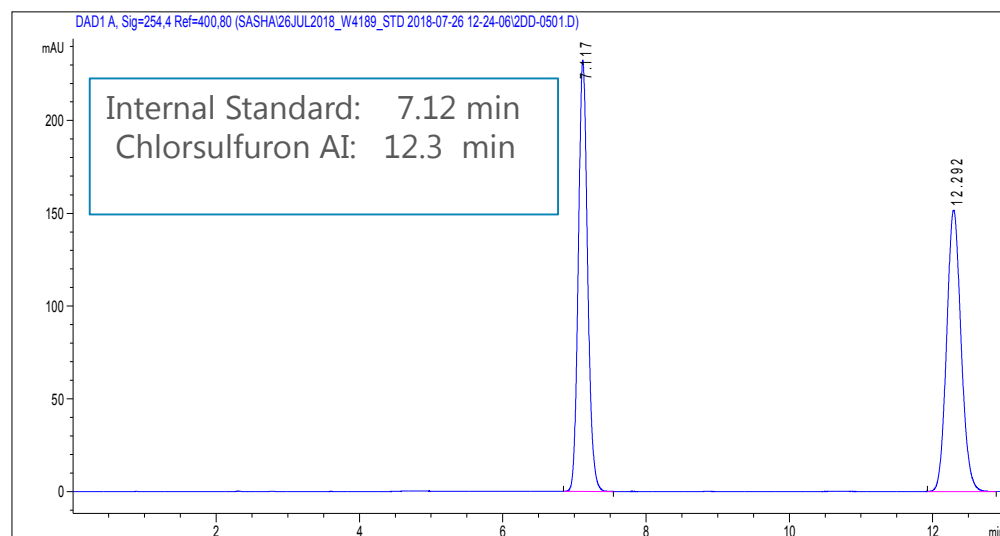
Linearity Summary

Compound	Method Type	Correlation Coefficient	Y Intercept	Slope	Internal Std Retention (min)	AI Retention (min)
Chlorantraniliprole	GLP Enforcement	0.9996	0.016	384.2	3.7	4.2
	Multi-Analyte	0.9996	0.016	384.2	3.7	4.2
Bifenthrin	GLP Enforcement	0.998	-25.66	1478	N/A	14.05
	Multi-Analyte	1.000	-9.98	1550	N/A	12.4
Cyantraniliprole	GLP Enforcement	1.0000	0.055	719.8	4.1	11.0
	Multi-Analyte	0.9999	0.021	719.7	1.56	3.53
Indoxacarb	GLP Enforcement	0.9995	0.010	502.5	10.2	7.2
	Multi-Analyte	0.9997	0.008	419.6	9.75	8.09
Flutriafol	GLP Enforcement	0.9991	-23.65	1095	N/A	8.14
	Multi-Analyte	0.9999	82.87	1089	N/A	3.159
Triflusulfuron	GLP Enforcement	0.9999	0.001	95.8	2.3	4.3
	Multi-Analyte	0.9999	0.006	97.11	4.67	5.59
Azimsulfuron	GLP Enforcement	0.9993	-0.014	2.64	4.11	6.23
	Multi-Analyte	0.9992	-0.004	2.63	2.06	3.42
Chlorsulfuron	GLP Enforcement	0.9999	0.014	633.6	7.12	12.3
	Multi-Analyte	0.9997	0.043	613.6	3.09	4.20

