FACILITY FOCUS

Best Industry Practices for Retrofitting Legacy Filling Lines with RABS Barriers

3rd Annual DME Facility Focus Program

04/18/2018, 1:00 PM - 2:00 PM

Technical Conference Stage 1, Booth 1076, Exhibit Hall

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Speakers

Hite Baker Speaker/Moderator	• Principal Process Engineer • DME
Les Edwards Discussion Panel	• VP, Technology & Business Dev. • SKAN US, Inc.
John Erdner Discussion Panel	• VP, Liquid Fill • SP Scientific
Alexander Haig Discussion Panel	• Director, Engineering • Catalent, Inc.
Steve Nole Discussion Panel	• VP, Operations • Grand River Aseptic Mfg. (GRAM)
Max Cesarini Discussion Panel	• Max Cesarini, Global Sales Manager • Comecer S.p.A.

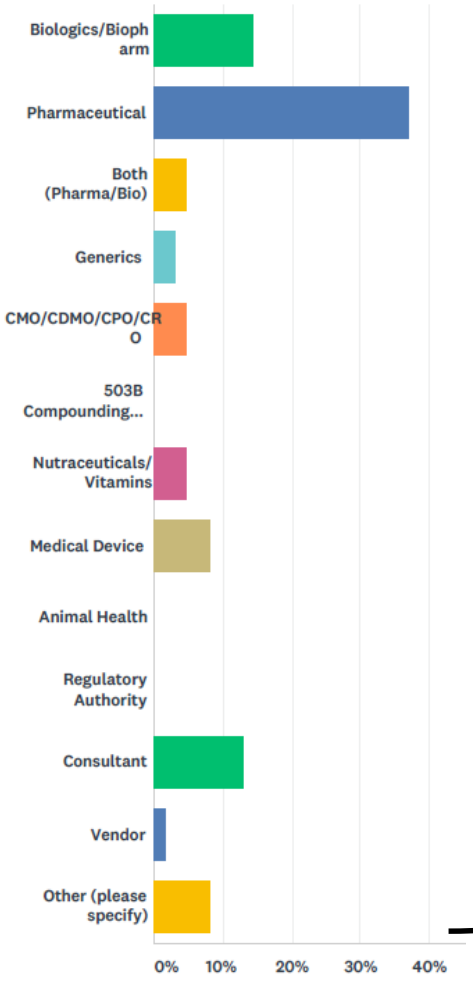
About DME Facility Focus

- 3rd Annual INTERPHEX 2018 Technical Education Program
- Surveys
  - Invited engineers, manufacturers, and other life sciences professionals like you to express views on trends and technologies affecting our industry.
  - Three Surveys, executed Q4 2017.
    - *Flexibility by Design: GMP Manufacturing for the Diverse Product Portfolio*
    - *Central Utilities for GMP Manufacturing: A Practical Dialog on Cost and Reliability*
    - *Best Industry Practices for Retrofitting a Legacy Filling Line with RABS Barrier*
- Whitepapers to be issued May 2018.
- Presentations with Distinguished Industry Panels.
    - *Flexibility by Design: GMP Manufacturing for the Diverse Product Portfolio*
    - *Central Utilities for GMP Manufacturing: A Practical Dialog on Cost and Reliability*
    - *Best Industry Practices for Retrofitting a Legacy Filling Line with RABS Barrier*

2017-18 Survey Results

Survey Participant Affiliation

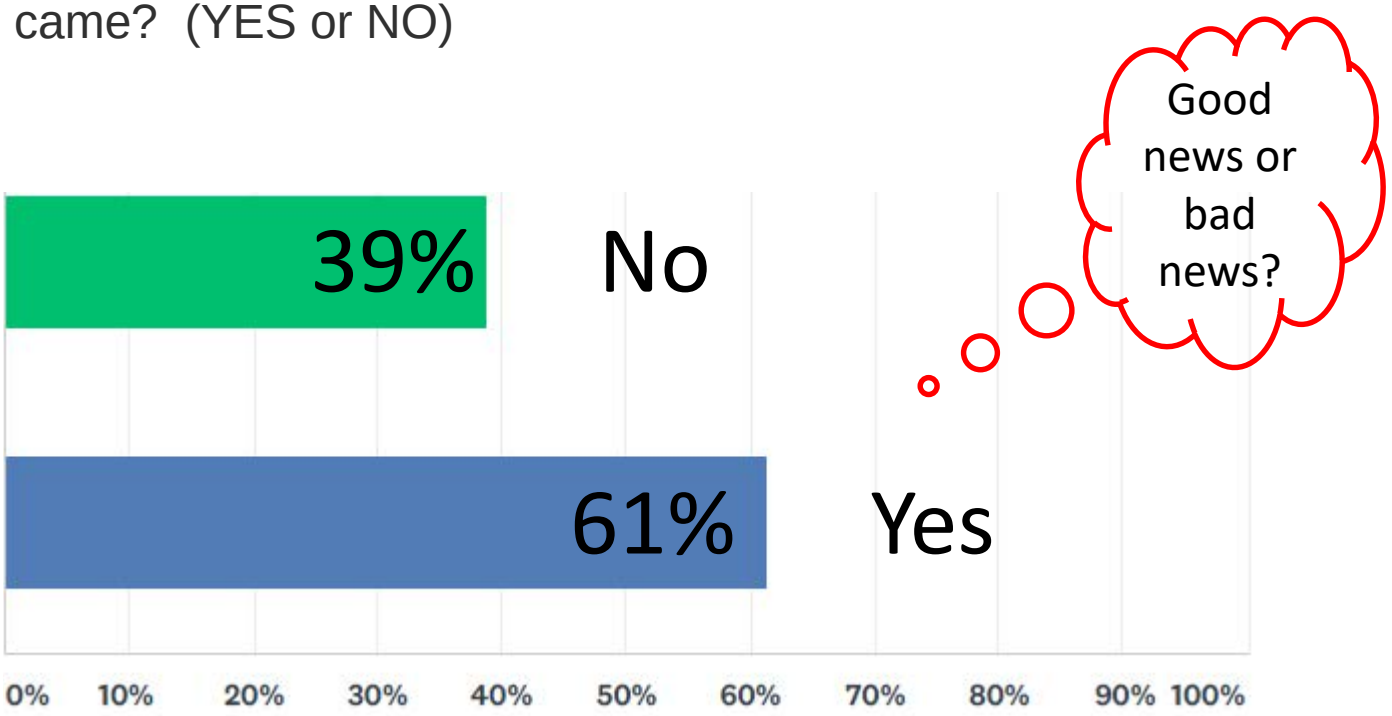
What is your primary affiliation?



