

# Using finite element analysis to determine blister permeability from tooling design

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# About us



# kp's global footprint



**18**  
countries

**32**  
plants

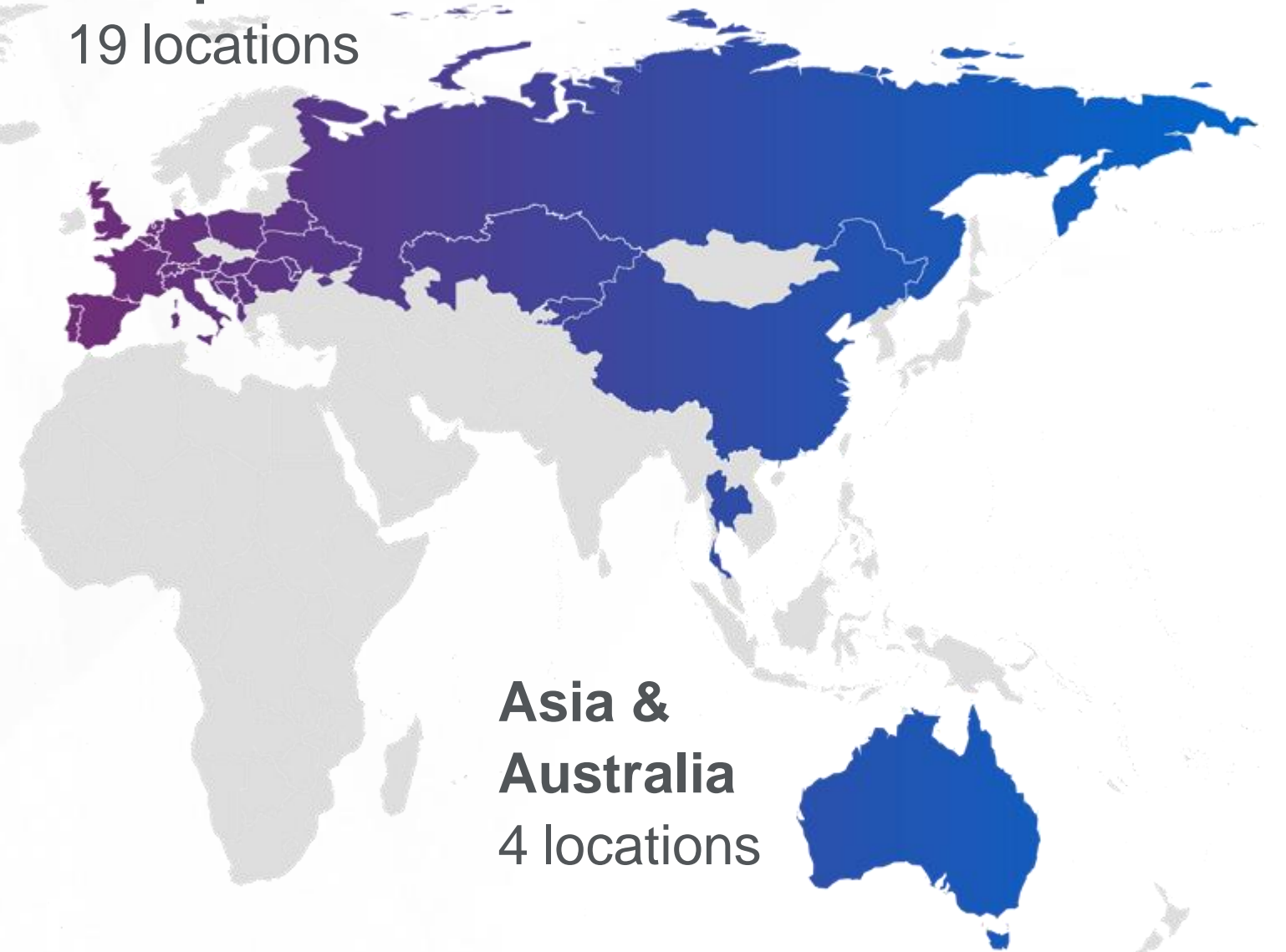
**~€2 bn**  
annual revenue

**6,200**  
employees



**The Americas**  
9 locations

**Europe**  
19 locations



**Asia &  
Australia**  
4 locations







# BlisterPro® XCEL services: definitions



BlisterPro XCEL® are a suite of services, moving from prediction to prototyping to assist on stability and packaging development.

The main idea behind this set of services is to accurately select the packaging materials that pass stability and reduce the time to market

BlisterPro® lite is a quick MVTR calculator based on material volume preservation. It is a “back of the envelope” calculation. Less accurate

BlisterPro® FEA is a MVTR calculator based on finite element analysis predictions for material thickness distribution. Is the most precise modeling technique for package development, contemplating viscoelastic constants of multiple materials and their effects on packaging permeability

