Agency for Science, Technology and Research
SINGAPORE

Biologics Pharma Innovation Programme Singapore (BioPIPS)

Grant Call for Compliant Agility

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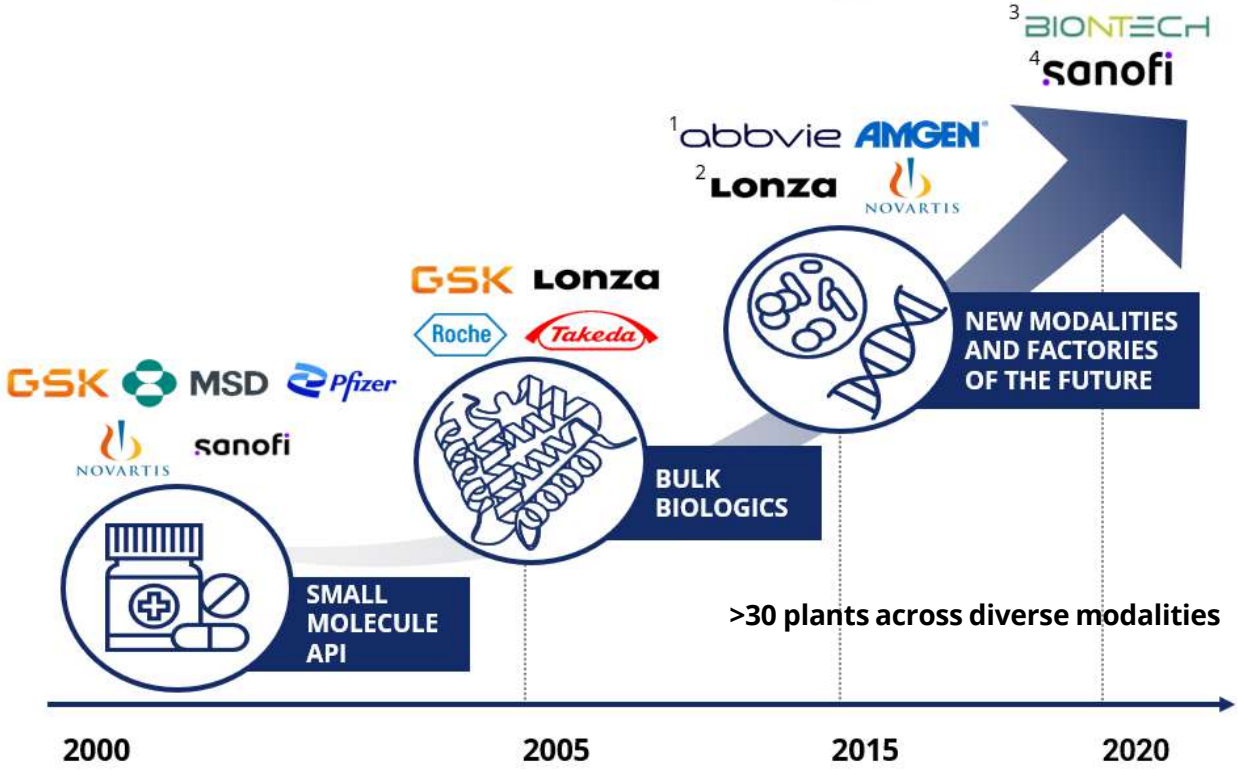
Biopharmaceutical Manufacturing in Singapore



1. Cell therapy CDMO (Contract Development and Manufacturing Organisation)
2. First-of-its-kind SUT (Single Use Technology) facility globally
3. mRNA facility
4. Modulus Facility

2023 BIOPHARMA SECTOR PERFORMANCE

Manufacturing Output

S$14.6B

Value Add

S$9.4B

Employment

>9,100 employees

Multi-Pronged Strategy

Helping companies meet new needs and enhancing Singapore's competitiveness

Technology

Driving productivity, encouraging introduction of new products and enabling manufacturing of new modalities

Strengthening existing manufacturing base via process and technology innovations

Preposition Singapore for manufacturing of new therapeutic modalities

Manpower

Growing and strengthening our base of manufacturing talent

Preparing an industry-ready workforce

Equipping workers with the right skills through local and overseas on-the-job training