BioPharm	15%
Pharmaceutical	37%
Consultant	13.%
SUBTOTAL	65%
THE REST	35%

Definition of “Compliant RABS”?

Does your company have an adequate definition of a “compliant” RABS (or an adequate definition of a “compliant” RABS retrofit), compliant in both design and operation, sufficiently understood to execute a successful RABS project if the time came? (YES or NO)



Elements of “Compliant RABS”

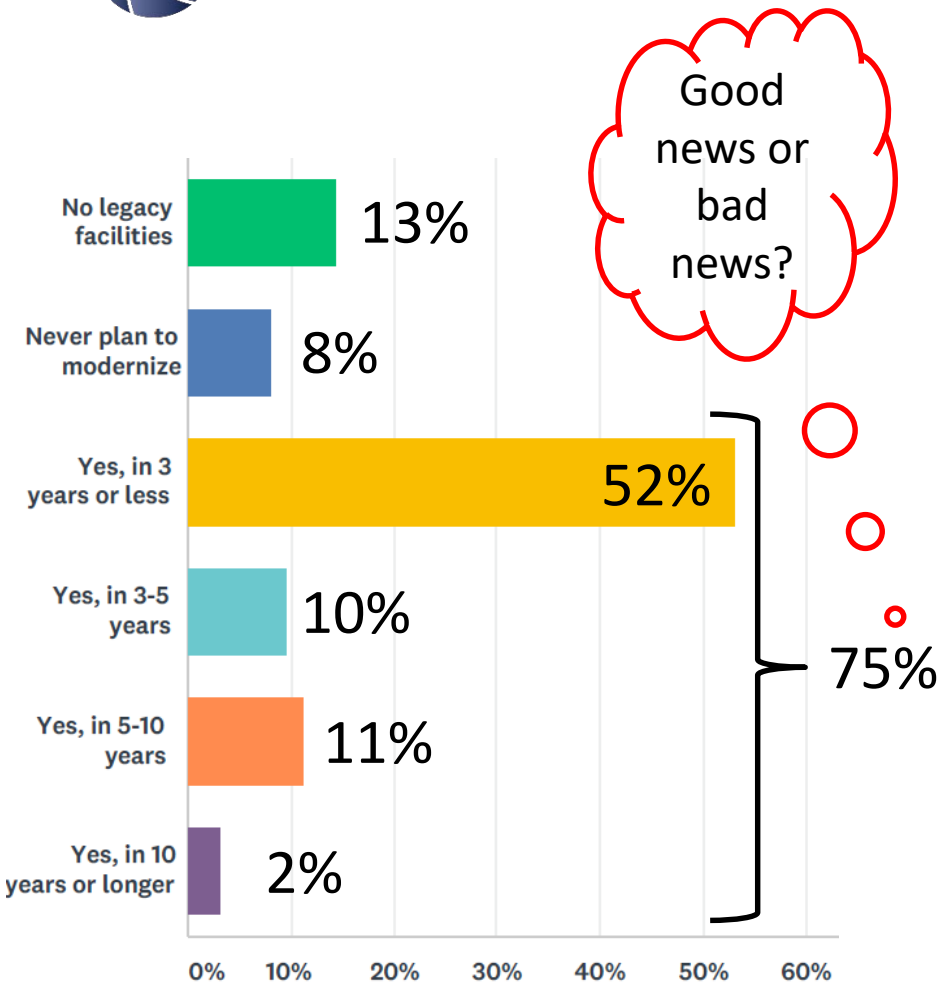
A high level view

Equipment Challenges		Facility Challenges	
RABS walls & doors	Plywood mock-up	Nested clean zones	Air changes / hour
HEPA air supply	Manual clean&decon	Facility programming	Transfers stopper etc
Grade A critical zone	Matls of construction	Enough head room	1-way gowning, MAL
Glove ergonomics	Hardware bits, hinge	Personnel AL & MAL	Repack vials, stopper
Closed door ops	Modifying old equip	Grade A door swings	Environ monitoring
Downtime	Set-up & changeover	Grade A passiveRABS	Grade B background
Transfers in/out		Smoke studies	

Is “Compliant RABS” Well Defined?

- What are the origins (or basis) of the definition of a “compliant RABS”?
- What are main elements of a “compliant RABS”?
- Why “closed door” operation the main element?
- What does 100% closed door operation mean?
- What are the remaining key elements to the design and operation of a “compliant RABS”?

Is Modernization Inevitable?

