

# A Comparison of Near-Infrared (NIR) Feasibility Study Analyzing Pharmaceutical Drug Product Using Near-Infrared (NIR) Method Development Approaches Using a Drug Product on Different Spectrophotometers and Chemometric Software Algorithms

Assad J. Kazeminy<sup>1</sup>, Saeed Hashemi<sup>1</sup>, Roger L. Williams<sup>2</sup>, Gary E. Ritchie<sup>3</sup>, Ronald Rubinovitz<sup>4</sup>, and \*Sumit Sen<sup>5</sup>  
 1. Irvine Pharmaceutical Services, Inc., 10 Vanderbilt, Irvine, CA 92618  
 2. United States Pharmacopeial Convention, 12601 Twinbrook Parkway Rockville, Maryland 20852  
 3. Former United States Pharmacopeial Convention, 12601 Twinbrook Parkway Rockville, Maryland 20852  
 4. Buchi Corporation, 19 Lukens Drive, New Castle, DE 19720  
 5. United States Food and Drug Administration, 18701 Fairchild, Irvine, CA 92612  
 \*Corresponding Author: sumit\_sen@hotmail.com

## Abstract

A study protocol was designed, using a common data set consisting of four formulations of Ibuprofen (200 mg): two branded and two store-branded Ibuprofen (200 mg) Immediate Release Tablets, involving three investigating parties, namely, the United States Food and Drug Administration (US FDA), the United States Pharmacopeia (USP), and Irvine Pharmaceutical Service, and three different NIR instruments. Each model consisted of 192 calibration samples and 64 test set samples developed for each NIR instrument.

## Methods

The instruments that were used included a Bruker Vector 22N FT-NIR spectrometer a Buchi NIRFlex Solids and FOSS XDS Rapid Content Analyzer. The Software used from each instrument, respectively, were OPUS™ 5.5, NIR Cal®, NIRCal® 5.2 and Vision™ 3.4. The Unscrambler® 9.7, a stand-alone multivariate analysis and experimental design software package was used as referee software to assist in developing a common model.

## Abstract

Table 1 – Sources of Samples for Study

Lot	Brand - Advil	Brand - Motrin	Generic - CVS	Generic - Rite Aid
1	B04691 2 x 200 = 400 tablets	PGAT109 3 x 100 = 300 tablets	6E1012 2 x 250 = 500 tablets	P45002 1 x 500 = 500 tablets
2	B07194 2 x 200 = 400 tablets	GLA103 3 x 100 = 300 tablets	6E1015 4 x 100 = 400 tablets	P44309 1 x 500 = 500 tablets
3	B04691 3 x 100 = 300 tablets	PGAT209 3 x 100 = 300 tablets	6E1012 1 x 750 = 750 tablets	P44608 1 x 250 = 250 tablets
4	4 x 75 = 300 tablets	10 x 24 = 240 tablets	1 x 750 = 750 tablets	1 x 250 = 250 tablets
5	2 x 150 = 300 tablets	3 x 100 = 300 tablets	3 x 100 = 300 tablets	3 x 100 = 300 tablets
6	2 x 150 = 300 tablets	3 x 100 = 300 tablets	1 x 500 = 500 tablets	1 x 500 = 500 tablets
7	3 x 100 = 300 tablets	5 x 60 = 300 tablets	1 x 500 = 500 tablets	2 x 120 = 240 tablets
8	2 x 200 = 400 tablets	5 x 100 = 500 tablets	3 x 100 = 300 tablets	5 x 50 = 250 tablets
9	9 x 24 = 216 tablets	2 x 100 = 200 tablets	1 x 500 = 500 tablets	5 x 50 = 250 tablets
10	B01989 2 x 100 = 200 tablets	LAA309 2 x 100 = 200 tablets	TRE908 1 x 500 = 500 tablets	P44608 2 x 100 = 200 tablets