# Introduction to permeability models

# Influential factors of barrier performance



$$\text{MVTR} = \frac{[\Delta C] * A * D_{ab}}{t}$$

- Apply fundamental concepts from Fick's Law of Diffusion

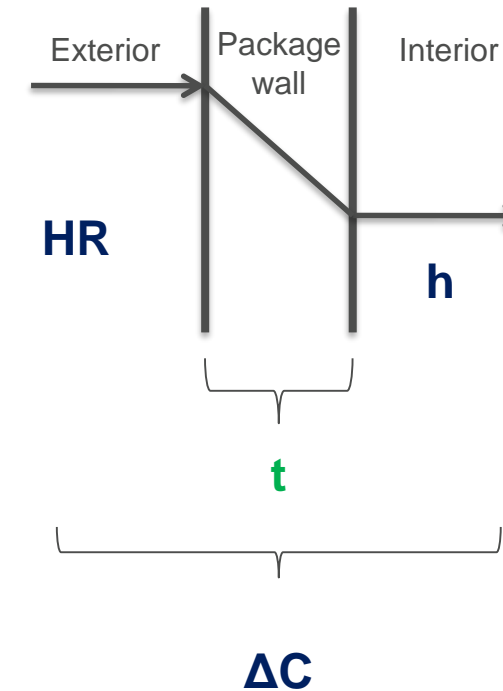
Flat Film MVTR =  $f(D_{ab}, \Delta C, T, A, t)$

- Transform flat film rates into blister rates

Blister MVTR =  $f(\text{flat film MVTR, blister area, blister wall thickness})$

- Examine the influence dimensions & blister geometry

- film thinning (as film thins, transmission goes up)
- cavity surface area (as area increases, transmission goes up)
- draft angles (as draft angle goes up surfaces goes up, thickness goes up, transmission goes down)
- corners, radii, fillets





# Geometry calculations

# Packaging geometry assumptions: *ASAPprime*®



- Capsules' blister area comes from tables hardcoded inside *ASAPprime*®
  - See custom tab of the Dosage section. Refer to pull down menu
- Tablet's areas come from formula relating mass, volume and area of blister
  - Volume assumption uses a density of 1g/ml
- All volumes independently of the form are adjusted to reflect the size of the blister

## Material (Blister)

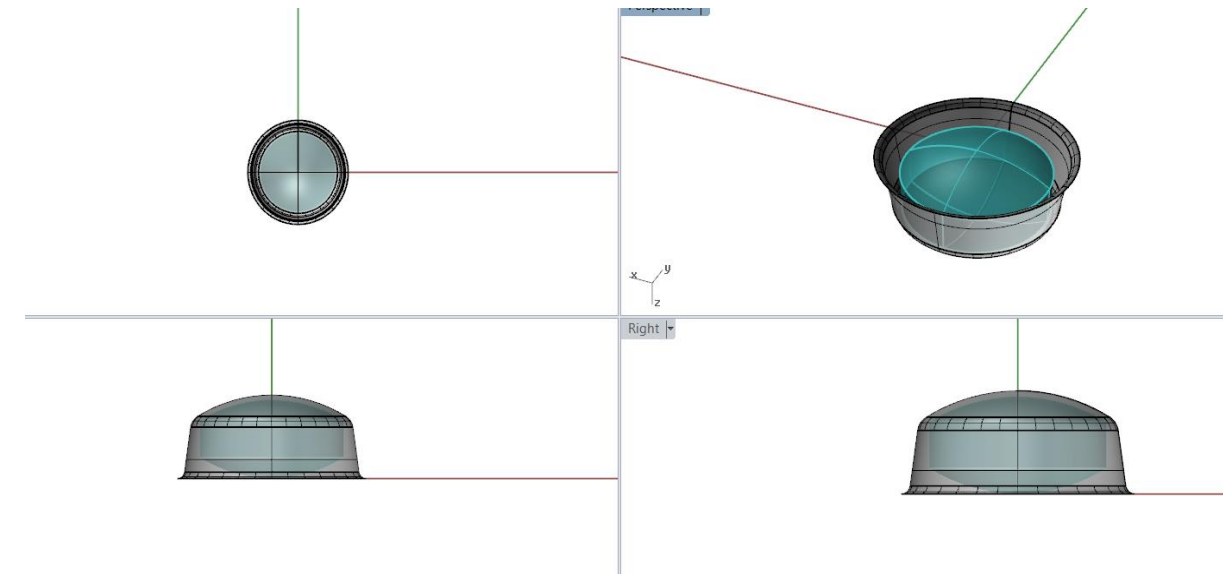
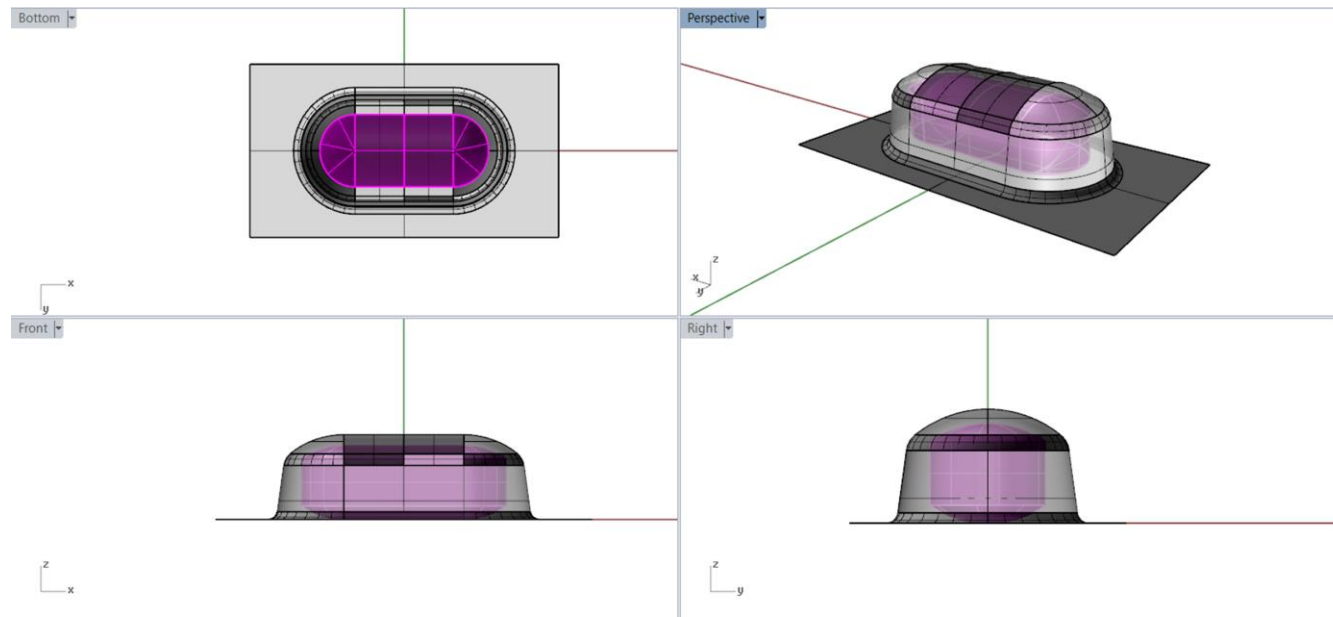
The user can select from among a number of [blister](#) materials. These data should be viewed as approximate since the exact cavity used and the quality of the seals will have a significant impact. More exact calculations, using the blister tooling, are available for many of the blister options through a partner company and can be accessed by enquiring with FreeThink (see ["Help"](#)).