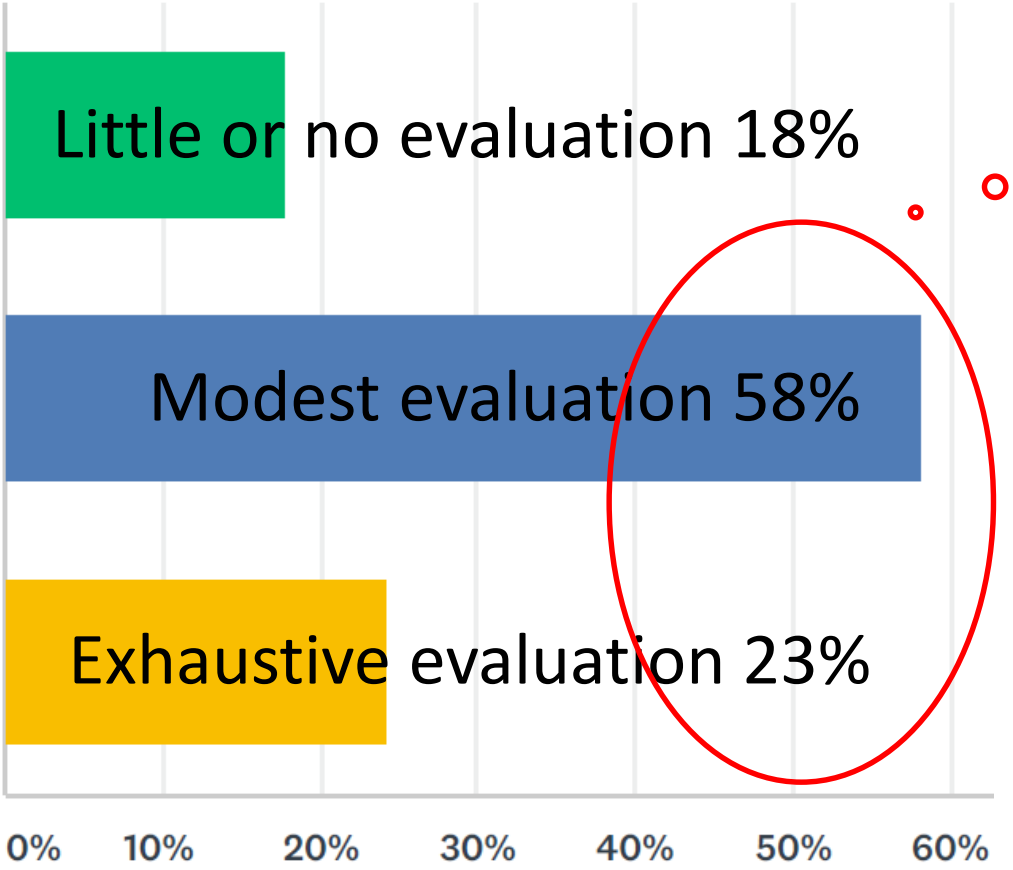


"Legacy sterile facilities" are defined as having filling lines based upon older conventional aseptic technology and/or have cleanrooms where gowned personnel enter directly into Grade A critical zones, and frequently do not meet cGMP's because sterile product and/or sterile components are exposed to gowned personnel and/or the surrounding environment. It is estimated there are 1000+ legacy sterile facilities in the world. Is it inevitable that your company must eventually modernize its "legacy sterile facilities" to use RABS-based or isolator-based filling equipment? (Check one)

GMPs versus cGMPs?

- GMP Regulation is law, cGMP guidance is “advice” … so why modernize?
- Does our industry actively believe that “protecting the product” is good business? Is it?
- Define “advanced aseptic technology” versus “conventional aseptic technology”.
- Do you believe legacy sterile facilities are living on “borrowed time”?

How Much Evaluation will be Needed to Decide between Isolators and RABS?

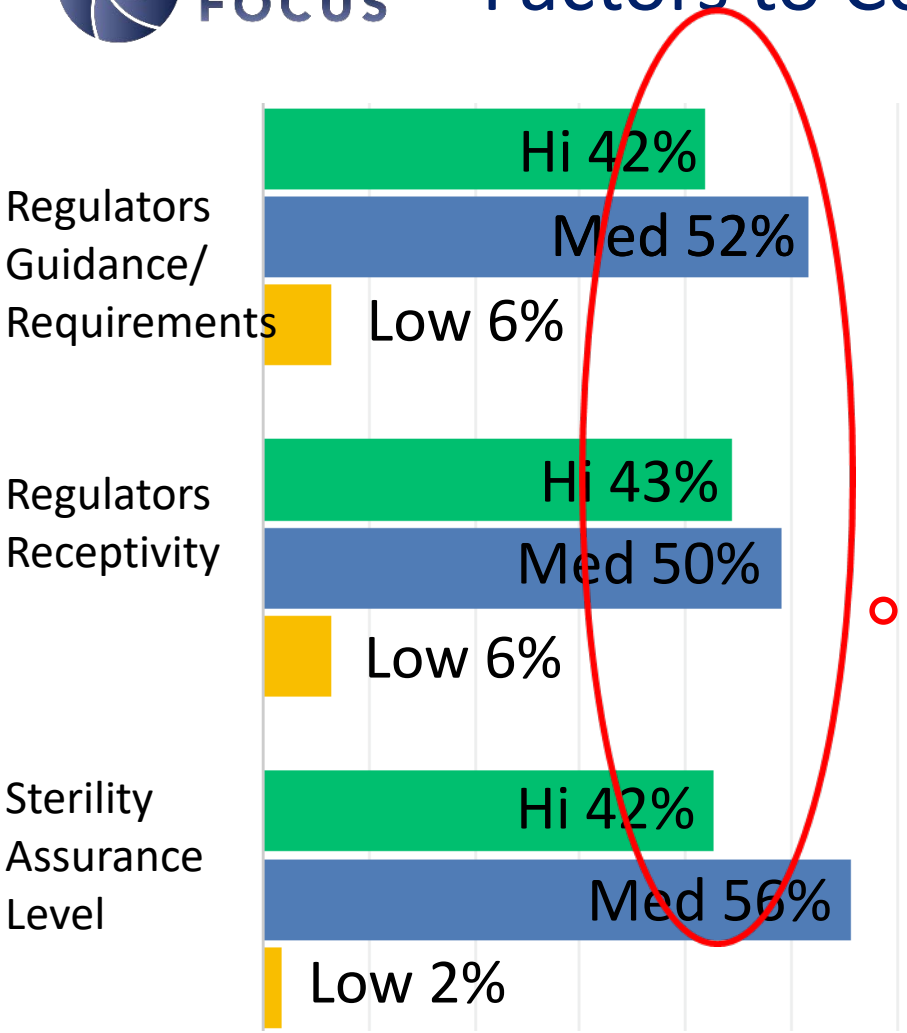


Good news or bad news?

If/when it becomes necessary to modernize your legacy sterile filling facility, would your company evaluate both Isolators and RABS before deciding which kind of barrier technology to use? (Check one)

Factors to Consider RABS vs Isolators?

