BIOINCUBATE

# Forge Track

## Detailed Challenge Document

Revolutionizing Detection of Microbial Contaminants to Accelerate Biomanufacturing

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## Contents



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Lonza

*Built by:*

STUDENT BIOLAB ZURICH

# Program Overview

*Ideate Phase:* Teams draft their proposal and have the opportunity to meet relevant experts to gain feedback on their ideas. The submission deadline for proposals is Midnight on October 26th. Proposals will be screened and the top 6 teams will be invited to pitch in front of a judging panel on November 9th. The top two teams will be selected and admitted into the Build Phase.

*Build Phase:* The two admitted teams will have 5 months to further develop their conceptual solution and basic proof-of-concept according to their proposal. Each team will receive CHF 10,000 project budget, access to a BSL1 laboratory & core facility services in Zurich, and mentorship from experts in Lonza, ETH and UZH.

*Final Pitch:* The Build Phase will culminate in a Final Pitch in early May 2024 when the teams compete for the 1st Place Grand Prize of CHF 30,000 and 2nd Place Prize of CHF 10,000

## TIMELINE

### Ideate

*SEPTEMBER OCTOBER NOVEMBER*

**4 KEY DATES FOR IDEATE PHASE**

**OCTOBER 11, 18:00 - 20:30**
**Expert Review Workshop**
An opportunity for teams to meet experts from Lonza & academia to discuss and troubleshoot your proposals

**OCTOBER 26, 23:59**
**Proposal Submission Deadline**

**NOVEMBER 2**
**Top 6 teams invited to pitch at Selection Event**

**NOVEMBER 9, 18:30 - 21:30**
**Ideate Selection Event**
6 teams are invited to pitch to a panel of judges. Two teams will be selected at the event to enter the Build Phase. Dinner & Apero provided during the event.

### Build

*NOVEMBER -- APRIL 2024*

**BUILD PHASES**

**NOVEMBER**
**Lab Intro & Ordering**
Lab and safety introduction, experimental design and purchasing of consumables.

**NOVEMBER - APRIL**
**Prototyping & Development of Solution**

**APRIL**
**Submit final written report on results**

### Pitch

*END OF MAY 2024*

**FINAL PITCH EVENT**

**Prizes Awarded**
1ST: CHF 30K
2ND: CHF 10K

**Memorable Occasion**

## STUDENT ELIGIBILITY & COMMITMENT

- **Student Requirement:** Each team must have at least one active student member (Bachelor, Master, PhD).
- **Team Size:** Teams are expected to be 3-6 members. If you are seeking additional members, join the BioIncubate Slack by registering your team on our website: bioincubate.ch/register
- **Time Commitment:** BioIncubate is designed to run alongside ongoing studies, PhD work, internships or other commitments. While teams are encouraged to balance their participation with existing responsibilities, they are expected to dedicate meaningful effort to progress their projects throughout the program duration.
- **Questions:** For any questions about team eligibility please contact: bioincubate@studentbiolab.ch

# Revolutionizing Detection of Microbial Contaminants to Accelerate Biomanufacturing

## CHALLENGE SUMMARY

LONZA, a global leader in biomanufacturing, is seeking out-of-the-box solutions to disrupt and redefine a crucial industry problem: the rapid detection of biological contaminants during biomanufacturing of drugs. Your challenge is to design a method to rapidly and comprehensively test for all potential biological contaminants, while maintaining comparable performance to current detection methods. Successful solutions should consider multidisciplinary, innovative concepts that leverage expertise from various backgrounds. The details below elaborate on the key aspects of the challenge.

## BACKGROUND ON BIOMANUFACTURING & CONTAMINANT TESTING

Biomanufacturing involves the production of vaccines, antibodies and other drugs using engineered cell lines grown in industrial-scale bioreactors. To ensure patient safety, drug manufacturing is highly regulated and subject to stringent testing to ensure no 'adventitious agents', such as bacteria, fungi, viruses and mycoplasma are present in the manufactured drug. However, standard tests suffer from lengthy turnaround times, ultimately slowing the release of biotherapeutics and delaying patient access to crucial treatments.

*Why is this challenge important?* The future of the industry is shifting towards "continuous, integrated biomanufacturing" - enabling more efficient drug production and moving away from the traditional batch-based approach. Continuous biomanufacturing improves drug yield, reduces costs & ultimately delivers safe drugs to patients faster. To enable continuous biomanufacturing, adventitious agent testing technologies and strategies need to be revolutionized to allow rapid turnaround of results. Thus, this challenge is seeking novel detection technologies that will help enable the future of biomanufacturing.