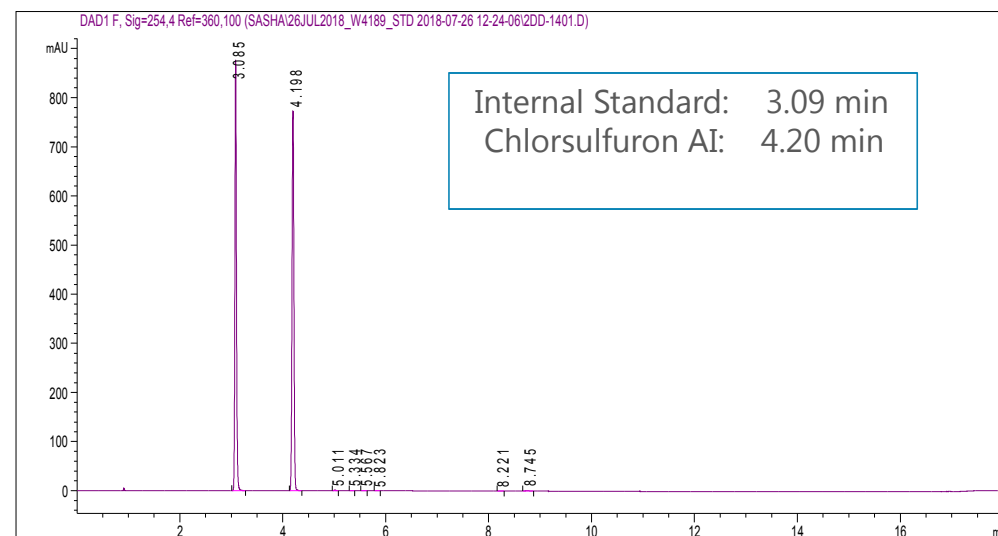


Chromatographic Comparison Example

GLP Enforcement Method



Multi-analyte Method



Instrument and Analyst Precision

Data



Precision Results

Compound	Method Type	Average Weight Percent (%)	RSD: Analyst n = 8 preparations	RSD: Instrument n = 8 injections	Modified Horowitz Limit %RSD _r	Passed?
Chlorantraniliprole	GLP Enforcement	99.46	0.77	0.21	1.34	Yes
	Multi-Analyte	99.46	0.77	0.21	1.34	Yes
Bifenthrin	GLP Enforcement	100	1.18	0.14	1.34	Yes
	Multi-Analyte	99.45	0.45	0.09	1.34	Yes
Cyantraniliprole	GLP Enforcement	98.11	0.86	0.19	1.34	Yes
	Multi-Analyte	98.67	1.17	0.22	1.34	Yes
Indoxacarb	GLP Enforcement	98.59	1.05	0.07	1.34	Yes
	Multi-Analyte	98.20	1.08	0.05	1.34	Yes
Flutriafol	GLP Enforcement	100.97	0.41	0.71	1.34	Yes
	Multi-Analyte	99.77	0.27	0.23	1.34	Yes
Triflusulfuron	GLP Enforcement	99.23	0.21	0.06	1.34	Yes
	Multi-Analyte	99.25	0.28	0.04	1.34	Yes
Azimsulfuron	GLP Enforcement	100.97	0.53	0.06	1.34	Yes
	Multi-Analyte	101.19	0.52	0.17	1.34	yes
Chlorsulfuron	GLP Enforcement	97.32	0.69	0.20	1.34	yes
	Multi-Analyte	97.74	0.60	0.11	1.34	yes

Accuracy

Data



Accuracy Results

Compound	Method Type	Average Weight Percent (%)	RSD n = 6	Modified Horowitz Limit %RSD _r	Passed?
Chlorantraniliprole	GLP Enforcement	99.95	0.68	1.34	Yes
	Multi-Analyte	99.95	0.68	1.34	Yes
Bifenthrin	GLP Enforcement	99.53	1.14	1.34	Yes
	Multi-Analyte	100.32	0.87	1.34	Yes
Cyantraniliprole	GLP Enforcement	100.18	0.85	1.34	Yes
	Multi-Analyte	97.99	0.50	1.34	Yes
Indoxacarb	GLP Enforcement	98.41	0.80	1.34	Yes
	Multi-Analyte	97.45	1.28	1.34	Yes
Flutriafol	GLP Enforcement	98.94	0.45	1.34	Yes
	Multi-Analyte	99.02	0.33	1.34	Yes
Triflusulfuron	GLP Enforcement	99.12	0.52	1.34	Yes
	Multi-Analyte	99.25	0.45	1.34	Yes
Azimsulfuron	GLP Enforcement	100.17	0.23	1.34	Yes
	Multi-Analyte	100.16	0.37	1.34	Yes
Chlorsulfuron	GLP Enforcement	98.61	0.48	1.34	Yes
	Multi-Analyte	98.51	0.61	1.34	Yes

TMIC

Duplicate samples prepared at 3 separate concentrations, averaged.
75%, 100% and 125% of the concentration of the sample solution preparation.