Blister MVTR data were all obtained at two temperatures with an [Arrhenius](#) fit to determine the slope and intercept values of the [permeability](#) stored. The original data were obtained from blisters sized for #1 capsules. The data assumes the lid stock is effectively impermeable. The program corrects for the size of blister using a two-thirds power rule to relate volume to surface area.

$$P = \exp \left[ \text{intercept} + \frac{\text{slope}}{273.15 + \text{temp}} \right] (\text{volume})^{2/3}$$

How the volume is calculated depends on the formulation type ([Custom tab](#) of the [Dosage Panel](#)). For tablets, a nominal density of 1 g/mL is used for the volume. For capsules, the volume is based on the capsule #. For powder, volume is based on a nominal density of 0.5 g/mL. All volumes are then adjusted to reflect the size of the blister that contains them.

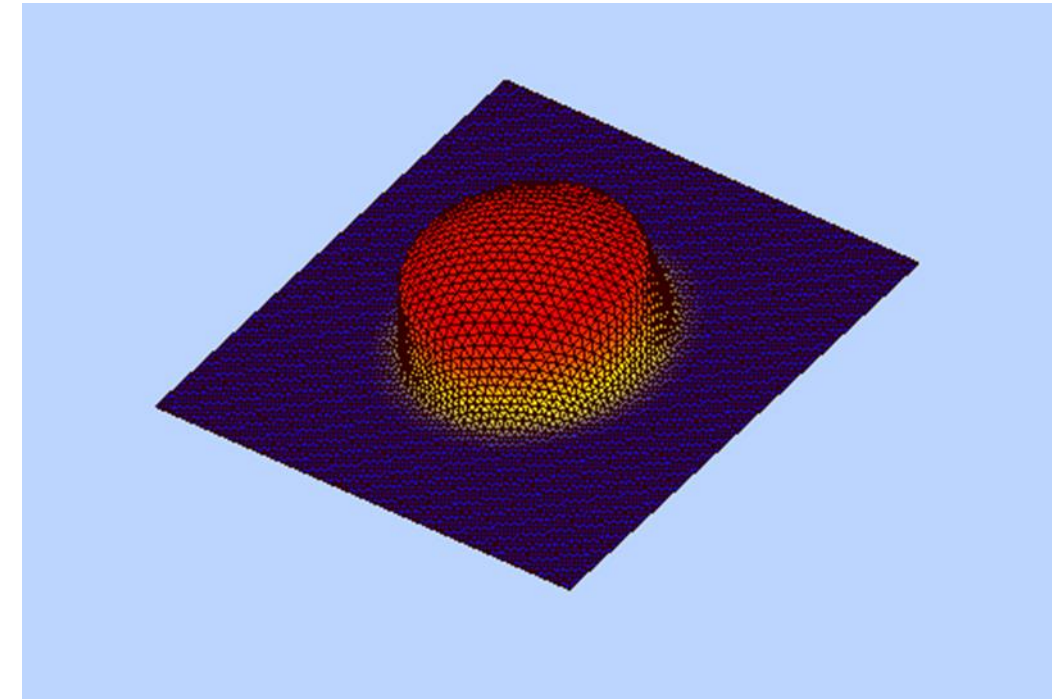
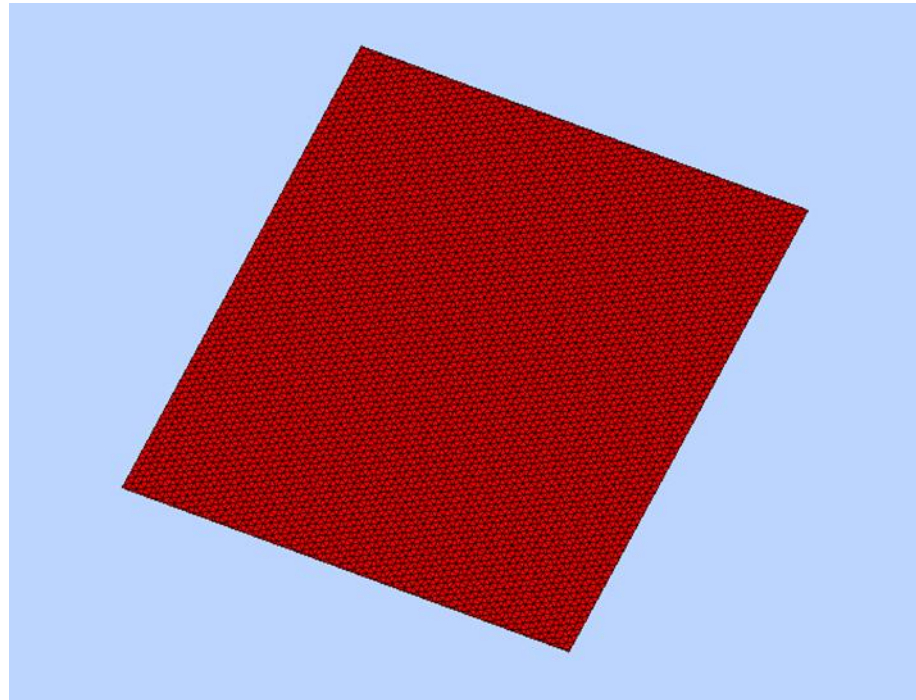
# Packaging geometry assumptions: BlisterPro® lite