Enabling workers to build a career across various levels of experience

Infrastructure

Providing industry with innovative capacity solutions

Increasing outsourced development and manufacturing capacity in Singapore

Providing flexible infrastructure options

Supplier Ecosystem

Diversifying the supplier and supply chain ecosystem

Identifying critical supply gaps in the supplier ecosystem

Encouraging new suppliers who can meet these needs to set up in Singapore

Sustainability

Supporting sustainable growth and operations in Singapore

Advancing decarbonisation pathways for industry

Expanding capabilities in circular economy

Growing an enabling environment to support sustainability needs

About BioPIPS

Objectives

Leverage public sector R&D capabilities to –

- ***Address problem statements*** from local biologics manufacturing facilities
- ***Enhance manufacturing productivity and operational efficiency***

Desired Outcomes

Transform the existing biologics manufacturing operations in Singapore so that the manufacturing sites are –

- ***Best-in-class*** within their respective manufacturing network
- Well positioned for the ***introduction of new products and novel manufacturing technologies***

Case for BioPIPS

Leverage strong foundation to launch BioPIPS

- ***Synergies*** in operations, resources, learning and collaboration of technologies with PIPS
- ***Interest*** from companies to form the consortium

Definition of Workstreams through Industry Roundtable Discussions

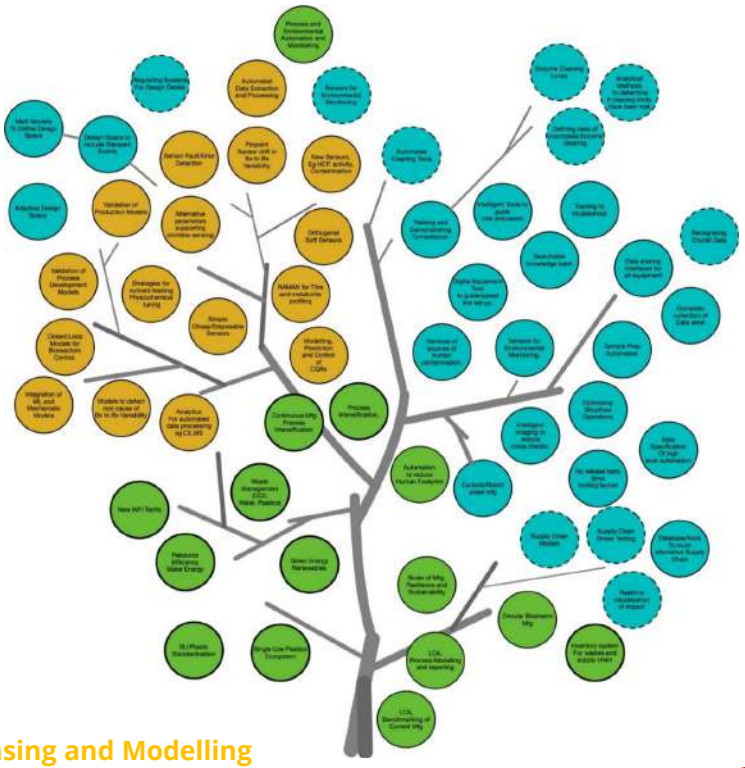
BIONTECH GSK sanofi

These workstreams are generated through discussion to address the dual challenge of (1) Directing research to improve productivity of existing manufacturing capabilities and (2) Exploring solutions to fundamentally improve the long-term resilience and sustainability of vaccines and biopharmaceuticals manufacture.

Sensing and Modelling – focuses on generating fast, in-process and automated workflows to translate process performance into actionable knowledge. Specifically, the aim is to improve the accuracy and robustness of sensing technologies and facilitate the incorporation of AI and modelling approaches into manufacturing processes to enable quicker and more effective product and process control.

Sustainability – focuses on technologies to achieve sustainability targets. These include using models to identify bottlenecks in manufacturing and supply chain, exploring impact of new technologies to reduce resource utilisation and re-thinking the expanded utility of single-use equipment through the lens of materials science and circular economy considerations.

Compliant Agility – focuses on removing manual tasks to achieve greater productivity in the manufacturing facilities while maintaining compliance status by using solutions, e.g. robotics and advanced analytics.