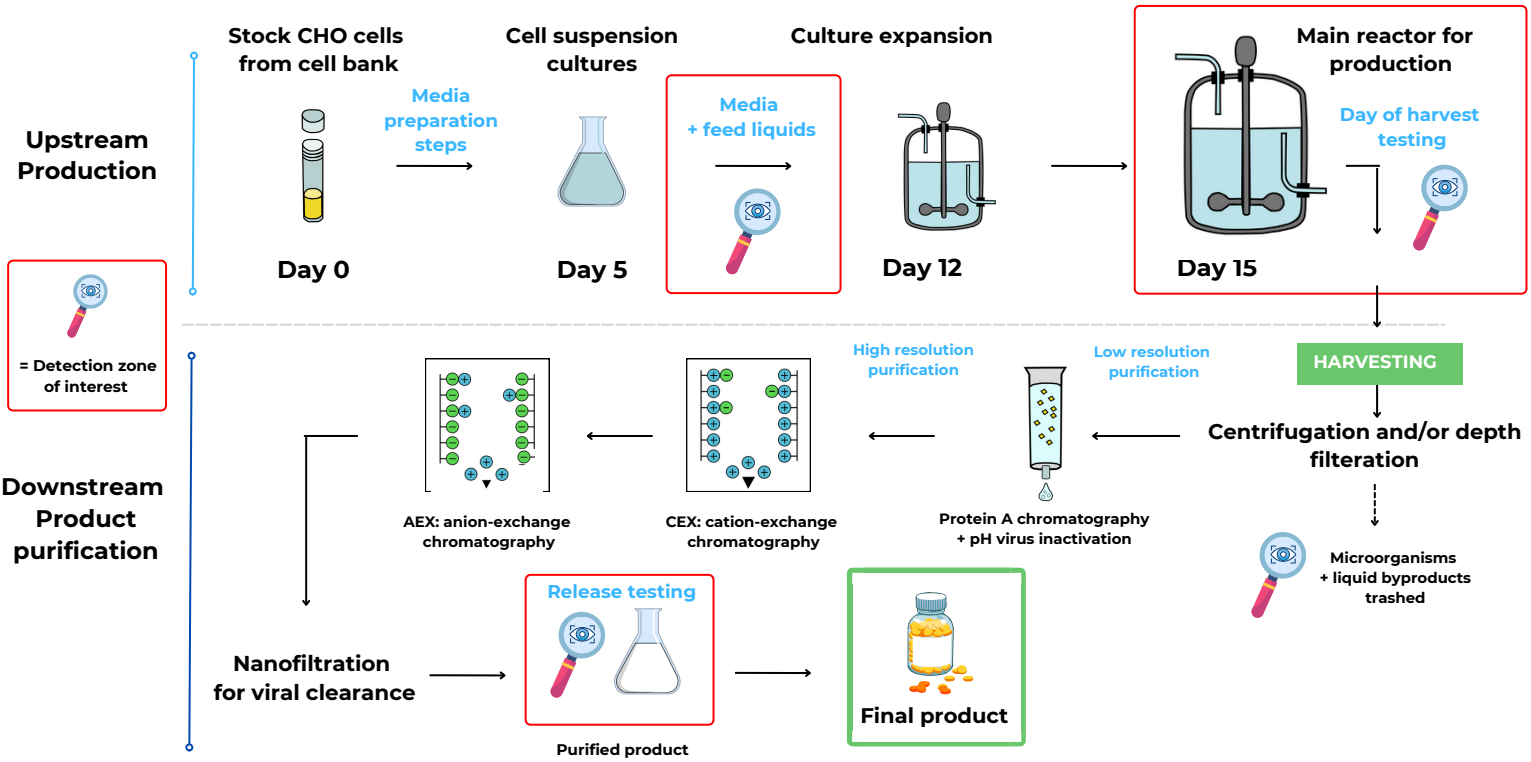
## CONTAMINANTS & TESTING STAGES

Adventitious agent testing mainly takes place at two stages during the manufacturing process: (1) before forward processing of intermediates during inoculum expansion and bioreactor operation prior to purification (Upstream Processing) and (2) on the finished product after purification and before market release. For viruses and mycoplasma, testing usually occurs at the end of stage 1 only. As drug purification takes approximately 1 week, a testing turnaround time of < 1 week is essential to ensure the safe release of the purified drug for stage 2. For bacteria and fungi (known as bioburden), testing is performed at stage 1 and stage 2. To accelerate the final product release, a desired bioburden test time is < 24 hours. The Figure on the next page shows an overview of the biomanufacturing pipeline with potential timepoints of testing highlighted and areas for possible contamination emphasized. Please note the figure is a visual aid for the biomanufacturing process but should not constrain solution proposals.

