The Next Generation of Product Performance Tools- Combining Formulation Function with Effect

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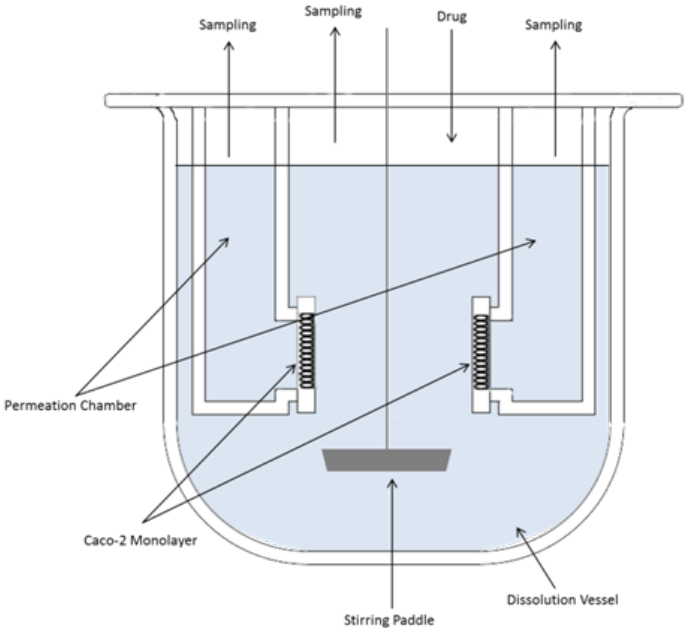
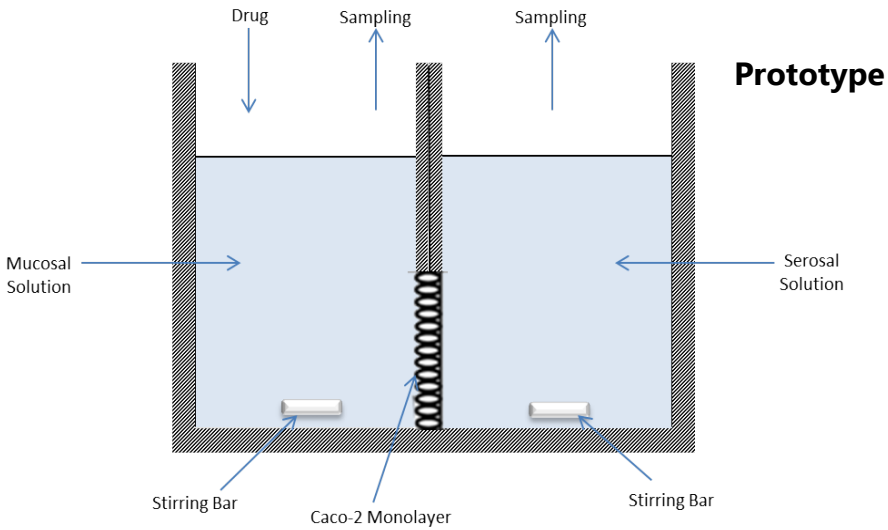
IDAS: Biopharmaceutics Dissolution with Better *In Vivo* Correlation





- *In Vitro* **Dissolution Absorption System** combines traditional dissolution testing with a means to **determine and quantify** interactions with a bio-relevant membrane.
- **Absorption, Biomarker Regulation, Metabolism**

Challenge

- Presenting a finished dosage form and maintaining reasonable SA/Volume ratio

Characterized and Validated System

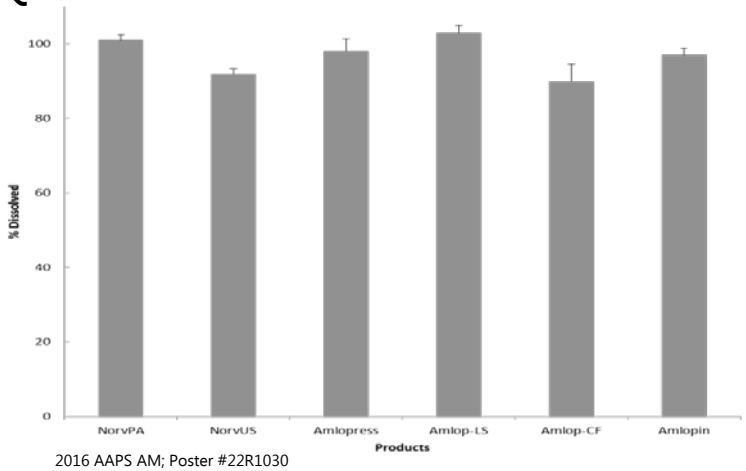
- Multiple Dissolution Media
- Over 20 compounds

Applications

- Formulations, Food Effects, Local GI

Application: Formulation Comparison with Better *In Vivo* Correlation

Batch Release Data for Product A-
Q value was similar for different manufacturers