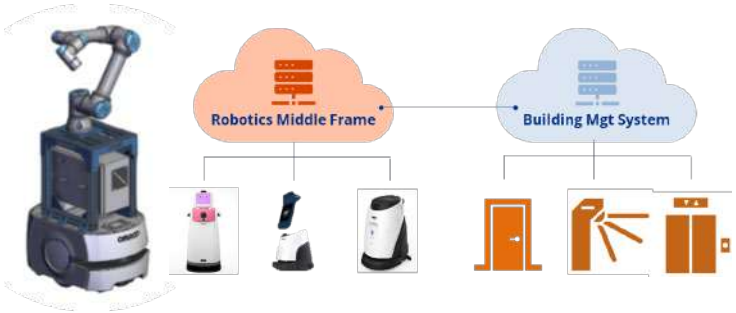


Sensing and Modelling
Sustainability
Compliant Agility

Compliant Agility

Underpinning medicine supply is the trust in the efficacy and safety of the manufactured products which need to comply to regulations. In the **Compliant Agility** workstream, the focus is on **removing manual tasks** to **achieve greater productivity** in the manufacturing facilities while **maintaining compliance** by using solutions, e.g. robotics, automation and advanced analytics.

Bioprocessing facilities require stringent cleaning and disinfection protocols to maintain Good Manufacturing Practice (GMP) standards. Cleanrooms, which are crucial for bioprocessing, need regular cleaning and disinfection to ensure product quality and safety. These tasks, while essential, are manual and laborious activities which divert the attention of trained production personnel from more critical functions.



Classified zones	Frequency	Maximum permitted number of particles per m³ equal to or greater than the tabulated size			
		At Rest		In Operation	
		0.5 µm	5.0 µm	0.5 µm	5.0 µm
Grade A	During critical operation	3,520	10[2]	3,520	10[2]
Grade A Supply	During critical operation or Weekly[1]	3,520	20	3,520	20
Grade C	Weekly / Monthly	352,000	2,900	3,520,000	29,000
Grade D	Monthly	3,520,000	29,000	35,200,000	290,000

[1]At least once per working week (in static condition) for Grade A LAF and BSC when there is no critical operation.
[2]Action level for Grade A isolators reduced by 50% due to presence of 3-way valves which influenced the recovery of particles as per VQD-REF-023283 v1.0 Interim status report on the Total Particle Tubing Qualification as per Requirement EU Annex 1 2022.

Defect Detection of Single-Use Systems

Problem Statement

The growing use of single use (SU) assemblies and bags in biomanufacturing has improved operational flexibility and reduced cleaning demands. However, it has also amplified the need for robust and reliable quality assurance. SU systems remain vulnerable to defects which can compromise product quality, process continuity and regulatory compliance. These defects often require extensive manual visual inspection which is labour intensive, operator dependent and susceptible to variability. As regulatory expectations increasingly demand objective evidence of inspection quality, there is pressing need for reliable and automated inspection solutions capable of detecting these priority defects before SU assemblies enter manufacturing processes. Advanced inspection technologies and other automated technologies will strengthen manufacturing consistency, reduce waste, support compliance and improve the reliability and safety of bioprocessing operations.

Defect Detection of Single-Use Systems

Objectives

This grant call seeks proposals to develop solutions which can –

1. **Automate the detection of defects** within SU assemblies and bags, in particular for those listed below (see Annex A for details) but not limited to –
   a. Incomplete or mis-assembly, such as missing or incorrect components, improper component orientation
   b. Incomplete points of sealing, e.g. port seal and film seal
   c. Embedded particles (>100 µm present in SU assemblies or bags)

2. **Improve repeatability and reduce operator variability** associated with manual visual inspection through the use of, but not limited to, imaging, computer vision, machine learning, optical sensing, spectroscopic methods or other relevant detection modalities

3. **Support regulatory compliance** by generating objective, reproducible inspection records suitable for GMP or regulated bioprocessing environment

Defect Detection of Single-Use Systems

Scope

1. **Defect Characterisation and Data Handling**
    a. Focus on technologies capable of detecting defects
    b. Solutions may involve, but are not limited to, imaging, computer vision, machine learning, optical sensing, spectroscopic methods or other relevant detection modalities
    c. Design systems to inspect SU components prior to use in manufacturing operations, including pre-installation, post-installation (before use) of SU components
    d. Micro-defects or pinholes detection is **out of scope**