- Blister area could come from existing design or from an optimized kp design
  - Criteria differs on draft angles, head spaces, radius and geometries
- Thickness distribution assumes ideal conditions of volume preservation
  - Material flows ideally, preserving the same thickness across the cavity
- MVTR slopes and intersects come from kp's extensive lab data library



# Packaging geometry assumptions: BlisterPro® FEA



- Blister area could come from existing design or from an optimized kp design
  - Criteria differs on draft angles, head spaces, radius and geometries
- Thickness distribution assumes ideal conditions of volume preservation at an elemental level (there are ~5000 elements in this mesh)
  - Material flows varies with film's temperature, COF, forming pressure (speed) and viscoelastic constants. Plug assist presents more optimal results
- MVTR slopes and intersects come from kp's extensive lab data library



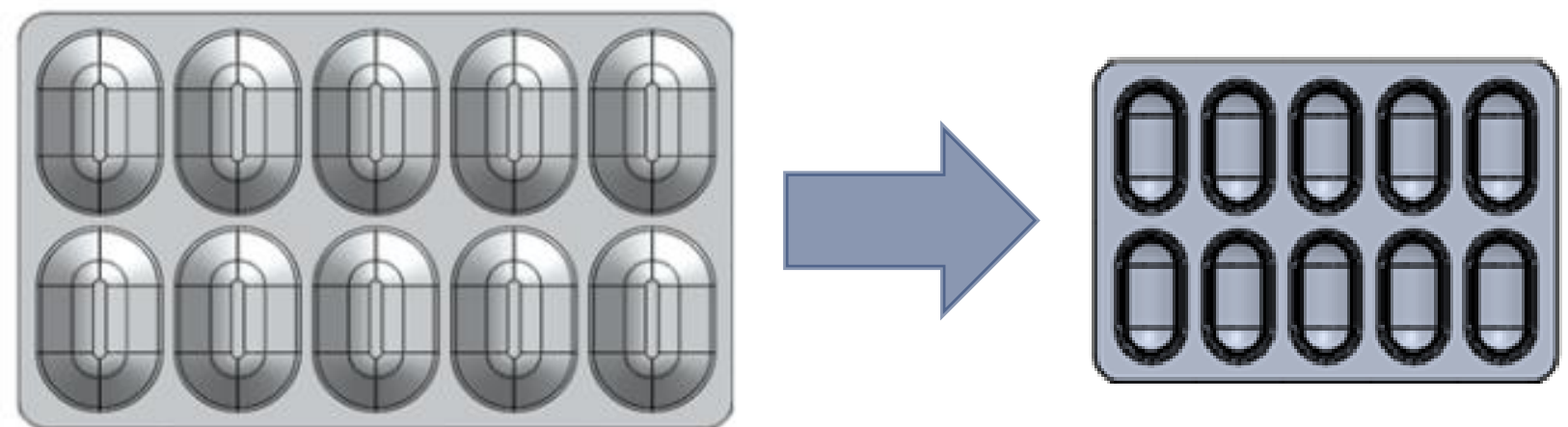
# Examples

# Capsule size 1 example



- Cephalosporin antibiotic, capsule size 1, presently packed in CFF
  - Produced in one place distributed around the planet
- How *ASAPprime*® and *BlisterPro*® packaging models affect the probability percentages of passing stability?
  - All conditions remain the same for all cases
- Slightly high  $E_a$  and B terms
  - Drives accelerated stability conditions to very high barrier requirements