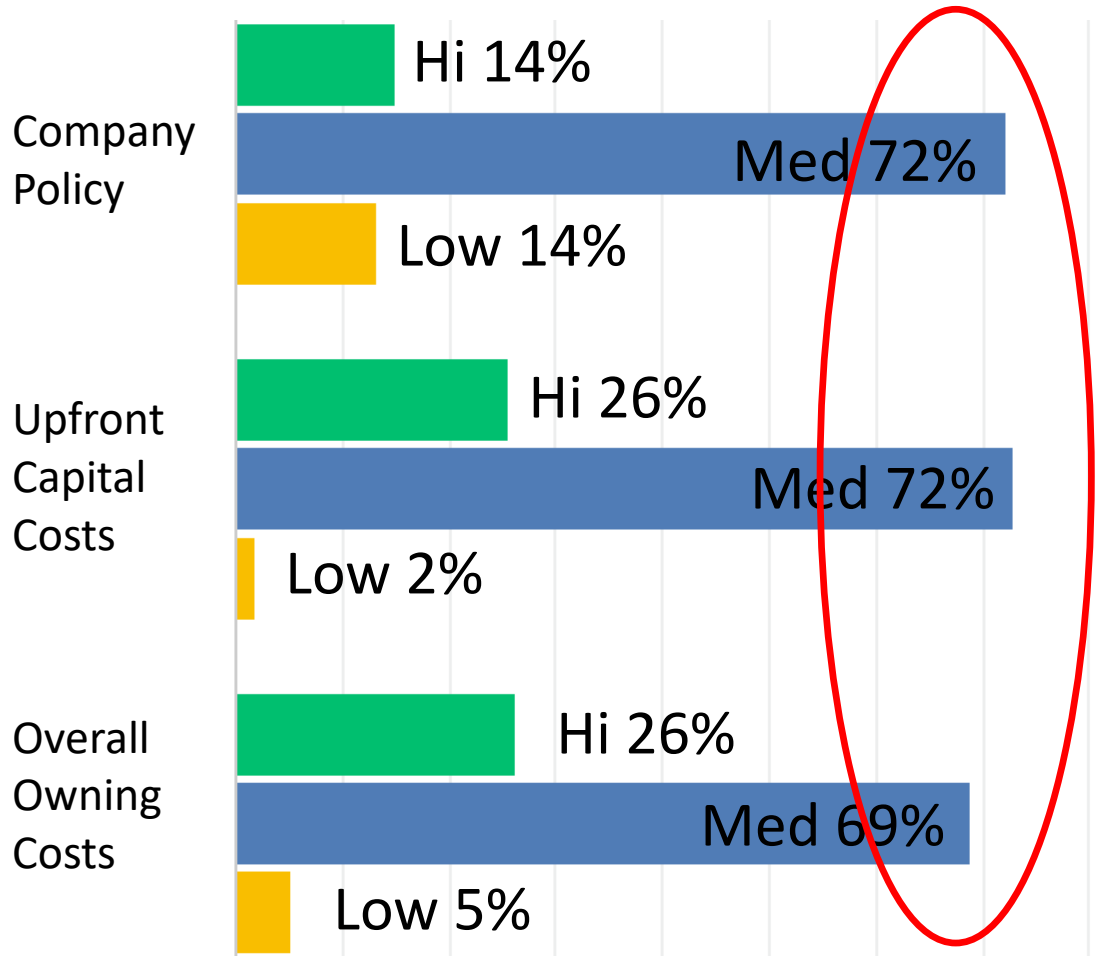
Regulatory Driver Factor Factors?



What are the Primary Factors to consider when deciding between RABS-versus-Isolators?(Rank high, medium, low)

Take home message: nearly everybody wants to do the right thing?

Factors to Consider RABS vs Isolators?

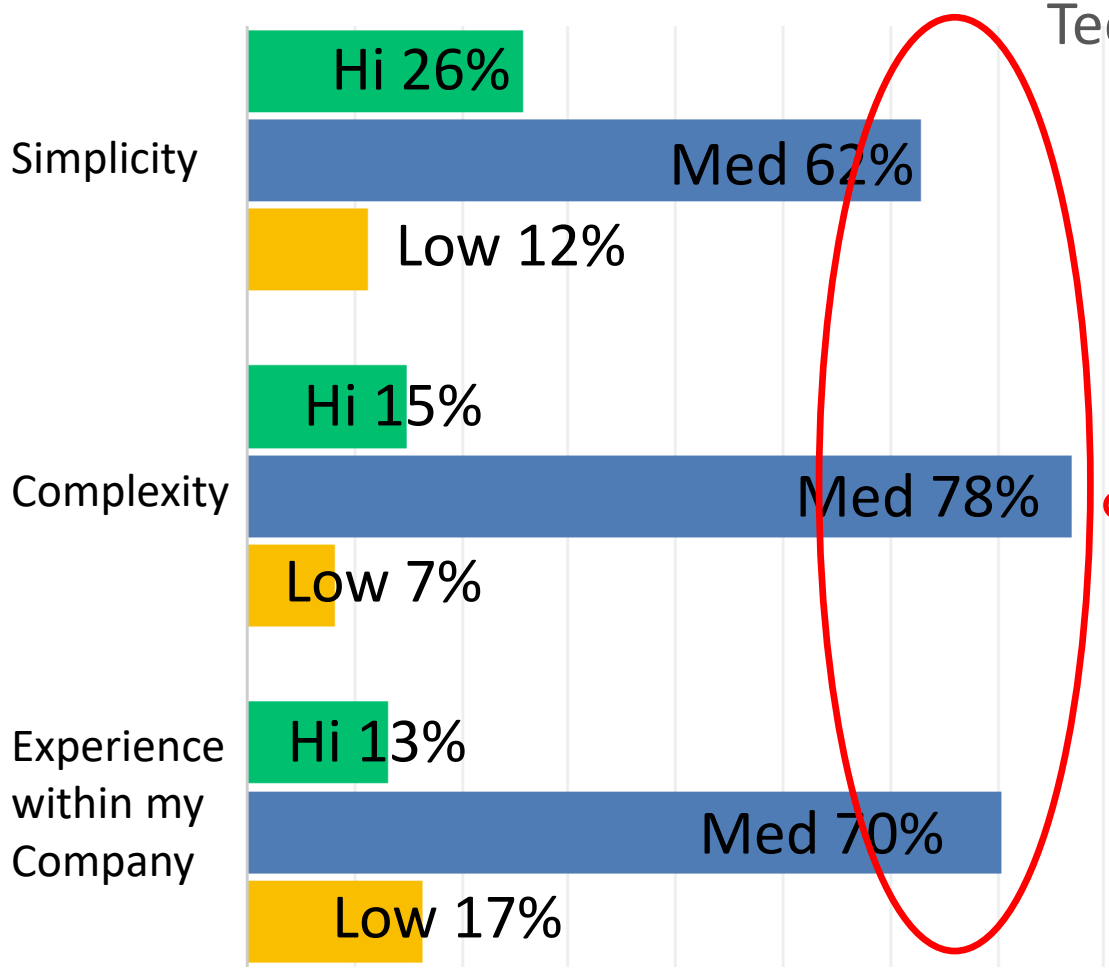


Policy/business Factors?