2. **Technology Development and Integration**
    a. Develop and validate automated inspection systems for real-time or near-real-time detection of macro-level SU defects
    b. Consider ergonomics, throughput and ease of integration onto existing shopfloor workflows
    c. Ensure compliance with relevant standards and practices expected in GMP or regulated bioprocessing environments

3. **Usability, Reliability and Data Output**
    a. Demonstrate improved inspection consistency and efficiency (20%) over manual visual inspection
    b. Offer traceable and auditable inspection data output
    c. Explore user interface designs to support operator adoption and minimise training burden

Defect Detection of Single-Use Systems

Desired Outcome (in order of importance)

1. Reliable, validated and automated inspection technologies capable of detecting critical SU system defects

2. Enhanced detection accuracy and earlier identification of defects to reduce waste and prevent SU in-use failure

3. Reduction in inspection labour hours and human variability to improve operational efficiency

4. Improved compliance readiness through objective inspection data and consistent documentation

5. Scalable solutions for adoption by end-users to elevate quality assurance practices across the bioprocessing value chain

Defect Detection of Single-Use Systems

Specifications (in order of importance)

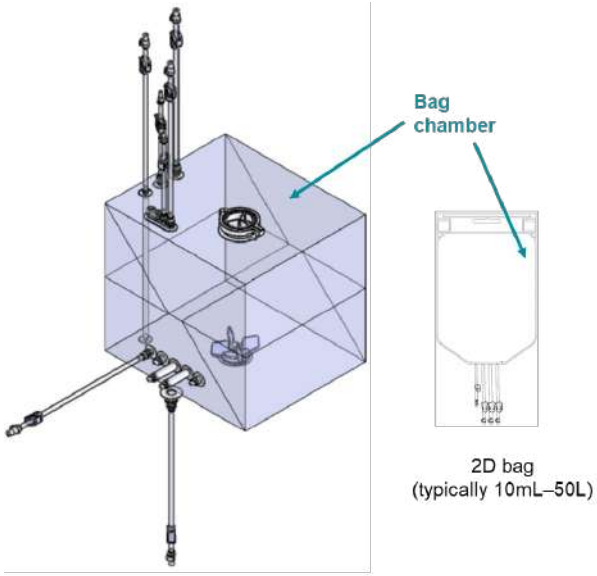
1. Able to scan/image large SU bags up to 2,000 L
2. Able to complete scanning/imaging on the order of minutes (not hours)
3. Easy to use and train new users on
4. Able to scan assemblies and transfer sets to accurately identify individual components within each unit, i.e. are the units/ports accurately supplied and assembled against the approved reference SU drawings?
5. Ergonomic design and safety considerations, e.g. cleanable surfaces, standards, moveable, non-greased, dust-free surfaces, guarded pinch-points
6. Suitable for use in a cleanroom environment – compatible with disinfectant used on shopfloor
7. Retrievable and validated scanning data
8. [Advantageous to have] Able to scan assemblies and transfer sets supplied through multiple layers of vendor packaging, i.e. foam to Right-First-Time

Defect Detection of Single-Use Systems

Annex A – Illustration of Components in Assembled Single-use Systems

Possible defects may include mis-assembly, missing or incorrect components, or improper component orientation of components in the assembled single-use system