Table 2 – Study Design

Laboratory / Instrument	Experimental Samples	Innovator Manufacturer Advil	Innovator Manufacturer Motrin	Generic Manufacturer CVS	Generic Manufacturer Rite Aid	Total
United States Pharmacopeia/ FOSS	Calibration Set	6 tabs x 8 lots = 48	6 tabs x 8 lots = 48	6 tabs x 8 lots = 48	6 tabs x 8 lots = 48	192
	Test Set	2 tabs x 8 lots = 16	2 tabs x 8 lots = 16	2 tabs x 8 lots = 16	2 tabs x 8 lots = 16	64
	Validation set	20 tabs x 2 lots = 40	14 tabs x 2 lots = 28	20 tabs x 2 lots = 40	20 tabs x 2 lots = 40	148
United States Pharmacopeia/ Bruker	Calibration Set	6 tabs x 8 lots = 48	6 tabs x 8 lots = 48	6 tabs x 8 lots = 48	6 tabs x 8 lots = 48	192
	Test Set	2 tabs x 8 lots = 16	2 tabs x 8 lots = 16	2 tabs x 8 lots = 16	2 tabs x 8 lots = 16	64
	Validation set	20 tabs x 2 lots = 40	14 tabs x 2 lots = 28	20 tabs x 2 lots = 40	20 tabs x 2 lots = 40	148
FDA/ Irvine Pharmaceutical Services, Inc./ Buchi	Calibration Set	6 tabs x 8 lots = 48	6 tabs x 8 lots = 48	6 tabs x 8 lots = 48	6 tabs x 8 lots = 48	192
	Test Set	2 tabs x 8 lots = 16	2 tabs x 8 lots = 16	2 tabs x 8 lots = 16	2 tabs x 8 lots = 16	64
	Validation set	20 tabs x 2 lots = 40	20 tabs x 2 lots = 40	20 tabs x 2 lots = 40	20 tabs x 2 lots = 40	160
Total		312	288	312	312	1224

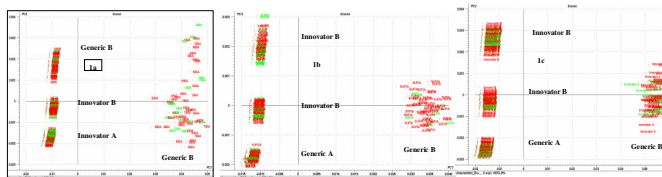
Table 3 – Data Pretreatment from 1000 nm – 2500 nm (Cluster)

Spectra Treatment (1000 nm-2500 nm)	Innovator A	Innovator B	Generic A	Generic B
Untreated Spectra	+	+	-	-
Baseline Correction	+	+	+	+
First Derivative	+	-	+	+
Second Derivative	+	+	-	-
Baseline Corrected First Derivative	+	+	-	-
Baseline Corrected Second Derivative	+	-	+	+

Table 4 – Data Pretreatment from 1400 nm – 1500 nm (Cluster)

Spectra Treatment (1400 nm-1500 nm)	Innovator A	Innovator B	Generic A	Generic B
Untreated Spectra	+	-	-	-
Baseline Correction	+	+	+	+
First Derivative	+	+	+	+
Second Derivative	Yes	-	-	-
Baseline Corrected First Derivative	+	+	+	+
Baseline Corrected Second Derivative	+	-	+	+

Figures 1a., 1b., and 1c. – Unscrambler® 9.7 PCA Score Plots of Buchi (1a), FOSS (1b), and Bruker (1c) Calibration and Test



Figures 2a., 2b., and 2c. – Unscrambler® 9.7 PCA Score Plots of Buchi (2a), FOSS (2b), and Bruker (2c) Calibration and Test

