

LyoSeal®

ISLFD

14 April 2011

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Delivering Innovative Solutions

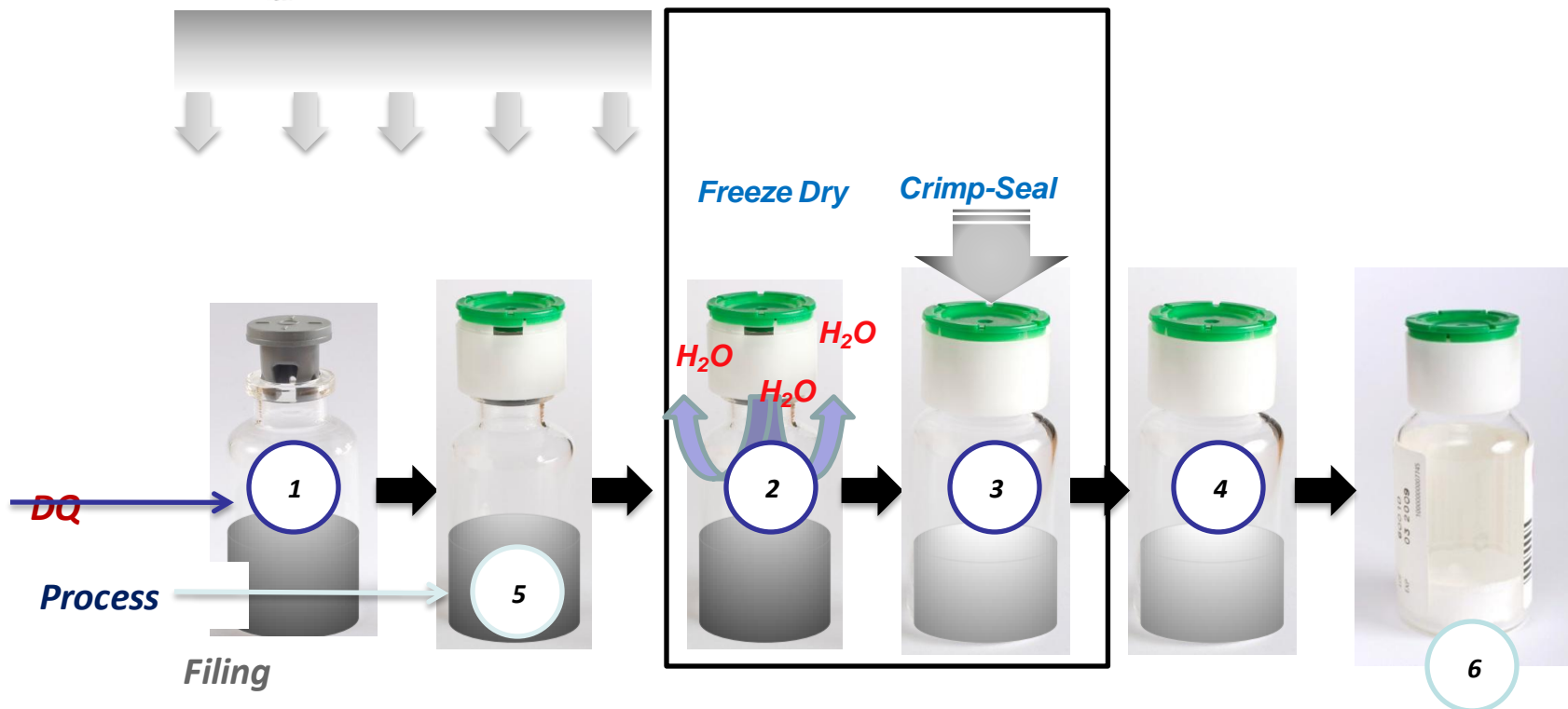
West Pharmaceutical Services and LyoSeal

- **2010: West and Biocorp sign an agreement under which Biocorp grants West an exclusive and worldwide license for sales and marketing of its LyoSeal™ family of closure products.**
 - **With the LyoSeal family of closure products, we are strengthening our product portfolio within our Injectable Container Solution platform. This platform includes West's industry leading products such as West FluroTec® barrier film, Westar® RS/RU stoppers, West Envision™ automated inspection, LyoTec™ stoppers and West Spectra™ and Flip-Off® seals.**
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LyoSeal[®]: Concept

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1	Compatibility with vials & closure	Compatible with standard ISO/GPI components
2	Incidence on sublimation	No incidence on validated lyophilization cycles
3	Crimping performance	100% crimping in F-Dryers 10 -450 sq.ft
4	Container closure integrity	CCI assessed Helium, μ Bio, P. decay & dim. challenge
5	Compatibility with Process	Gravity feed & Pick and Place
6	Regulatory filing	CBE 30



