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A Practical Approach to Media Fills

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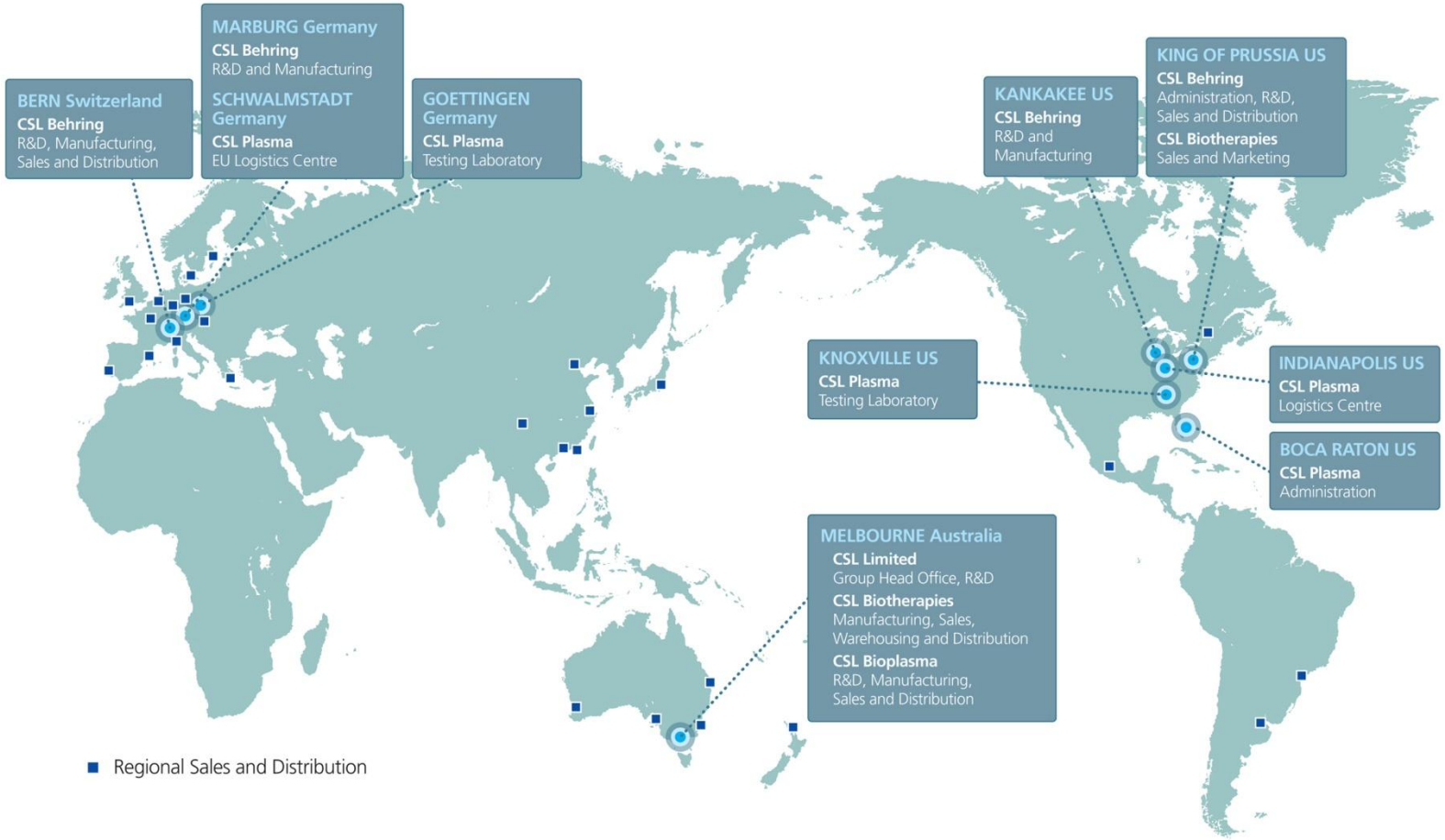
CSL - Global Biopharmaceutical Company

- Leading manufacturer in the plasma protein industry
- Major manufacturer in the influenza vaccine industry
- GARDASIL® licence of key HPV intellectual property