What are the Primary Factors to consider when deciding between RABS-versus-Isolators?(Rank high, medium, low)

What role are business factors playing in technology selection … large or small?

Factors to Consider RABS vs Isolators?



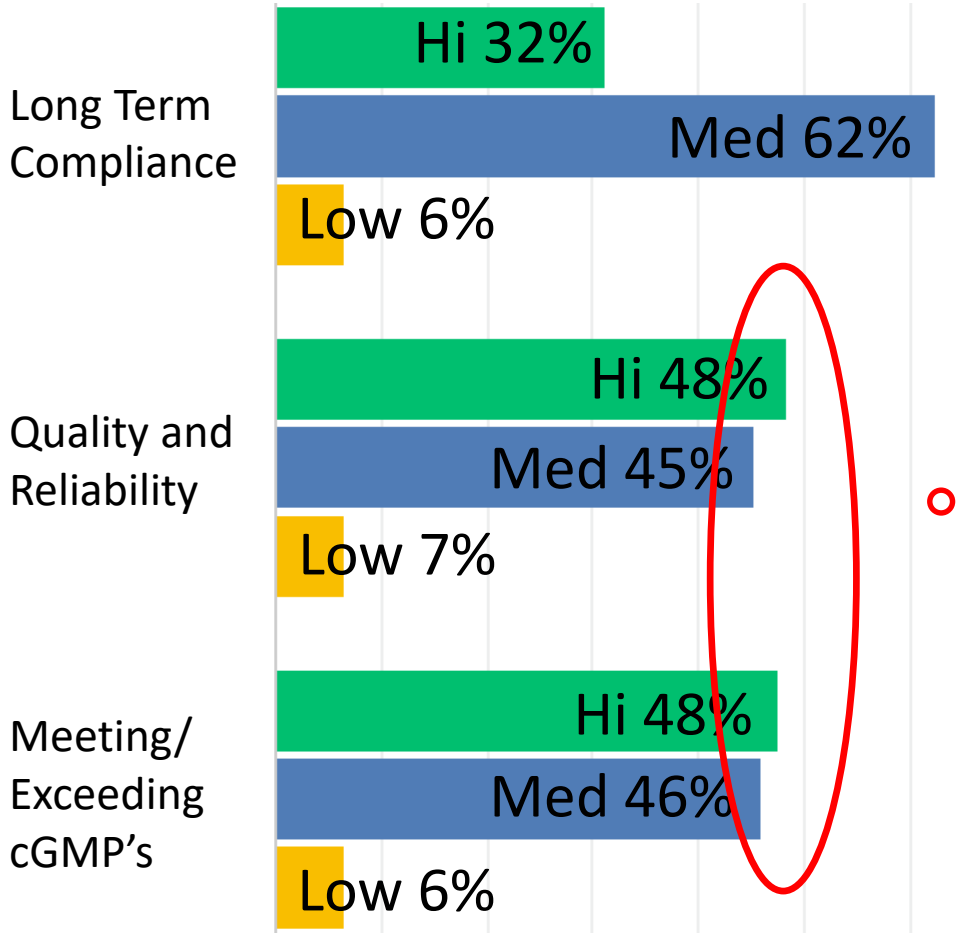
Technology Fear Factor?

What are the Primary Factors to consider when deciding between RABS-versus-Isolators?(Rank high, medium, low)

Are owners still cautious/ fearful of barrier technology? Should they be?

Factors to Consider RABS vs Isolators?

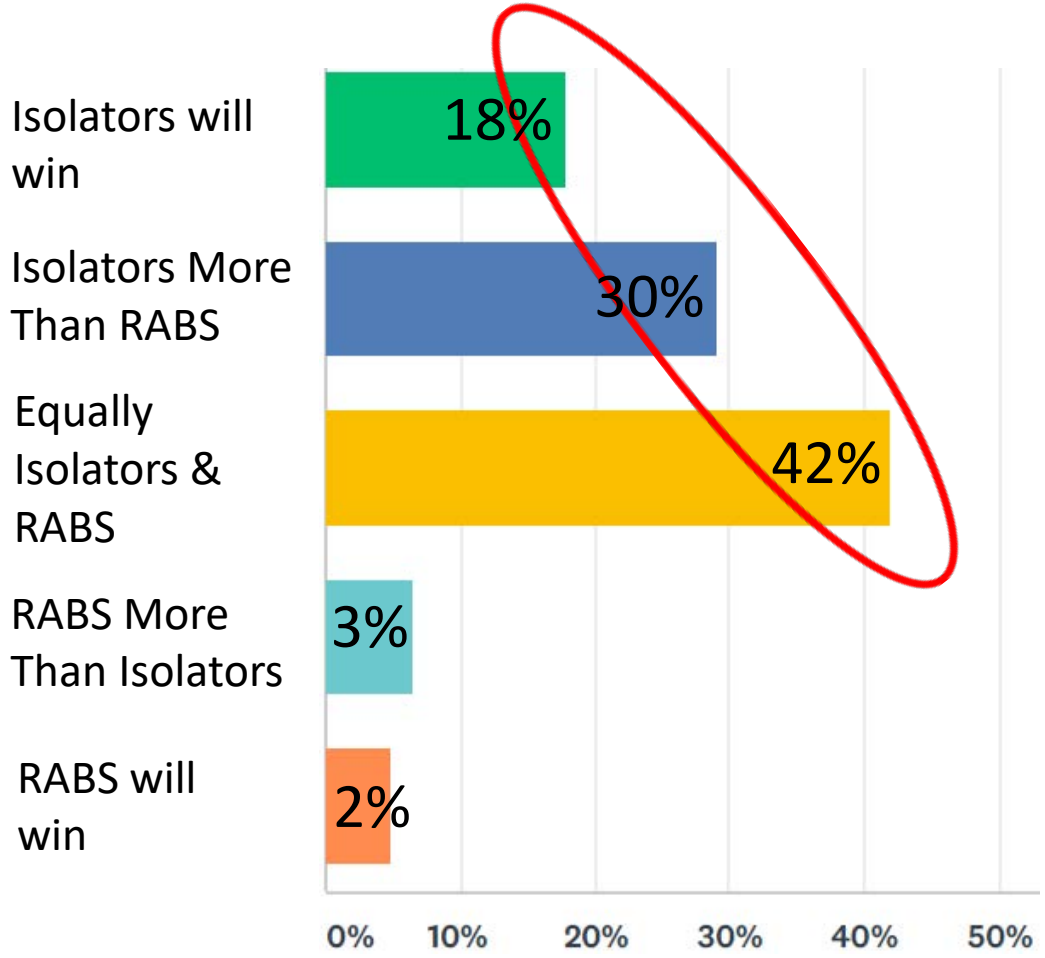
Regulatory Driver Factors?