Bag Assembly Anatomy

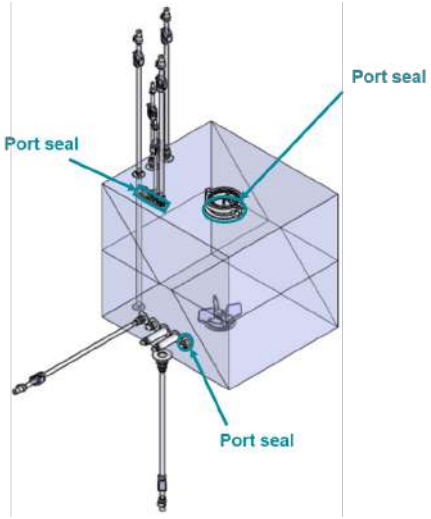


Defect Detection of Single-Use Systems

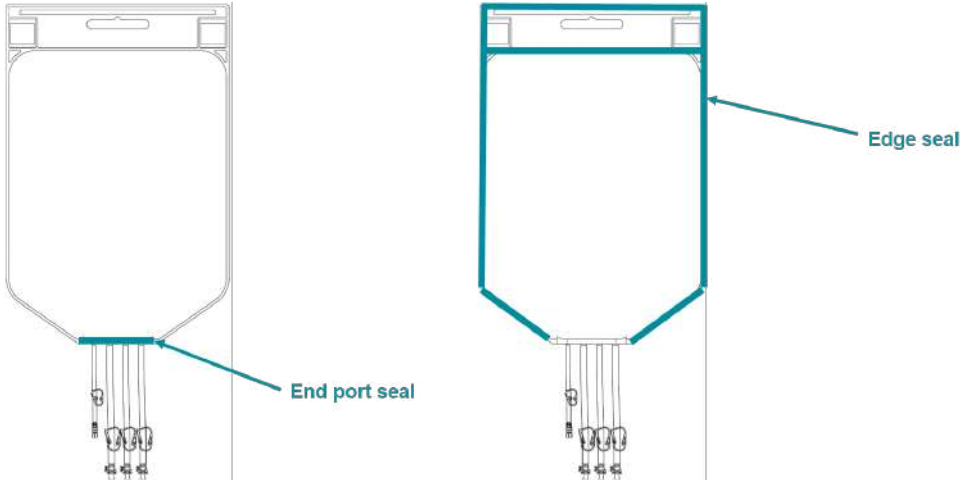
Annex A – Illustration of Seals in Single-use Systems

Possible incomplete seal around the ports and around the bags

Bag Assembly Anatomy



3D bag (typically 25 – 5,000 L)

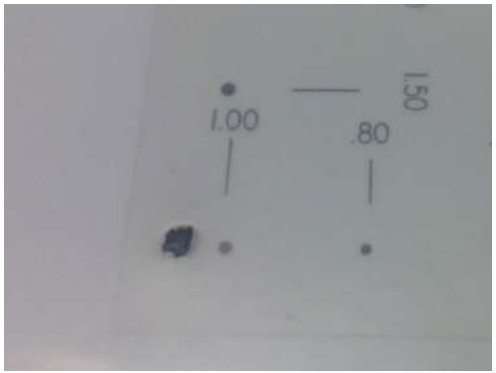


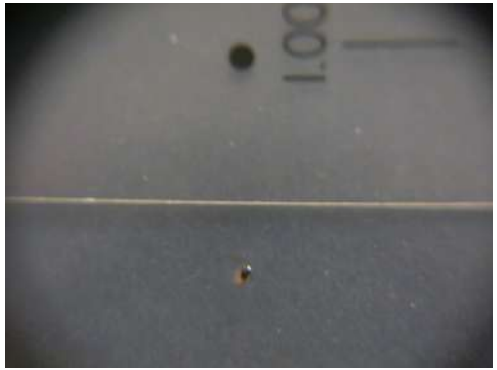
2D bags (typically 10 mL – 50 L)

Defect Detection of Single-Use Systems

Annex A – Illustration of Embedded Particles in Single-use Systems

Possible inclusion of embedded particles appearing as coloured material contained within the film which cannot be dislodged





Visual Observation Library

Embedded particle. TAPPI size estimation chart in the background.

Defect Detection of Single-Use Systems

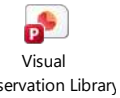
Annex A – Possible Defects in Single-use Systems

Defects of primary interest to this grant call –

1. Incomplete or mis-assembly
2. Incomplete port seal/film seal
3. Embedded particles

Other defects which could be of interest to this grant call –

1. Gel
2. Crease
3. Zipper
4. Scratch
5. Cut
6. Puncture
7. Abrasion
8. Rupture
9. Incomplete film seal
10. Damaged port
11. Kinked tubing
12. Loose particles



Defect Detection of Single-Use Systems

Useful References

1. Single-use systems bag assembly leakage and defect toolkit.

2. Product: The 2014 Particulates Guide: Recommendations For Testing, Evaluation and Control of Particulates From Single-Use Process Equipment: BPSA

3. https://www.sartorius.hr/media/cyzbxyra/manual_flexsafe-str_single-use-bags_50l-2000l-2667752-000-00_-e.pdf

Redesigned Manufacturing in Compliant Agility

Problem Statement

Biopharmaceutical manufacturing is at an inflection point. Advances in automation, digitalisation and process intensification offer major opportunities while medicine modalities continue to diversify, e.g. mAbs, peptides, oligonucleotides, RNA and vaccines. However, most current facilities are built around large-batch, human-centric production models which constrain automation, sustainability and operational flexibility. Strict aseptic requirements make human interaction a contamination risk. Yet, existing layouts — designed for manual operations — limit the effective deployment of robotics. Robotic systems themselves introduce technical challenges, e.g. particle shedding, sterilisation compatibility, cleanroom movement constraints, etc.