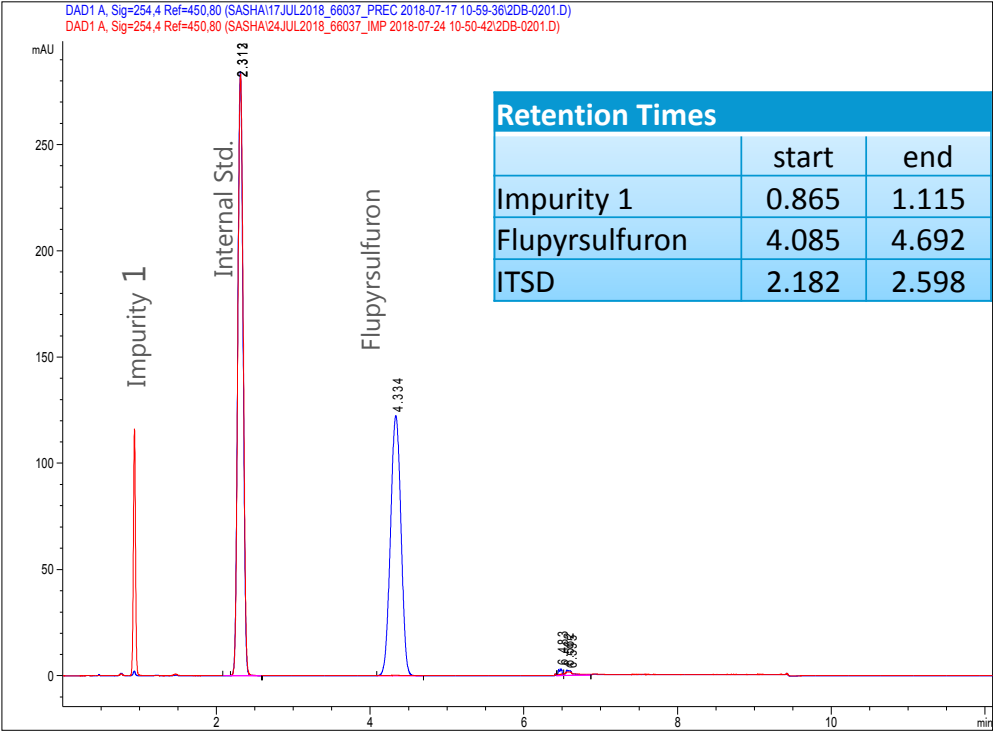
Specificity

Example

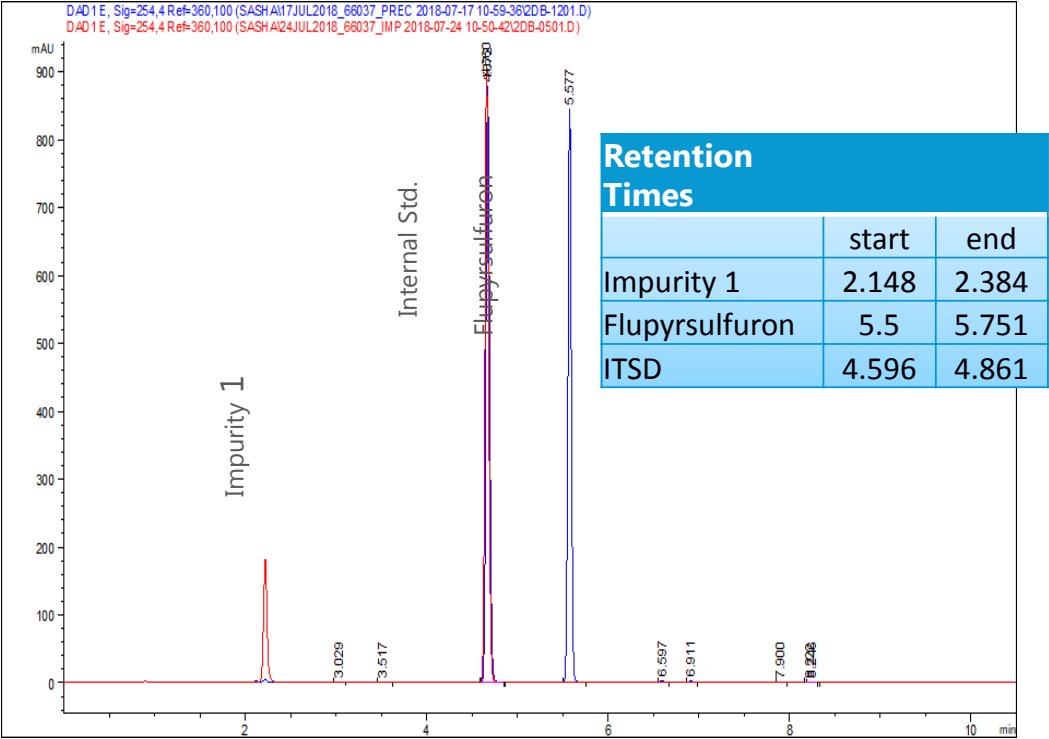


Specificity Example: Flupyrsulfuron

GLP Method



Multi-Analyte Method



Conclusions

- The Multi-Analyte method shows great promise in meeting GLP statistical requirements.
- Little or no change in precision, accuracy or linearity.
- Needs to be continually tested for specificity with each active.
- This work needs to extend to formulations of each active where the method will receive the most use by regulatory and country laboratories.

Special Thanks

- Jim Garvey, Ireland Department of Agriculture and Food Laboratories
- FMC Co-authors: Erin Ennis and John Groce
- Vassar Summer 2018 Student at FMC: Sasha Czarnick



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	Column Type	Length	Diameter	Particle Size	Flow Rate	Detection	Sample Concentration	Diluent