What are the Primary Factors to consider when deciding between RABS-versus-Isolators?(Rank high, medium, low)

Good news … these are the highest rankings in the entire survey?

Where will Most Growth Occur: Isolators or RABS?



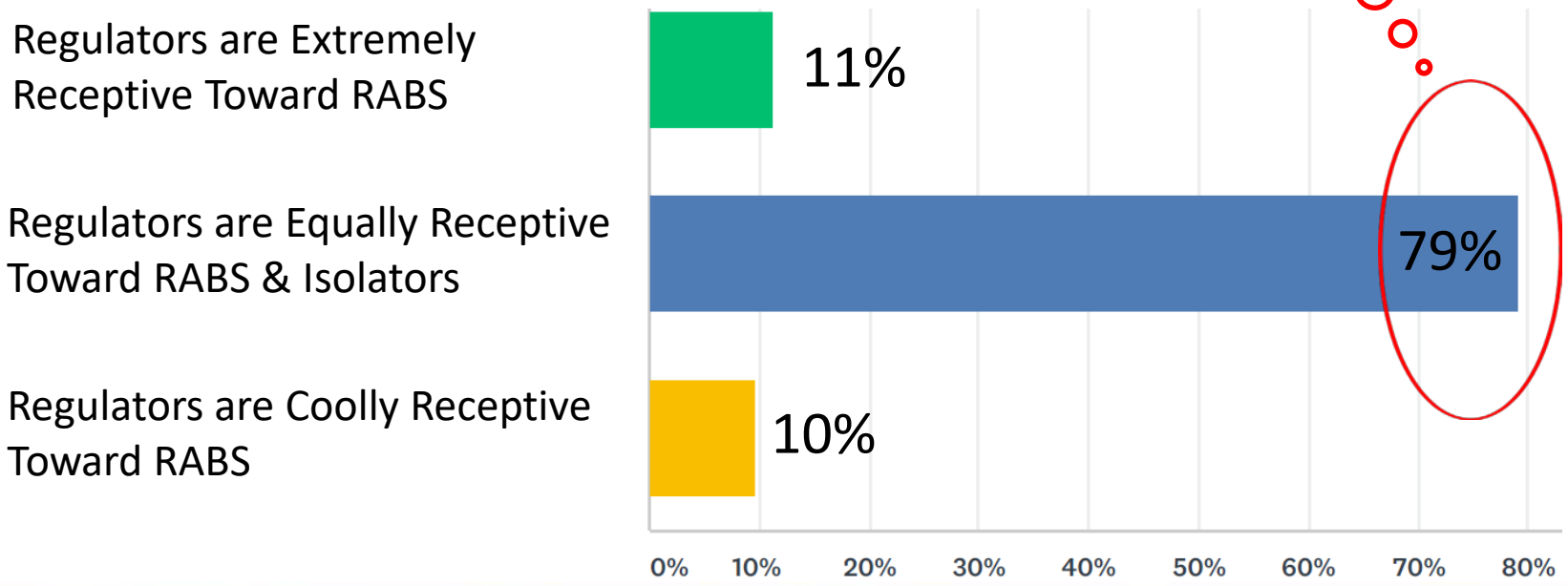
Who will win?

What is your perception, i.e. your prediction, whether RABS or Isolators will grow more in the next 5-10 years? (Check one)

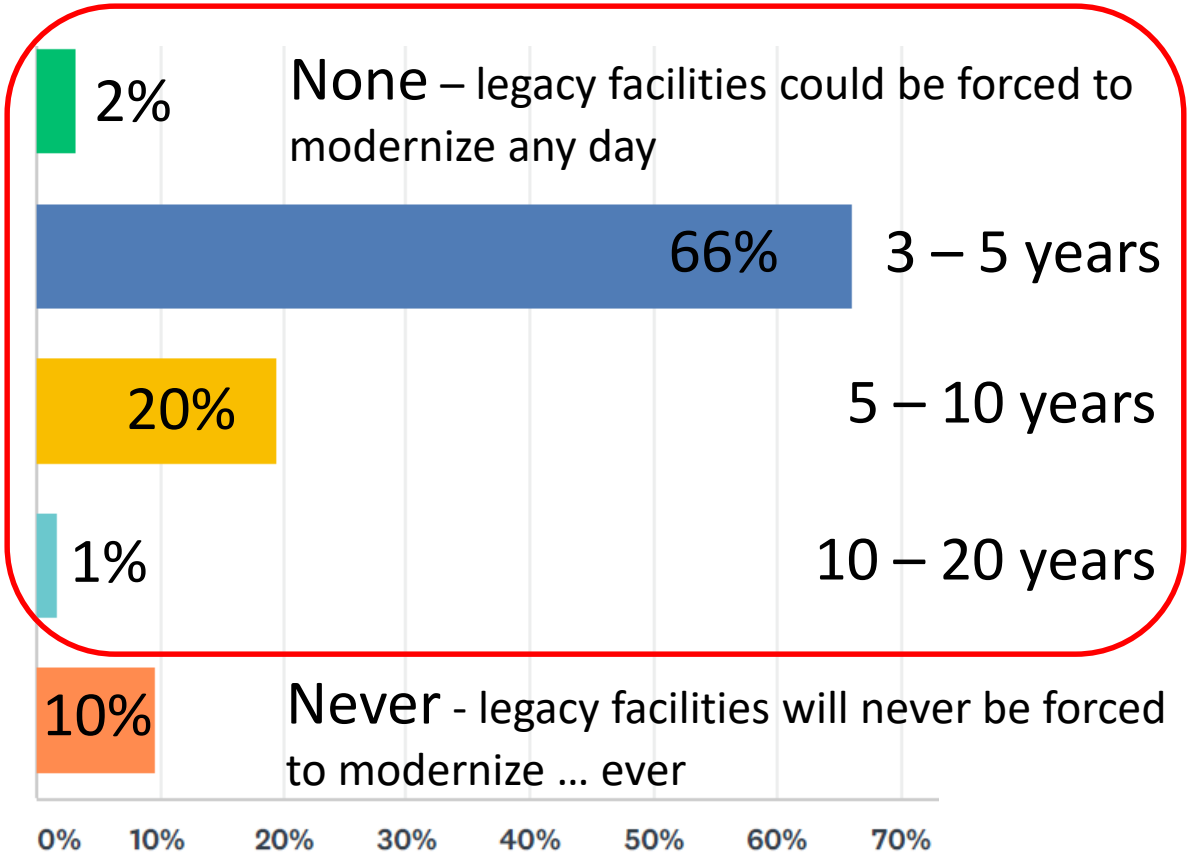
Are Regulators Receptive toward RABS?