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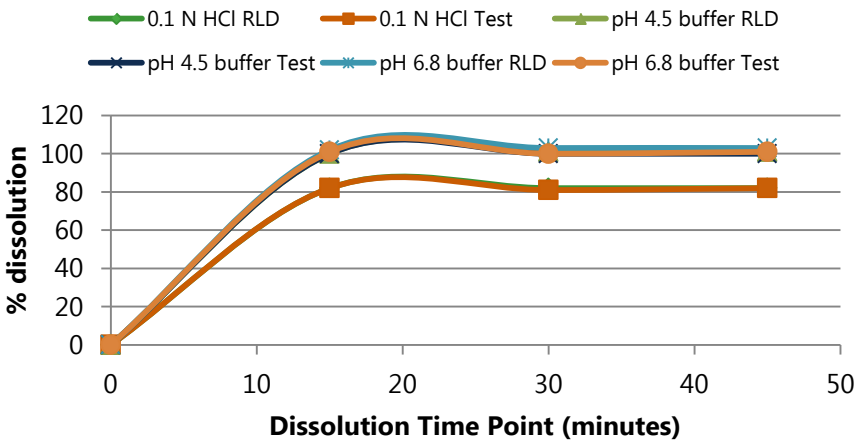
Data using IDAS shows marked differences in AUC and % permeated for different manufacturers

Product	AUC (0-2 hours)	% Permeation (0-2 hours)
FF15-025	**7304.8 ± 407.1**	**2.33 ± 0.52**
FF15-027	4001.3 ± 590.1*	0.25 ± 0.13*
FF15-028	2166.1 ± 756.8*	0.51 ± 0.16*
FF15-029	5043.8 ± 1157.7*	0.55 ± 0.35*
FF15-030	6477.0 ± 1031.9	0.51 ± 0.16*

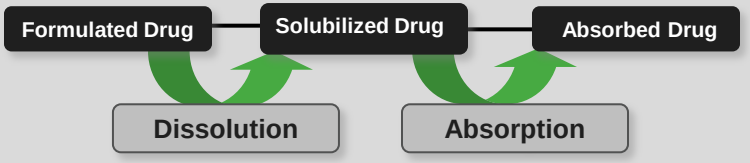
*: $p < 0.05$

IDAS Achieves Relevant Discrimination

Dissolution for Compound B [BCS III]



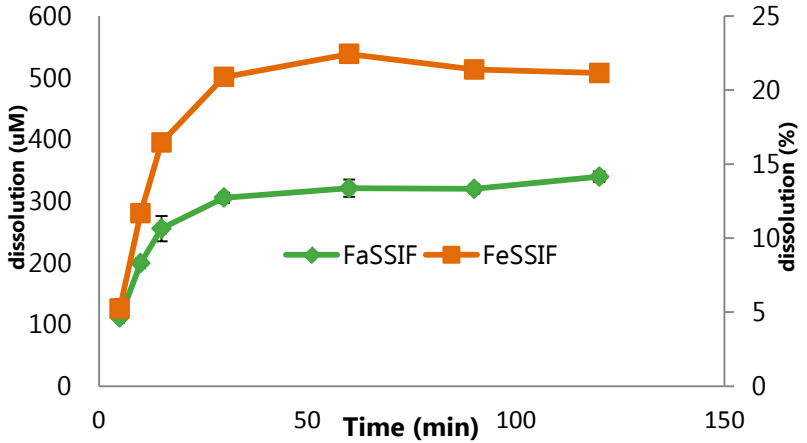
- The **test product failed bioequivalence.** The test product was **below the 90%** confidence interval for **C_{max} and AUC**
- IDAS – **dual gated process**



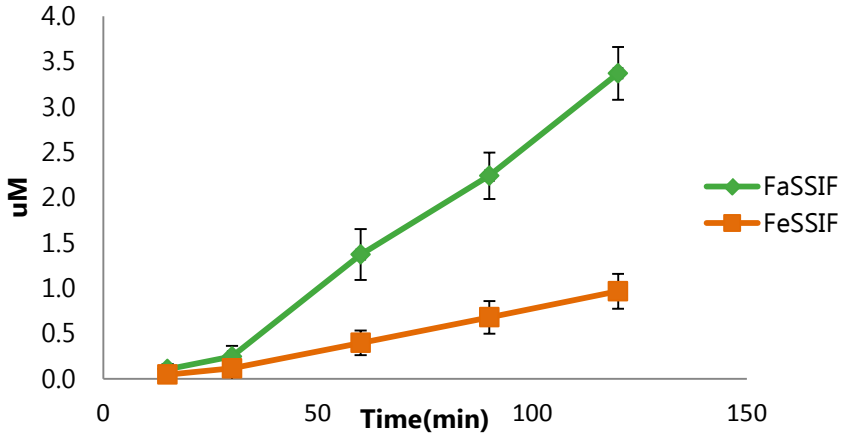
POTENTIAL

Application: Food Effects with Better *In Vivo* Correlation

Effect of Food on Dissolution of Saquinavir Mesylate
[EXPECTED]