Arrhenius	Values	SD
LnA	41.343	+/- 9.12
$E_a$	31.3	+/- 6.208
B	0.052	+/- 0.01
$R^2$	0.902	
$Q^2$	0.778	



# Capsule size 1: ASAPprime® and BlisterPro® results



## 2 year shelf-life

	Product	ASAP Requirement	M570/01 (254)	P250/40	P250/60	PA160/02 (254/15)	PA180/02 (254/20)	PA190/02 (254/23)	PA200/02 (254/51)	PA300/02 (254/76)	PA400/02 (254/102)	PA600/02 (254/152)	kpMax (127/102/150/127)
1.5% initial WC	FlatSheet_MVTR_38C_90RH-0RH [g/sq.m/day]		2.79	0.75	0.55	0.372	0.279	0.217	0.1071	0.064738518	0.05472	0.03636	0.035
	FlatSheet_MVTR_40C_75RH-0RH [g/sq.m/day]		2.411	0.6481	0.4753	0.3215	0.2411	0.1875	0.102	0.0732	0.0575	0.0401	0.0302
	FlatSheet_MVTR_30C_75RH-0RH [g/sq.m/day]		1.3237	0.3558	0.2609	0.1765	0.1324	0.103	0.0485	0.0291	0.0186	0.0099	0.0166
	FlatSheet_MVTR_30C_65RH-0RH [g/sq.m/day]		1.1472	0.3084	0.2262	0.153	0.1147	0.0892	0.042	0.0252	0.0161	0.0086	0.0144
	FlatSheet_MVTR_25C_60RH-0RH [g/sq.m/day]		0.3782	0.1017	0.0746	0.0504	0.0378	0.0294	0.0186	0.013	0.0116	0.0047	0.0047
	FlatSheet_OTR_23C_100RH [cc/sq.m/day]		14.1	1.35	0.8	20.2	20.2	20.2	20.2	20.2	20.2	20.2	0.18
	Blister_MVTR_40C_75RH-0RH [mg/day]	0.1425	1.6207	0.4357	0.3195	0.2161	0.1621	0.1261	0.0686	0.0492	0.0387	0.0270	0.0203
	Blister_MVTR_30C_75RH-0RH [mg/day]	0.0390	0.8898	0.2392	0.1754	0.1186	0.0890	0.0692	0.0326	0.0195	0.0125	0.0066	0.0112
	Blister_MVTR_30C_65RH-0RH [mg/day]	0.0675	0.7712	0.2073	0.1520	0.1028	0.0771	0.0600	0.0283	0.0169	0.0108	0.0058	0.0097
	Blister_MVTR_25C_60RH-0RH [mg/day]	N/A	0.2542	0.0683	0.0501	0.0339	0.0254	0.0198	0.0125	0.0088	0.0078	0.0031	0.0032
	Blister_OTR_23C_100RH [mm3/day] (100% out / 0% in)		9.4783	0.9075	0.5378	13.5789	13.5789	13.5789	13.5789	13.5789	13.5789	13.5789	0.121
	Flat Film Thickness [my]		254	274	286	269	274	277	305	330	356	406	452
	Blister Draw Ratio		2.04	2.04	2.04	2.04	2.04	2.04	2.04	2.04	2.04	2.04	2.04
	Average Film Thinning [% of Original]		49.1	49.1	49.1	49.1	49.1	49.1	49.1	49.1	49.1	49.1	49.1
	Initial Area [mm2]		162	162	162	162	162	162	162	162	162	162	162
	Surface Area [mm2]		330	330	330	330	330	330	330	330	330	330	330
	Average Thickness [my]		125	135	140	132	135	136	150	162	175	199	222
	FEA - no plug												
	Blister_MVTR_40C_75RH-0RH [mg/day]							0.1309	0.0728				
	Blister_MVTR_30C_75RH-0RH [mg/day]							0.0719	0.0346				
	Blister_MVTR_30C_65RH-0RH [mg/day]							0.0623	0.0300				
	Blister_MVTR_25C_60RH-0RH [mg/day]							0.0205	0.0133				
	FEA - W/ plug												
	Blister_MVTR_40C_75RH-0RH [mg/day]							0.1209	0.0658				
	Blister_MVTR_30C_75RH-0RH [mg/day]							0.0664	0.0313				
	Blister_MVTR_30C_65RH-0RH [mg/day]							0.0575	0.0271				
	Blister_MVTR_25C_60RH-0RH [mg/day]							0.0190	0.0120				

### % Prob to Pass (ASAP): Using PA200/02

ASAP film menu	90.34
ASAP/BP 'Lite'	86.93
ASAP/BP FEA N/P	86.18
ASAP/BP FEA W/P	87.44