How receptive do you perceive FDA/EU regulators are to RABS and RABS retrofits? (Check one)

When did RABS and isolators become nearly equally respected? Why?



How Much "Borrowed Time" do Legacy Sterile Facilities Have?



If legacy sterile manufacturing facilities are on "borrowed time" because they are falling farther and farther behind cGMP standards, how much time until they will be "forced" to modernize by regulators? (Check one)

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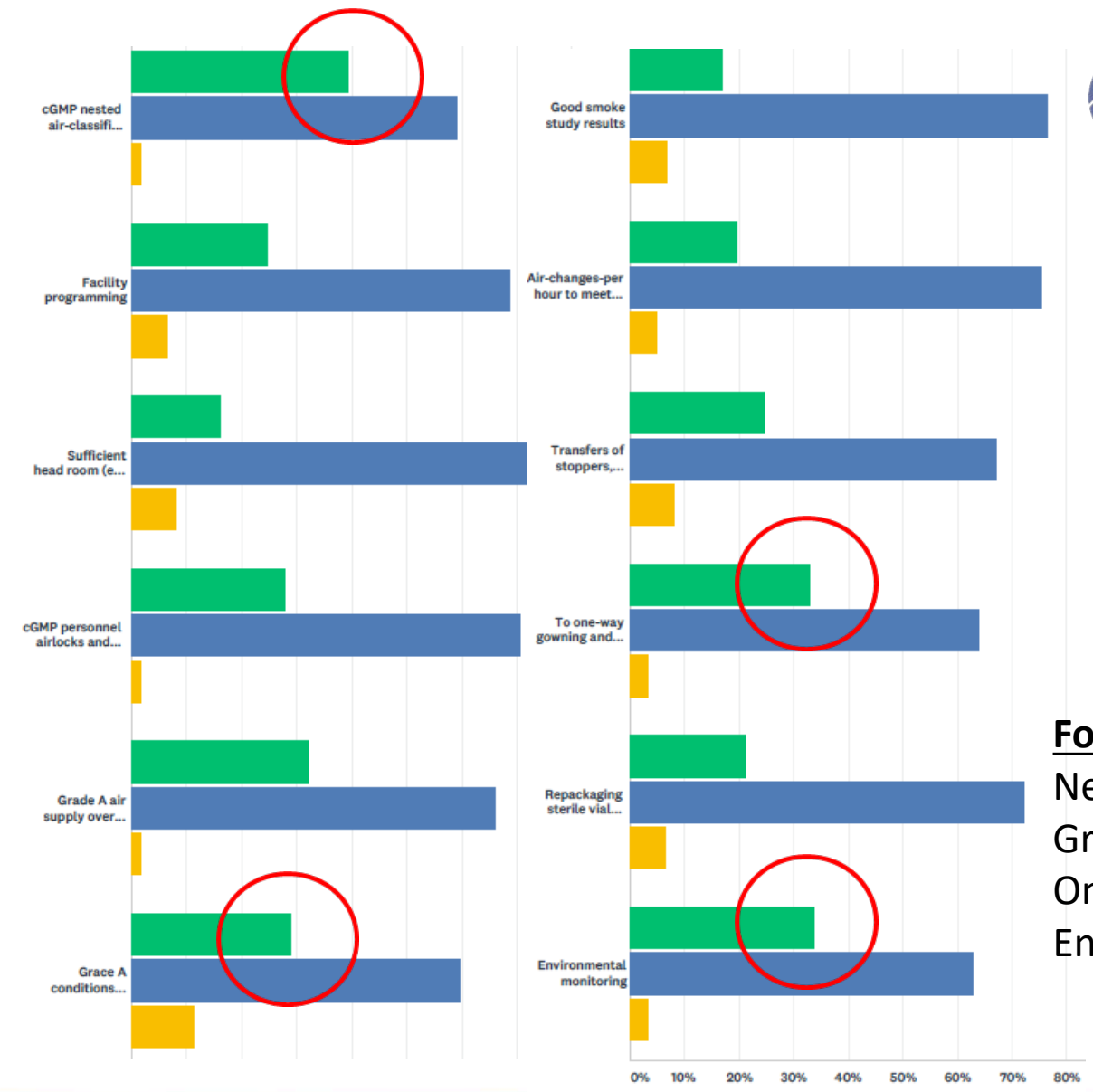
Equipment Challenges?

No big deal?

What are the primary equipment challenges for RABS retrofits?(Rank high, medium, low)

<u>Four Highest Retrofitting Challenges</u>

Achieving Grade A
Ergonomics of glove ports
Modifying legacy/ older equipment
Set-up and changeover



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Facility Challenges?

Mostly not a big deal?