Cyantraniliprole	Xbridge [®] C18	150 mm	4.6 mm	3.5 µm	1.2 mL/min	254 nm	1.0 mg/mL	ACN
Triflusulfuron	Zorbax [®] SB C8	150 mm	4.6 mm	5.0 µm	2.0 mL/min	254 nm	1.0 mg/mL	50:50 ACN/0.01N NH ₄ OH
	Zorbax [®] SB C8	75 mm	4.6 mm	3.5 µm	2.0 mL/min	254 nm	0.7 mg/mL	ACN
Indoxacarb	Zorbax [®] SB C8	150 mm	4.6 mm	3.5 µm	1.0 mL/min	240 nm	0.375 mg/mL	ACN
	Zorbax [®] SB C8 Solvent Saver	250 mm	3.0 mm	5.0 µm	0.65 mL/min	280 nm	0.5 mg/mL	ACN
Azimsulfuron	Zorbax [®] SB C8	150 mm	4.6 mm	5.0 µm	2.0 mL/min	254 nm	1.0 mg/mL	50:50 ACN/0.01N NH ₄ OH
	Zorbax [®] SB C8	75 mm	4.6 mm	3.5 µm	2.0 mL/min	254 nm	0.7 mg/mL	ACN
Metsulfuron Methyl	Zorbax [®] SB C8	150 mm	4.6 mm	3.5 µm	1.0 mL/min	240 nm	0.375 mg/mL	ACN
Chlorantraniliprole	Ace [®] 3 C18	150 mm	4.6 mm	3.0 µm	1.8 mL/min	275 nm	1.0 mg/mL	50:50 ACN/0.005 M NaH ₂ PO ₄