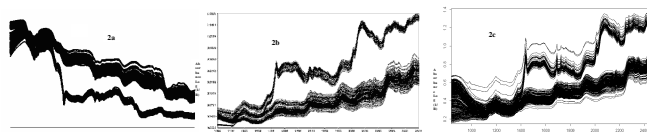
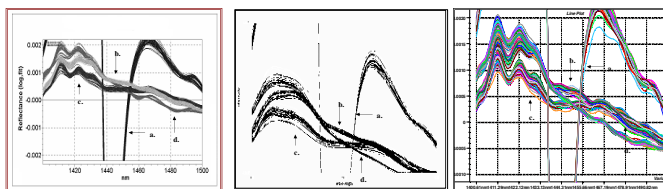


Figure 3., Expanded view of Buchi, FOSS, and Bruker Derivative Spectra of Calibration and Test Set c.b. Buchi



## Results

It was found that using Savitsky-Golay, first derivative, 21 point smoothing, third order polynomial, pretreated spectra and either Principal Component Analysis (PCA) or Factorization model resulted in different models but possessing the same accuracy capabilities for predicting samples comprising similar validation sets. Each model correctly and accurately (100 %) predicted 160 validation samples using the Buchi model, and 148 validation samples using the Bruker and FOSS models. One validation sample set, a store-branded Ibuprofen (200 mg) Immediate Release Tablet, was correctly identified as not belonging to the sample represented in the calibration set by all three models. Based on these results and despite difference in instrument configuration number of spectral data points, PCA or Factorization algorithms, and validation modeling approach, exact and accurate spectroscopic results can be achieved using NIR spectroscopy for discriminate analysis.

## Conclusion

This study shows that the same NIR method spectral pretreatment parameters can be used, and that nearly the same multivariate models can be obtained, despite instrumental and software differences, to accurately predict the identity of pharmaceutical dosage forms.

## References

1. P. de Peinder, M.J. Vredenburg, T. Visser and D. de Kaste, "Detection Of Lipitor® counterfeit: A Comparison of NIR and Raman Spectroscopy in Combination with Chemometrics", *Journal of Pharmaceutical and Biomedical Analysis* 47, 688 (2008).
2. J. Luyten, D.L. Massart and Y. Vander Heyden, "Near-Infrared Spectroscopy Applications in Pharmaceutical Analysis", *Talanta* 72, 865 (2007).
3. V. Roggo, P. Chalusa, L. Maurea, C. Lena-Martinez, A. Edmonds and N. Jentia, "A Review of Near Infrared Spectroscopy and Chemometrics in Pharmaceutical Technologies", *J. Pharm. and Biomedical Analysis* 44, 693 (2007).
4. A. K. Desingh, "Pharmaceutical Counterfeiting", *Analyst* 130, 271 (2005).
5. D. A. Burne and E. W. Ciuczak, Ed. "Near-Infrared Spectroscopy in Pharmaceutical Applications", in *Handbook of Near-Infrared Analysis*, 3rd Ed., Practical Spectroscopy Series Volume 98, CRC Press, Boca Raton, London, New York, 585 (2008).
6. S. H. Scott and C. Pasquini, "Identification of Counterfeit Drugs Using Near-Infrared Spectroscopy", *Analyst* 126, 2218 (2001).
7. J. Workman Jr. and J. Brown, "A New Standard Practice for Multivariate, Quantitative Infrared Analysis-Part I", *Spectroscopy* 11(2), 48 (1996).
8. J. Workman Jr. and J. Brown, "A New Standard Practice for Multivariate, Quantitative Infrared Analysis-Part II", *Spectroscopy* 11(9), 24 (1996).
9. A. Savitzky and M. J. E. Golay, "Smoothing and Differentiation of Data by Simplified Least Squares Procedures", *Anal. Chem.* 36, 1627 (1964).
10. Davies, A.M.C. and C. Miller, 1988, "Tentative Assignment of the 1440-nm Absorption Band in the Near-Infrared Spectrum of Crystalline Sucrose", *Appl. Spectrosc.* 42 (4), 703-704.