What are the primary facility upgrade challenges for RABS retrofits? (Rank high, medium, low)

Four Highest Retrofitting Challenges

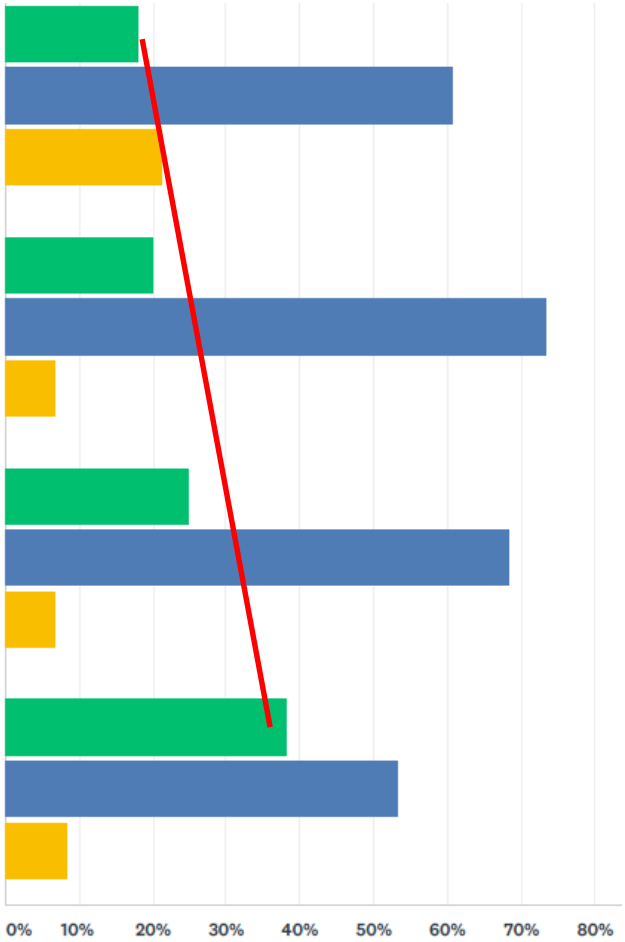
Nested cleanliness zones 40%

Grade A door swings 39%

One-way gowning and MALs 33%

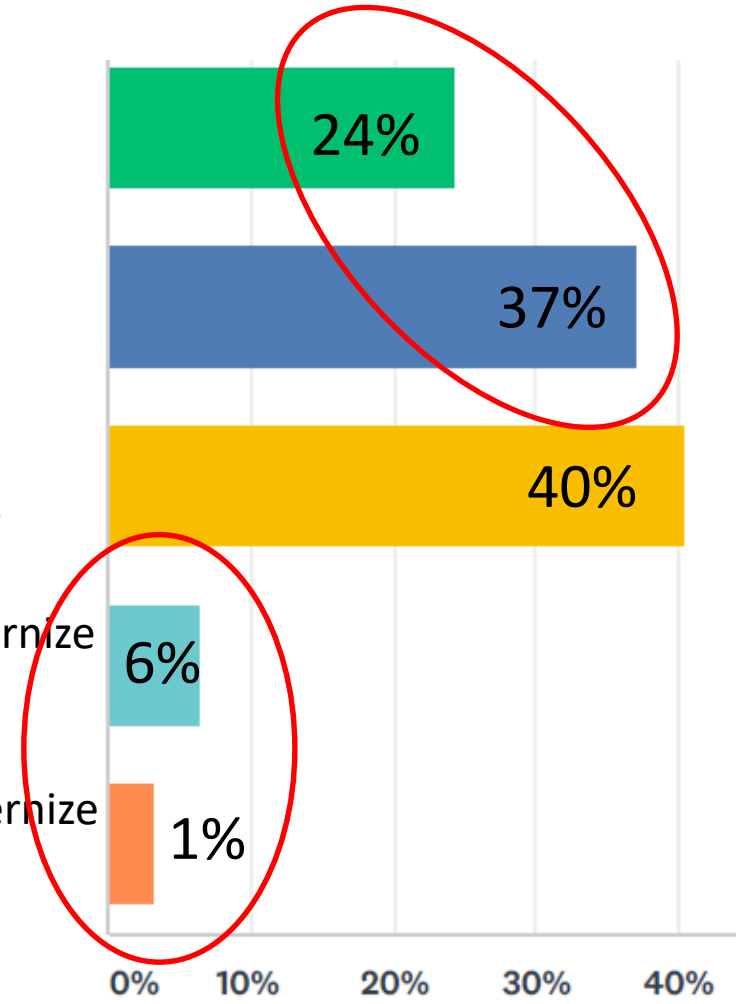
Environmental monitoring 34%

Preferred RABS Partners?



What preferred RABS supplier would you seek to assist you to conceive, measure-up, design, fabricate, install and qualify a new RABS enclosure onto a legacy filling machine?(Rank high, medium, low preference)

FDA Incentives



The FDA has provided incentives to modernize legacy sterile facilities that do not meet cGMP's for the past 10-15 years. These incentives generally take the form of increased scrutiny of legacy facilities, and less scrutiny and faster approvals for modern facilities using barrier technology (such as RABS and isolators) and automation to reduce direct human intervention. Are you aware the FDA provides incentives to modernize legacy sterile facilities?(Check all that apply)

Audience Input

- Was anything surprising?
- Any worries or concerns?
- What was useful?
- Did you change your mind about anything?
- What will you take back to your company?
- What did this survey miss?
- If the FDA were here, then what would you like them to learn from this survey?

Wrapup

- 2/3 majority feel that “compliant RABS” is sufficiently defined
- ¾ majority feel modernization is inevitable
- 80% + feel thorough evaluation of isolators vs RABS is still required
- 79% feel regulators are equally receptive to RABS or isolators
- Nearly 90% feel legacy sterile facilities are living on borrowed time
- Preferred RABS retrofit partners are equally divided among inhouse design, filling & isolator vendors and engineering firms
- Equipment and facility challenges for RABS retrofits do not seem to be a big deal
- FDA incentives to modernize legacy sterile facilities are not well known or understood, nor effective

For More Information

- Acquire DME Facility Focus survey whitepapers and copies of this presentation!
  - Available at www.dmeforlife.com/about-us/facility-focus after INTERPHEX.
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