## AVOIDING CONTAMINATION RISK & IMPLICATIONS OF FALSE POSITIVES/NEGATIVES:

Due to stringent control strategies used during the biomanufacturing process, in the vast majority of cases there is no contamination and tests return negative. If, however, a test is positive, the entire manufactured batch of drug (often millions of CHF worth of product) must be discarded and a thorough inspection and disinfection process of the whole manufacturing facility is required. Therefore, it is critical that novel testing methodologies protect against false positive results while still matching the performance of existing compendial tests to avoid false negatives.

# BIOMANUFACTURING PIPELINE




# LIMITATION OF CURRENT TESTING METHODS

The main issue with existing compendial adventitious agent tests are their slow turnaround time and lack of in-line integration. Separate methods are required for each contaminant and have extensive timeframes, ranging from days to weeks. Further, testing is often outsourced to external facilities to keep any source of contaminants, such as the organisms or material used as controls, separated from the biomanufacturing facility. Existing compendial tests are well-documented. Below is a brief summary of some of the key tests utilized in the industry (non-exhaustive list):

| Contaminating Agent | State of the Art | Testing Time | Drawbacks | Limit of Detection (LOD) |
|---|---|---|---|---|
| Bioburden (Bacteria & Fungi) | Agar plating and CFU counting on various types of media. | 1-2 Weeks | • Many organisms don't grow on defined media and require specialized or exotic media for growth.<br>• Outsourcing is required for testing due to test complexity and in order to keep organisms, used as controls, far from the manufacturing facility.<br>• Lengthy testing & time to turnaround results.<br>• Plating bias may lead to missing certain strains or variants | ≈1 CFU/mL |
| Viruses | qPCR and TEM | 3-4 weeks | • 28 day growth test<br>• Outsourcing necessary due to expertise and specialized knowledge requirements (particularly with TEM)<br>• qPCR is specific to individual viruses, lacking broad-spectrum detection capability | <1VPS/10^6 doses |
| Mycoplasma | qPCR | Days - 1 week | • Comparatively less problematic compared to Viruses and Bioburden testing due to current testing speed.<br>• Outsourced due to contamination risks associated with controls during testing.<br>• There is a potential to miss detection of 'hidden' variants | ≈1-10 organisms |

## IDEAL SOLUTION

Ideal Solutions should be rapid, in-line and enable Continuous Biomanufacturing. While traditional compendial methods are highly sensitive with an impressive Limit of Detection (LOD), they suffer from long turnaround times & external reliance on third-party testing facilities. Thus, proposed solutions to the challenge should focus on rapid turnaround time for results. The absolute "holy grail" solution would be a single, in-line test that can detect all contaminants regardless of species, would be 'blind' to the organism used to produce the therapeutic (e.g. for example CHO cells) and provide a near immediate readout to operators. Teams should aspire towards this ideal solution in any way possible.

## MANDATORY REQUIREMENTS FOR SOLUTION PROPOSALS

There are two pass/fail mandatory requirements for successful proposals:

**Exhibit High Sensitivity:** Very low quantities of contaminants can pose a risk throughout the entire biomanufacturing process. Thus, solutions must achieve a Limit-of-Detection (LoD) for contaminants that is extremely low and at least comparable to current compendial tests. Note that the bioreactor environment is 'messy' - containing a biological matrix of living cells, various proteins, nucleic acids, and nutrient media. Solutions must maintain sensitivity against this backdrop.

**Safeguard against False Positives and False Negatives:** As aforementioned, false positive or false negative results have vast implications on the biomanufacturing pipeline. Therefore, your solution must safeguard against these risks.

## FURTHER KEY ASPECTS TO CONSIDER:

In addition to the two mandatory requirements, the following key aspects are ***listed in order of priority***. Your solution should aspire to satisfy as many of these aspects as possible.

1. **Significantly Reducing Time to Results:** Solutions should reduce turnaround time for results as much as possible: Ideally less than 24 hr for bacteria and fungi, Ideally less than 7 days for viruses & mycoplasma
2. **Breadth:** Your solution should ideally detect all the potential biological contaminants in a species-agnostic or variant-agnostic manner.
3. **Feasibility at Scale & Economically Viable:** Your solution should integrate across different bioreactor volumes & stages, and be realistic on a cost basis for practical implementation.
4. **Non-specialist, User-Friendly Operation:** Your solution should be operable by non-specialist / non-expert employees.
5. **In-Line Testing & Eliminating Outsourcing:** To ensure streamlined testing, your solution should enable on-site operation & offer the potential for "in-line", "on-line" or "at-line" detection.
6. **Non-Invasive Approach:** The solution should be non-invasive and minimize the chances of contaminating the product.

