

# Dissolution Safe Space

In Silico trial to establish a dissolution safe space based on Bioequivalence outcome

June 2021 | Dissolution, Modeling & Simulation, Batch Release

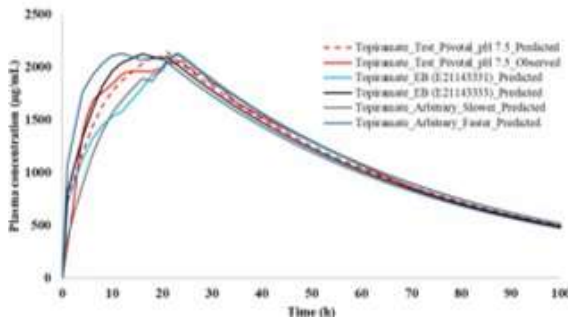
**Background:** The Sponsor intended to have a “dissolution safe space” based on the bio batch dissolution specifications. The Sponsor had performed a BA BE study and 90% CI is within the range of 80% - 125%.

**Question of Interest:** Could Modeling and Simulation establish a dissolution safe space without conducting actual BA BE study?

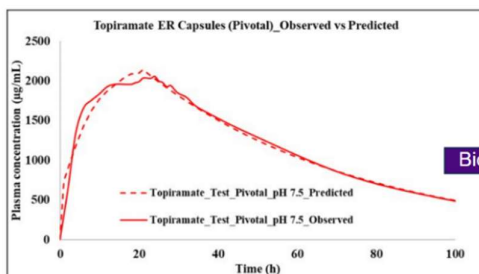
**Methods:** Could Modeling and Simulation establish a dissolution safe space without conducting actual BA BE study?

**Results:**

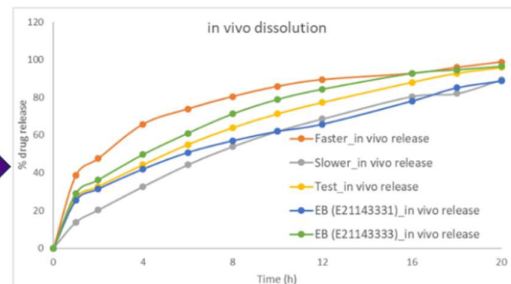
A validated IVIVC model (see figure) was developed and used to simulate the “Dissolution Safe Space”.



Spec.	Limits
1 h	10 – 30%
6 h	35 – 65%
18 h	NLT 75%



Bio equivalent



Drug Record	C <sub>max</sub> (ng/mL)			AUC (ng/mL*h)		
	Obs.	Pred.	% Pred. Error	Obs.	Pred.	% Pred. Error
Pivotal – Test sample	2058	2143	-4.13	1.39E+05	1.38E+05	0.217
Pivotal – Reference standard (Trokendi XR®)	2283	2495	-9.286	1.44E+05	1.39E+05	3.199
Specifications	Proposed Limits					
1 h	10 – 30%					
6 h	35 – 65%					
18 h	NLT 75%					

**Impact:**

- The Agency accepted the Sponsor’s M&S methodology including the “Dissolution Safe Space” proposal.
- The Sponsor reduced costs and timelines for the commercial batches by having wider dissolution specifications for batch release.