Geographically balanced sales

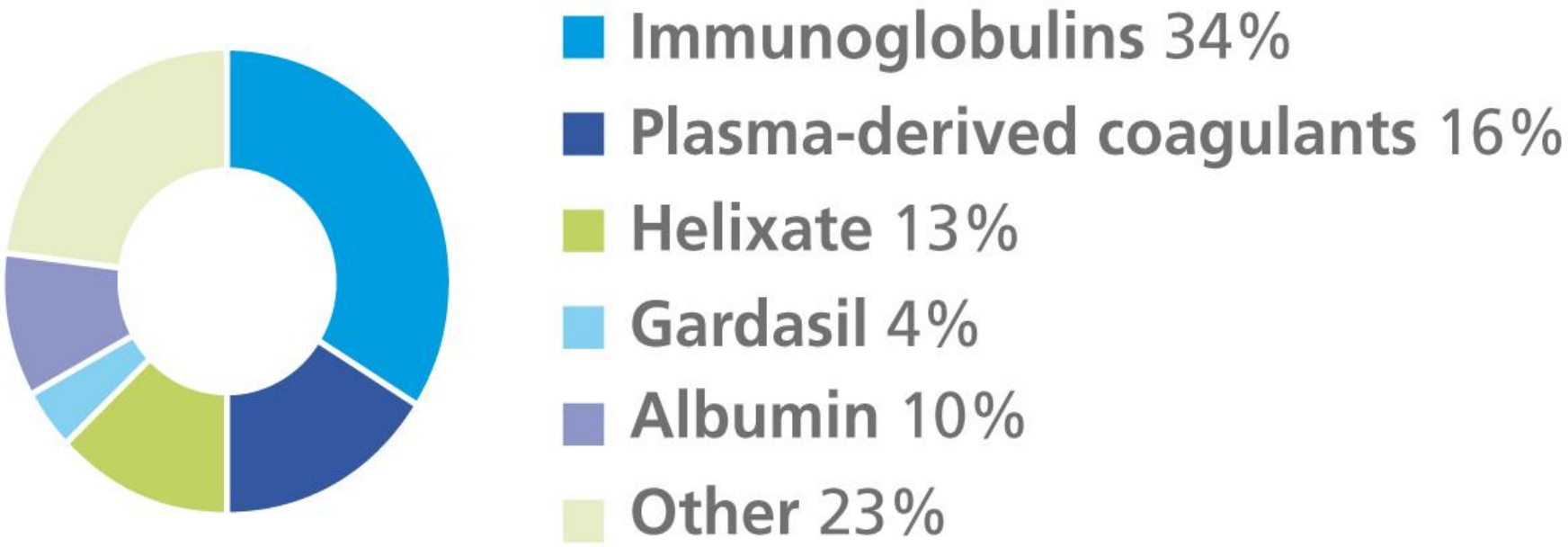
- North America 38%
- Europe 30%
- Australia 15%
- Asia 9%
- Other 8%

CSL's Global Network



CSL employs over 10,000 staff in 27 countries

CSL Group Sales by Major Products



CSL R&D Vision - We are dedicated to developing important, new protein-based medicines that save lives by preventing or treating serious medical conditions.

A practical approach to medial fills

- Regulatory requirements/guidelines
- Media fills – just one part of the equation
- Key elements of a media fill
- Bracketing
- Interventions
- Planning for a media fill
- Media fill protocol
- Executing the media fill

Key Pharmaceutical Regulations

- Annex 1 – PIC/S Guide to Good Manufacturing Practice for Medicinal Products
- FDA Guidance for Industry – “Sterile Drug Products produced by Aseptic Processing – cGMP”
- PIC/S: PI007-6 – “Recommendation on the Validation of Aseptic Processes”

Media fills – just one part of the equation

Media Fill

Personnel Qualification & Training

Aseptic Process

"Other"

Cleaning

Buildings & Facilities (HVAC)

"Validation"

Key elements of a media fill

- Number and frequency of runs
- Number of units to be filled
- Container size
- Fill volume
- Filling/Line speed – min/max
- Duration of media fill
- Environmental monitoring activities
- Interventions/worst case conditions
- Final incubation/visual inspection

Bracketing

- If applicable, bracketing can be your best friend and can be applied for the following:
  - Container/vial size
  - Source vessels
  - Filling speeds
  - Freeze dryers
  - Hold points
  - Other, based on your specific needs

Interventions

- Interventions pose a significant risk to the aseptic process
- Most interventions involve some form of operator involvement
- Interventions can be classified as: routine or non-routine
- Use a risk based approach to determine the frequency that interventions will be validated
- Validate both the intervention and the operator
- Consider those interventions that do not/have not happened before – plan and validate for the unexpected

Planning for a medial fill

- Begin planning well in advance as media fills do not occur regularly and can be a costly and time consuming exercise
- Consider if bracketing strategies can be applied to reduce the frequency of conducting media fills
- Include all routine requirements as well as taking the opportunity to plan for the future
- Ensure all staff are aware of their involvement in the media fill as part of their qualification program
- Document the requirements of the media fill in a protocol in accordance with your media fill master pan

Media Fill Protocol

- Any media fill should be considered as a validation activity
- Clearly define all aspects of the aseptic process that will be covered by the media fill (especially interventions)
- Ensure acceptance criteria is well defined, including actions to be undertaken in the event of a failure
- Communicate the details of the protocol to all staff involved
- Capture any requirements that are specific to the media fill and not part of routine operations
- Cross-check against your media fill master plan to ensure you have addressed all requirements

Executing the media fill

- Consider the benefit of recording the media fill for training and investigative purposes
- Allow adequate time to capture all the requirements as detailed in your media fill protocol
- Conduct extensive monitoring during the media fill to help identify areas of improvement
- Learn from each media fill to improve the next one

Thank you