Validation - Crimping Performance

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20mm	Surface Area (m ²)	Capping Pressure (kg/cm ²)	% Crimping
GEA Lyofill	2	Nominal	100%
Klee	Pilot scale	Nominal	100%
Heraus	20	Nominal	100%
GEA Lyofill	20	0.7	99.73%
Steris	35	1.4	99.5
Telstar	45	1.2	100%

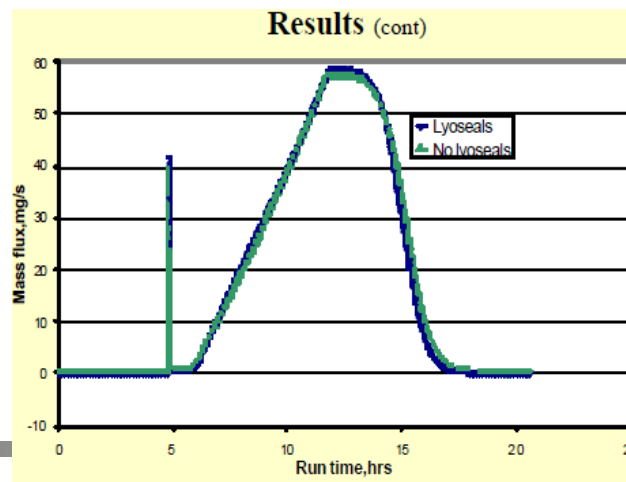


13mm	Surface Area (m ²)	Pressure (kg/cm ²)	% Crimping
IMA Edwards	45	0.9	100%

28mm	Surface Area (m ²)	Pressure (kg/cm ²)	% Crimping
Telstar	45	1.2	100%

Method		
Helium test		☑
Microbial Challenge	Sp Diminuta, E. Coli	☑
Vacuum Decay	- Container Closure integrity Study - Challenge Study - Aging study [ICH - 4C, 25C -, -20C, + 40C]	☑
Stacked tolerances Challenge		☑

Validation – Sublimation Rate



Data from poster presentation in Breckinridge 2008.
 Results from TDLAS
 S. Tchessalov, Hung-Chih Peng, C. Mohr, N. Warne
 Wyeth BioPharma, Andover, MA

QUALITY ASSURANCE

■ *Benefits of Early Container Closure Integrity*

- *Class A crimping*
- *Clean injection site*
- *Prevention of raised stoppers*
 - *Prevention of vacuum loss*
 - *Prevention of air ingress*
- *Prevention of crimping issues*

OPERATIONS

- ***Reduction of production cycle / burden***
 - ***Prevention of stopper sticking issues***
 - ***Suppression of the crimping work station & costs***
 - ***Suppression of class A costs***
 - ***Suppression of Aluminum caps preparation***
 - ***Reduction of staging and storage issues***
 - ***Reduction of downtimes***



LyoSeal 13 mm Validation (Proposed)

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TEST	METHOD	WORST CASE	REFERENCE
CLEANLINESS			
Bioburden	ISO 11737-1	n/a	WESTAR
Particulate matter	ISO 8871-3: 2003	n/a	WESTAR
Endotoxins	EUR. PH 2.6.14	n/a	WESTAR
Biocompatibility	X	n/a	DATA 20 mm
PERFORMANCE			
Sublimation	X		
Sterilization and drying	RH ≤ 0.2 % [80C-3 hr]		LYOSEAL 20
Crimping Performance	INDUSTRIAL FREEZE DRYER	LARGE FD Ø = 16mm	
Crimping: Temperature limit	CRIMPING TEST 5C-50C	n/a	
Terminal Sterilization	?		
CONTAINER CLOSURE INTEGRITY			
Microbial Challenge	PDA TECH REPORT 27		
Dye test	USP / EUR. PH.		
Helium test	WEST		
Vacuum Decay	ASTM 2338		
Stacked tolerance	X (INCLUDED IN EACH CCI VALIDATION)		
Aging Studies (After capping)	ICH Q1A (R2) / 37 MONTHS VACUUM DECAY [5 MICRONS]		

**BORDERLINE
STACKED
TOLERANCE**

**DEMANDING
STOPPER/ VIAL
COMBINATION**

**ALUMINUM
SEALS WITH LOW
RSF**



TEST	METHOD	WORSTCASE	REFERENCE
Misc.			
TRANSPORTATION (BULK)	VISUAL CONTROLS + PARTICULATE MATTER	TDB	n/a
TRANSPORTATION (AFTER CRIMPING)	?		
AGING (BULK) /SHELF LIFE	TDB [ICH – TEMP / UV]		
PRIMARY PACKAGING: CLEANLINESS	TBD	n/a	n/a
PRIMARY PACKAGING: SEAL INTEGRITY	ISO 11607, ASTM D882, F88, ISO 6383-1 INCLUDES SHELF LIFE [37 Mo]	PARAMETER BRACKETING	n/a