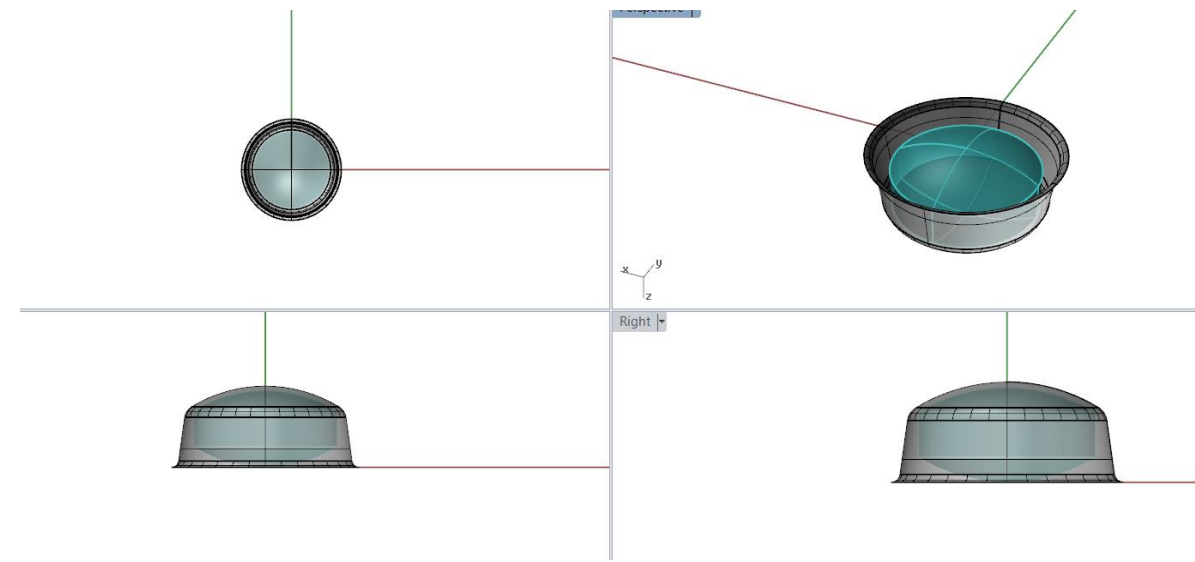
- Permeability required @ 30/75<0.675 mg / pack / day
- BP lite shows Aclar® PA200 passing, FEA no plug Aclar® PA200, FEA w plug shows Aclar® PA190...
- Initial water content of 1.5% meets production criteria
- ASAPprime® estimations are more optimistic by ~ 4% difference

# Rounded Tablet case 2



- Lower Ea and higher B term than in the case before
- How *ASAPprime*® and BlisterPro® packaging models affect the probability percentages of passing stability?
- Volume and Blister Area estimations in ASAP come from a cylindrical form
- BlisterPro® geometries where designed from the tablet using standard criteria to maximize packaging speed and barrier protection

Arrhenius	Values	SD
LnA	28.941	+/- 4.748
Ea	31.3	+/- 3.393
B	0.072	+/- 0.008
R <sup>2</sup>	0.973	
Q <sup>2</sup>	0.923	





# Capsule size 1: ASAP and BlisterPro® results



1.0% initial WC	<b>BlisterPro 'Lite'</b> 2 year shelf-life						
	Product	PA160/02 (254/15) PA190/02 (254/23) PA200/02 (254/51) PA300/02 (254/76)				PA400/02 (254/102)	PA600/02 (254/152)
	FlatSheet_MVTR_40C_75RH-0RH [g/sq.m/day]	0.3249	0.1875	0.1020	0.0732	0.0575	0.0401
	FlatSheet_MVTR_30C_75RH-0RH [g/sq.m/day]	0.1113	0.1030	0.0485	0.0291	0.0186	0.0099
	FlatSheet_MVTR_30C_65RH-0RH [g/sq.m/day]	0.0965	0.0892	0.0420	0.0252	0.0161	0.0086
	FlatSheet_MVTR_25C_60RH-0RH [g/sq.m/day]	0.0507	0.0294	0.0186	0.0130	0.0116	0.0047
	<b>Blister_MVTR_40C_75RH-0RH [mg/day]</b>	<b>0.1629</b>	<b>0.0941</b>	<b>0.0510</b>	<b>0.0366</b>	<b>0.0288</b>	<b>0.0201</b>
	<b>Blister_MVTR_30C_75RH-0RH [mg/day]</b>	<b>0.0558</b>	<b>0.0517</b>	<b>0.0242</b>	<b>0.0145</b>	<b>0.0093</b>	<b>0.0049</b>
	<b>Blister_MVTR_30C_65RH-0RH [mg/day]</b>	<b>0.0484</b>	<b>0.0448</b>	<b>0.0210</b>	<b>0.0126</b>	<b>0.0081</b>	<b>0.0043</b>
	<b>Blister_MVTR_25C_60RH-0RH [mg/day]</b>	<b>0.0254</b>	<b>0.0148</b>	<b>0.0093</b>	<b>0.0065</b>	<b>0.0058</b>	<b>0.0023</b>
	Flat Film Thickness [my]	269	277	305	330	356	406
	Blister Draw Ratio	1.93	1.93	1.93	1.93	1.93	1.93
	Average Film Thinning [% of Original]	51.7	51.7	51.7	51.7	51.7	51.7
	Initial Area [mm2]	134	134	134	134	134	134
	Surface Area [mm2]	259	259	259	259	259	259
	Average Thickness [my]	139	143	158	171	184	210
	FEA - no plug						
	<b>Blister_MVTR_40C_75RH-0RH [mg/day]</b>				<b>0.0378</b>		
	<b>Blister_MVTR_30C_75RH-0RH [mg/day]</b>				0.0150		
	<b>Blister_MVTR_30C_65RH-0RH [mg/day]</b>				0.0130		
	<b>Blister_MVTR_25C_60RH-0RH [mg/day]</b>				0.0067		
	FEA - W/ plug						
	<b>Blister_MVTR_40C_75RH-0RH [mg/day]</b>				<b>0.0340</b>		
	<b>Blister_MVTR_30C_75RH-0RH [mg/day]</b>				0.0135		
	<b>Blister_MVTR_30C_65RH-0RH [mg/day]</b>				0.0117		
	<b>Blister_MVTR_25C_60RH-0RH [mg/day]</b>				0.0061		