This initiative proposes a 'robotics-first' rethink of biomanufacturing –

- Designing facilities, equipment and material flows optimised for automation
- Reimagining single-use systems for automated setup, operation, cleaning and reconfiguration
- Integrating advanced sensing and modeling for performance and compliance
- Evaluating new production paradigms, e.g. high-volume/low-frequency versus low-volume/high-frequency
- Ensuring safety, quality and affordability remain uncompromised

Multidisciplinary collaboration, e.g. engineering, robotics, materials science, architecture, automation, social sciences, economics, etc is encouraged to define what 'compliant agility' looks like in next-generation biomanufacturing and to build the economic case for change.

Redesigned Manufacturing in Compliant Agility

Objectives and Scope of Work

Accepting that any human interaction with the manufacturing process presents a risk to contaminate the process and robotics systems could also present the same risk and limit the impact of automation to improve current factory concepts for biopharmaceutical manufacture, solutions are sought to –

1. Automate High-Risk Manual Operations

Develop solutions to reduce contamination risk and manual intervention in critical activities, such as –

- Media preparation
- Sampling
- Equipment configuration, setup and breakdown
- Materials and wastes handling

Proposals can include retrofit solutions for existing isolators and legacy processes as well as greenfield concepts

2. Minimise Contamination Across Sterile Boundaries

Design systems to safely manage robotic and materials movement between sterile and non-sterile zones through –

- Improved barrier technologies
- Segmented workflows
- Controlled transfer pathways
- Advanced environmental containment strategies

Solutions must maintain or improve current sterility assurance levels

Redesigned Manufacturing in Compliant Agility

Objectives and Scope of Work

3. Redesign Equipment For Robotics Operations

Redesign single-use and multi-use equipment for robotic manipulation and automated configuration by emphasising –

- Sterilisable and low-particle materials
- Modular and reconfigurable architecture
- Robot-compatible interfaces
- Simplified setup, operations and cleaning

Proposals can explore shifts from high-volume/low-frequency batch production, e.g. ≥1000 L towards low-volume/high-frequency or hybrid batch-continuous manufacturing models

4. Future-Ready Facility And Workflow Architecture

Propose facility concepts optimised for automation and 'lights-out' manufacturing, including –

- Robotics-enabled spatial configurations
- Separation of human and robotic workflows
- Alternative sterilisation zoning strategies
- Closed or near-closed production environments

Concepts can address both greenfield facilities and transformation pathways for existing plants

Redesigned Manufacturing in Compliant Agility

Objectives and Scope of Work

5. Define The Robotics Lifecycle In GMP Environments

Establish frameworks to manage robotic systems within regulated manufacturing environments, including –

- Sterility and particle control
- Maintenance and service models
- Power and charging strategies
- Human–robot interaction protocols
- Compliance validation and monitoring

Solutions must align with GMP requirements and regulatory expectations

Different types of collaboration are encouraged. Some ideas can be standalone research projects while others require pulling together different collaborators to take forward. Some of the ideas above are likely to need phasing or drawing from concepts already deployed in other industries, e.g. semiconductor, automotive or nuclear.

Eligibility

1. The Principal Investigator and Co-Investigators as defined in Grant Terms and Conditions must:
    a. Hold a primary appointment in a Singapore publicly funded research institution or an Institute of Higher Learning. The Principal Investigator must hold a primary appointment of at least 0.7 FTE in Singapore.
    b. Lead a laboratory or research programme which carries out research in Singapore
    c. Possess track record of leadership ability in coordinating research programmes and providing mentorship to research teams as well as having productive research outcomes. A track record in securing IRS will be advantageous.