Effect of Food on Permeation of Saquinavir Mesylate
[IDAS ADVANTAGE]



IDAS Achieves Relevant Discrimination

Cause: Entrapment

Compound	HBSS	FaSSIF	FeSSIS
Saquinavir Mesylate (BCS Class II)	**13%**	**80%**	**90%**
Minoxidil (BCS Class I)	**N/B**	**Minimal**	**Minimal**
Atenolol (BCS Class III)	**N/B**	**Minimal**	**Minimal**
Propranolol (BCS Class I)	**4%**	**44%**	**94%**

- Compound X, undergoes **extensive first pass metabolism** also demonstrates an **increase in the AUC and a reduction in C_{max}** when administered orally with a **high fat meal**.
- Possibility of **elucidating the interplay** between food and first pass metabolism using a **specialized bio-membrane**.

POTENTIAL

Application: PK & Local GI with Better *In Vivo* Correlation

IDAS Achieves Relevant Discrimination

Table 1. Comparison of in vitro IDAS results with in vivo human oral pharmacokinetics results

	Indomethacin	Submicron indomethacin	%Change
IDAS parameters			
k_D (min^{-1})	0.330	1.371	316
k_P ($min^{-1} \cdot cm^{-2}$, $x10^{-3}$)	2.282	2.967	30.0
D_{max} (ng/mL)	55325	64935	17.4
Human oral PK parameters*			
C_{max} ($ng \cdot mL^{-1} \cdot mg^{-1}$)	47.39	59.22	25.0
AUC ($ng \cdot h \cdot mL^{-1} \cdot mg^{-1}$)	155.2	152.8	-1.6

* Adapted from literature reference (2) and dose normalized.

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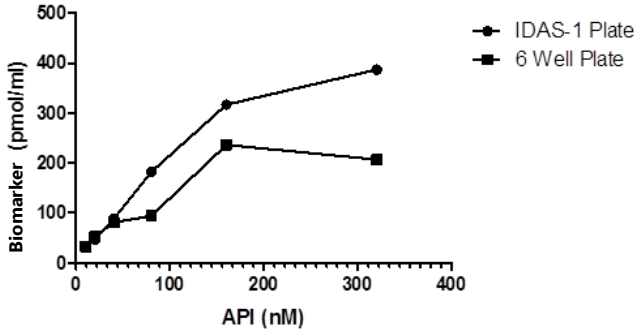
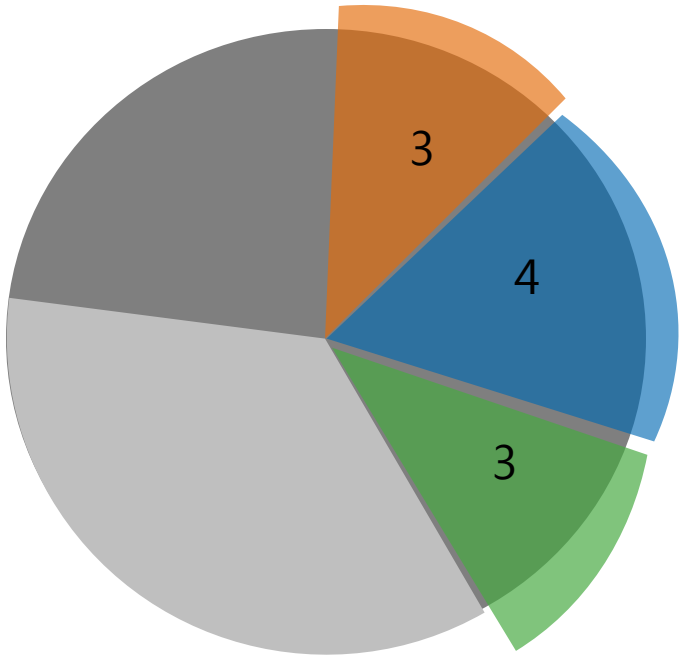
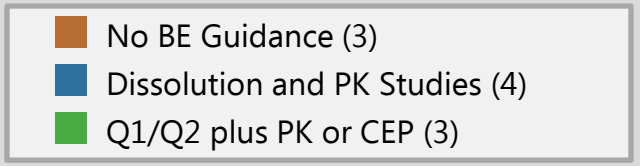
Biomarker Dose-Res to API (IDAS vs 6 Well Plate)



	IDAS-1 Plate	6 Well Plate
LogEC50	~ 95.95	~ 102.6

Local GI





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Support Needed