## % Prob to Pass (ASAP):

ASAP film menu	94.50%
ASAP/BP 'Lite'	93.91%
ASAP/BP FEA N/P	93.00%
ASAP/BP FEA W/P	<b>95.01%</b>

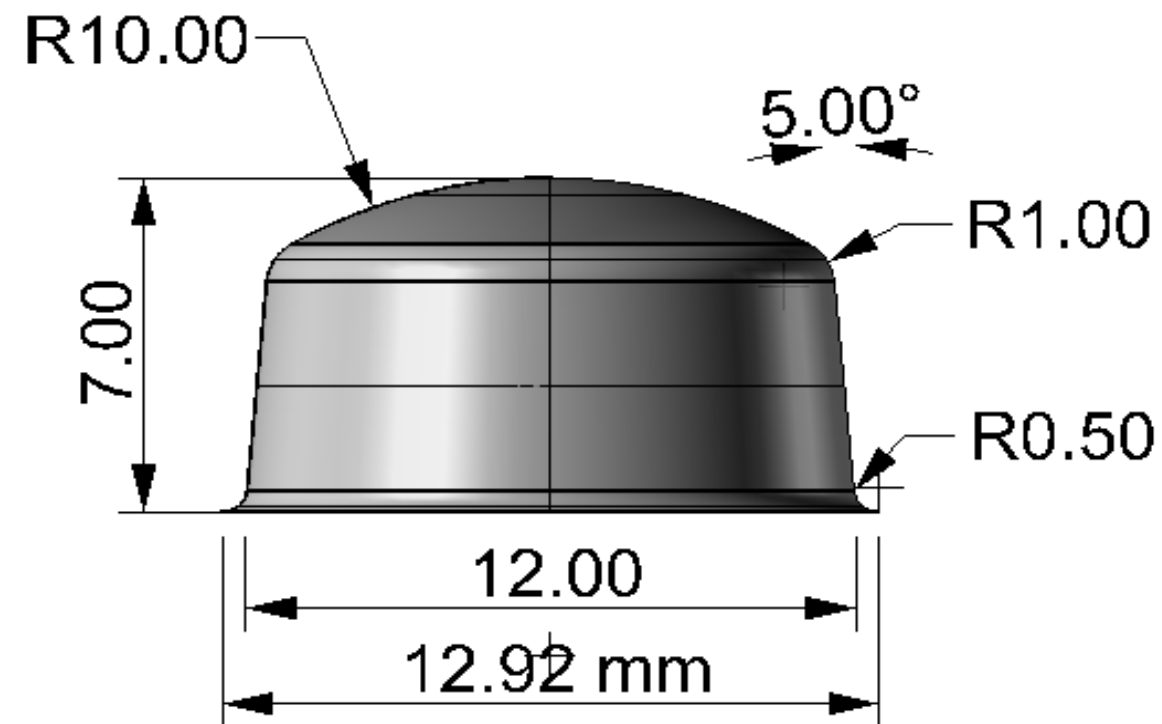
- Very small differences between estimations.
- Tablet is very close to a cylindrical shape
- Larger differences between zone IVA and IVB driven by larger B term

# Implications

# Safety margins need special considerations



- ASAPprime® is very accurate for ideal conditions and tabulated shapes.
- Differences between production and stability tools and machines or tools from different manufacturers are not contemplated



PA 200S03 (127/51/127)	7mm Depth	6mm Depth
Starting Thickness	305 $\mu\text{m}$	same
Initial Area for Forming	131 $\text{mm}^2$	same
Average Formed Thickness	130 $\mu\text{m}$	146 $\mu\text{m}$
Formed Area	308 $\text{mm}^2$	274 $\text{mm}^2$
Blister MVTR (40C, 75%RH)	0.053 mg/day	0.042 mg/day
Blister Volume	640 $\text{mm}^3$	542 $\text{mm}^3$
Headspace Water (22C, 50%RH)	0.11 $\mu\text{g}$	0.09 $\mu\text{g}$
Draw Ratio	2.35	2.09