2. Collaborators as defined in Grant Terms and Conditions are not eligible to receive funding
    a. Companies can participate in projects only as collaborators

3. Exceptions to the above eligibility criteria will be considered on a case-by-case basis. Please submit a request to the BioPIPS Programme Office at least 7 days before the closing date of the grant call.

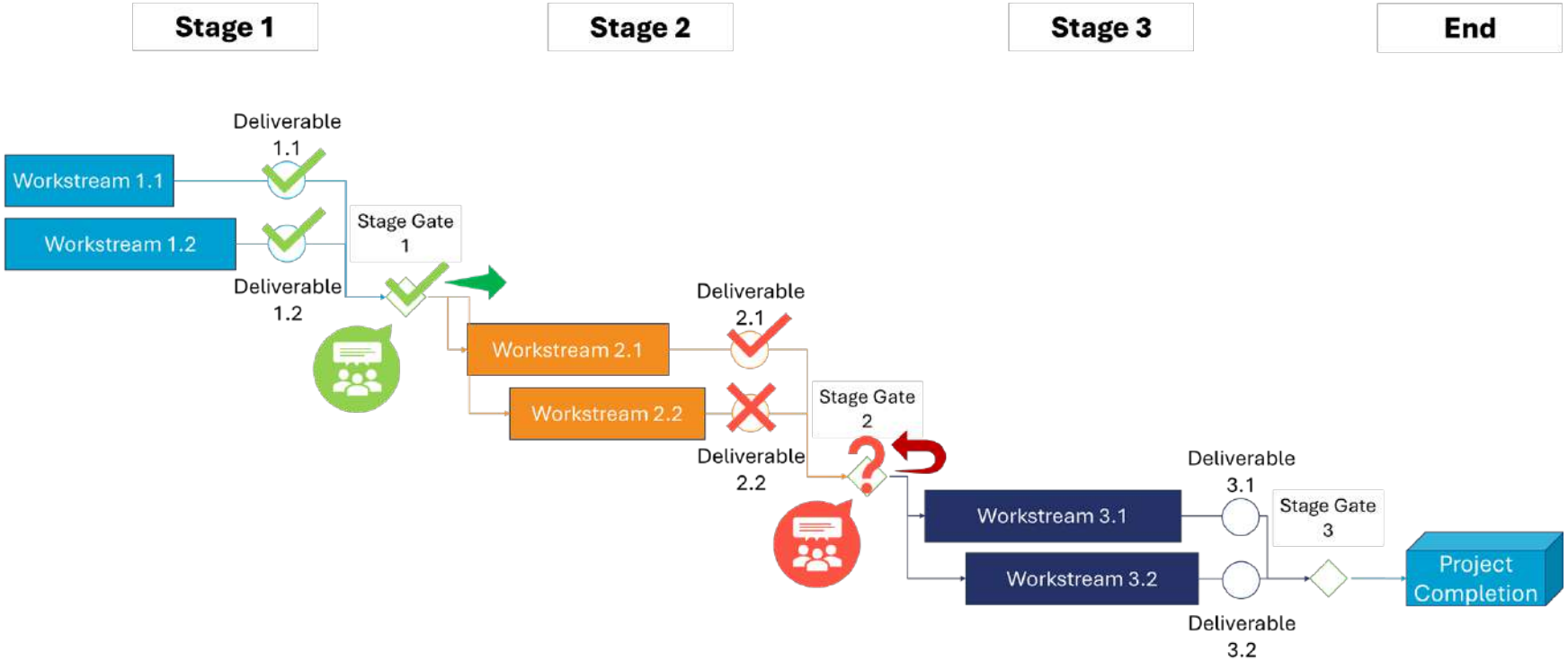
Important Notes

1. Applicants must use the latest version of the Letter of Intent (LOI)/proposal template

2. Submissions should clearly state milestones and deliverables. Industry collaborations are strongly encouraged.

3. Applicants shall comply with grant terms and conditions, including prevailing regulations

Example of Stage-Gated Project Management



Evaluation Criteria

1. Relevance to Problem Statement(s)
2. Potential for commercial adoption
3. Scientific quality and innovativeness
4. Experience and expertise of the team
5. Effectiveness of project management
6. Appropriateness of the requested budget
7. Strength of intellectual property (IP) strategy
8. International competitiveness

Contact Us

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BioPIPS website address –
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THANK YOU

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