## ENCOURAGING MULTIDISCIPLINARY, OUT-OF-THE-BOX INNOVATIONS

Fresh perspectives from diverse academic backgrounds can lead to out-of-the-box solutions. We invite students from various disciplines to collaborate on this problem to redefine the landscape of biomanufacturing. Potential solutions could involve: Software & Modeling; Materials Science Innovation; Optical and Spectral Innovations; Microchip Design and Electrical Engineering; Molecular Biology and Chemistry Solutions; to name just a few.

# Submission Requirements & Judging

## HOW TO APPLY

### #1: Team Registration

Register your team as soon as possible here: **www.bioincubate.ch/register**
Be sure your team meets the eligibility requirements.

### #2: Review the Forge Terms & Conditions

Review the Forge Terms & Conditions here:
**www.bioincubate.ch/forge-terms-conditions**
Applicants are required to agree to the terms of conditions, which include terms concerning potential IP, expectations & research use of the concepts.

### #3: Upload your Application Proposal Deadline October 26th at 23:59

Upload your application here: **https://6tr05wwscbj.typeform.com/to/x30faa5P**
Please review the application requirements & judging criteria on the next page.

## SELECTION OF BUILD PHASE TEAMS

After an initial screening round, the top 6 proposals will be invited to pitch their idea at the **Ideate Selection Event on November 9th.** Pitches will be 5 minutes followed by 5 minutes of questions from the panel. The two teams that win the Selection Event will be admitted into the Build Phase of BioIncubate, lasting from November through April.

## GRAND PRIZE AT FINAL PITCH EVENT AFTER BUILD PHASE

Two teams admitted into the Build Phase will be given further instructions regarding their requirements & process for development over the 5 months of Build. At the Final Pitch in May 2024, the two teams will pitch and compete to win the Grand Prize.

### 1st Place Winner - CHF 30,000 Cash

The team that emerges as the winner in May 2024 will have a highly innovative solution to the challenge & demonstrated a basic proof-of-concept in the lab. The winning team will receive a cash prize of CHF 30,000.

### 2nd Place Runner-Up - CHF 10,000 Cash

The runner-up team will receive a cash prize of CHF 10,000.

Regardless of the winner, both teams in the Build Phase will benefit from direct guidance and support from experts in Lonza & academia.

# Submission Requirements & Judging

## JUDGING CRITERIA & GUIDELINES

**Page Limit:** Proposals are limited to max 5 pages (Size 11 font; Arial), excluding references. The proposal should consist of the following:

### 1. Executive Summary & Project Outline

A concise summary of the project's objectives and innovative aspects of your solution.

### 2. Conceptual Component

Describe your well-researched and innovative solution and how it satisfies the following:

- Innovation: How novel & innovative is your approach? Think "out-of-the-box".
- Solution requirements: Does your approach satisfy the requirements & many of the "key priorities" listed on page x?
- Scientific Foundation: Are there scientific foundations that indicate your solution may work?
- The **conceptual component will be considered more important** than the lab component - please consider this for your ideation & planning

### 3. Lab Component

Design an experimental plan which focuses on prototyping and/or providing data to support an aspect of your conceptual solution:

- Simple yet impactful: Complement your conceptual proposal and produce preliminary data supporting a core feature(s)/theory developed
- Wet-lab and/or Dry-Lab: Various approaches are possible, including wet-lab experimentation, dry-lab prototyping and in-silico modeling. Review the facility details and resources here to guide your proposal: www.bioincubate.ch/lab
- Budgeting of CHF 10,000 within Timeline: Suggest a clear and concise experimental plan and budget breakdown detailing the intended utilization of allocated funds.
- Note: We do not expect teams to develop a full, working prototype of their solution in 5mo. Teams should develop an achievable experimental plan that will demonstrate a simple yet impactful part of their solution.

### 4. Team Structure & Experience

Describe how your team will be organized in the Build phase

- Team Roles: Identify team structure and responsibilities for members.
- Skills and Background: provide the academic backgrounds and previous experience of each member of the team.

**Questions? Email Us. bioincubate@studentbiolab.ch**

**WE WISH YOU THE BEST OF LUCK**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