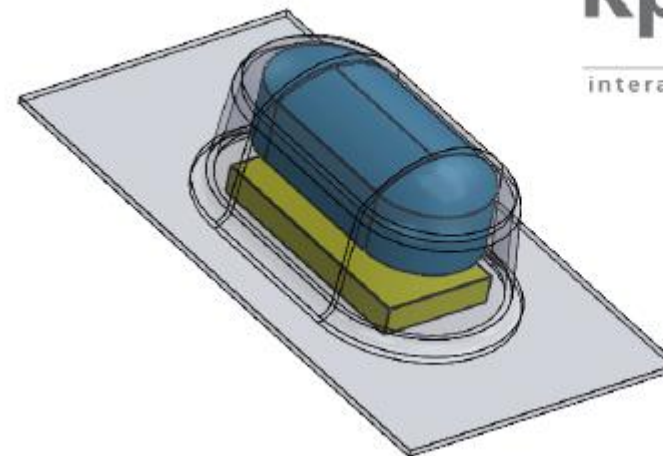
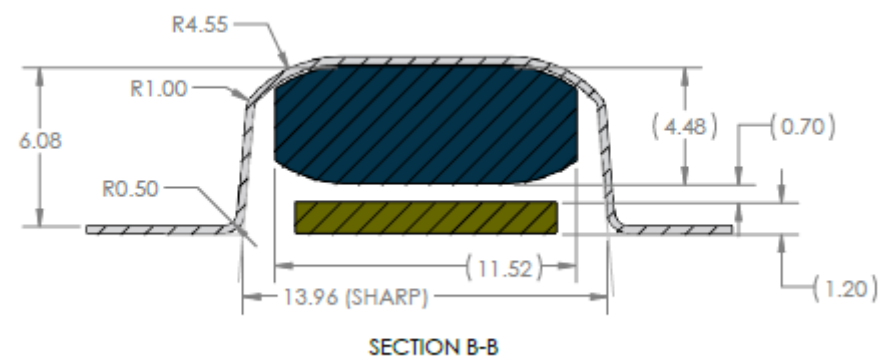
**Improvement in Blister MVTR**

**21%**

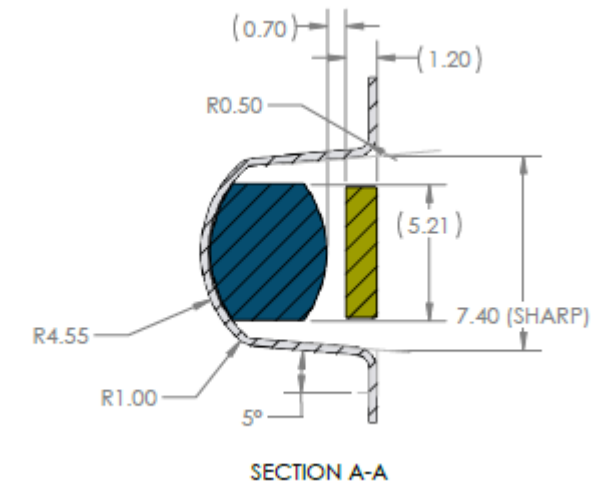
# Special designs geometries require different treatment



- Special forms and geometries like double capsules and Aptar CSP blisters are excluded from standard models.



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interaction. ideas. innovation.



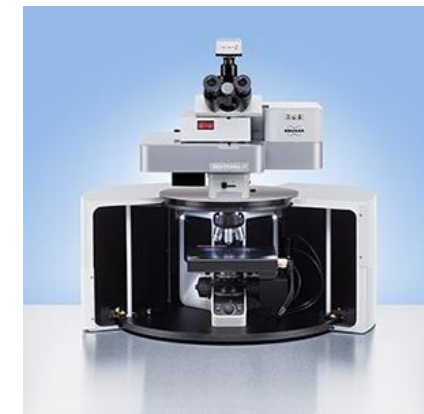
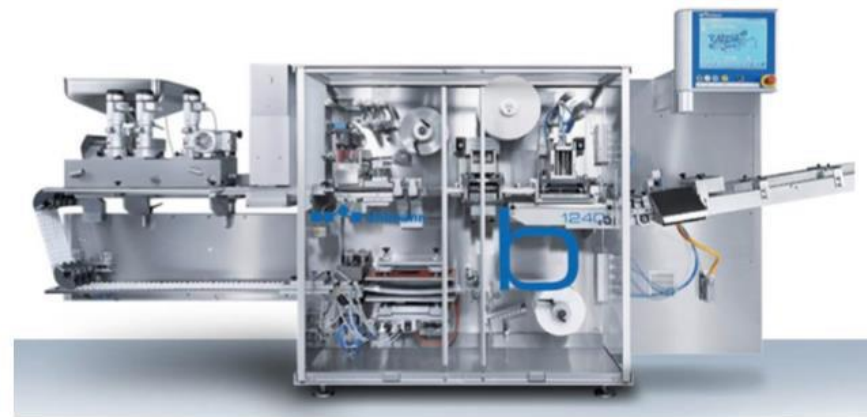
- All these special designs can be solved by kp and FTT using custom mode packaging design tab in *ASAPprime*® and **BlisterPro**® *XCEL* services



# Imagine: from design to prototype in one week



- The kp i.center team can design and prototype any package.
- Make samples for Child Resistance testing, Stability samples and other packaging analytical jobs like permeability or leachability in record time



Please visit us at: [https://www.kpfilms.com/en/Products\\_Solutions/Pharmaceutical\\_Packaging\\_Films-Pentapharm/Pentapharm\\_BlisterPro\\_XCEL\\_Services.php](https://www.kpfilms.com/en/Products_Solutions/Pharmaceutical_Packaging_Films-Pentapharm/Pentapharm_BlisterPro_XCEL_Services.php)

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