BENEFITS OF LYOPHILISED BEADS FOR STABILISING IN VITRO DIAGNOSTIC (IVD) ASSAYS

WHITE PAPER

BIOFORTUNA

FIVE KEY REASONS TO SPECIFY LYOPHILISED BEADS

1	Increase assay accuracy
2	Reduce risk of contamination
3	Increase speed to result
4	Reduce errors
5	Increase efficiency

WHAT ARE LYOPHILISED BEADS?

Lyophilised beads are durable spheres of freeze-dried material formed from accurately measured volumes of customisable formulation.

These single-dose beads, like all lyophilised formats, retain long-term stability at ambient temperature and therefore do not need expensive cold chain shipping or refrigeration during storage.

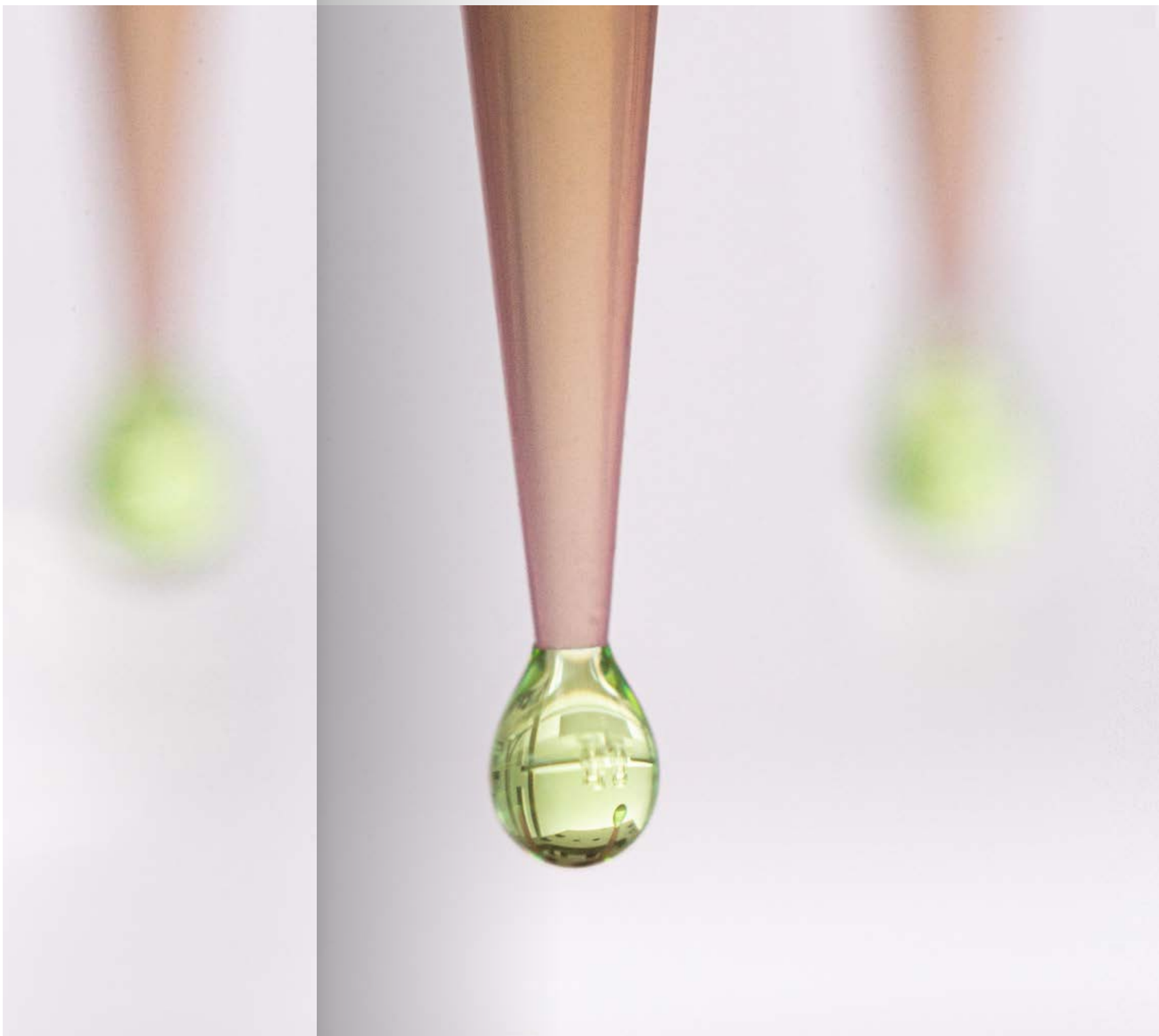
This significantly increases the accessibility of diagnostic testing for difficult-to-reach patients, facilitating regular near-patient testing in the community.

Lyophilised beads also present further performance and efficiency opportunities, particularly in terms of assay accuracy, speed and ease of process.

KEY BENEFITS OF LYOPHILISED BEADS

Lyophilised beads deliver the following performance, efficiency and cost benefits over traditional lyophilised formats:

1	Assay accuracy – the dose consistency of beads minimises the potential for variance.
2	Reduced risk of contamination - there is no central stock to corrupt.
3	Increased speed to result – beads reconstitute faster because of their volume-to-surface-area ratio.
4	Reduced risk of error - beads do not need aliquoting after reconstitution, significantly lowering the risk of dosing error.
5	Ease of handling – each all-in-one bead is pre-packaged and ready to use.
6	Reduced wastage – each bead contains an individual dose so there is no unnecessary reconstitution or exposure to moisture of any excess stock.
7	Simpler quality control. Quality control is quicker, easier, and more cost-effective with beads.
8	More efficient manufacturing - beads offer a much more efficient route to large-scale manufacture, especially for Point of Care devices.



BENEFITS OF LYOPHILISED BEADS FOR POINT OF CARE TESTING

Speed is critical in diagnosis. Clinicians must treat or manage the issue quickly and effectively. This urgency is particularly vital in cases of viral infection.

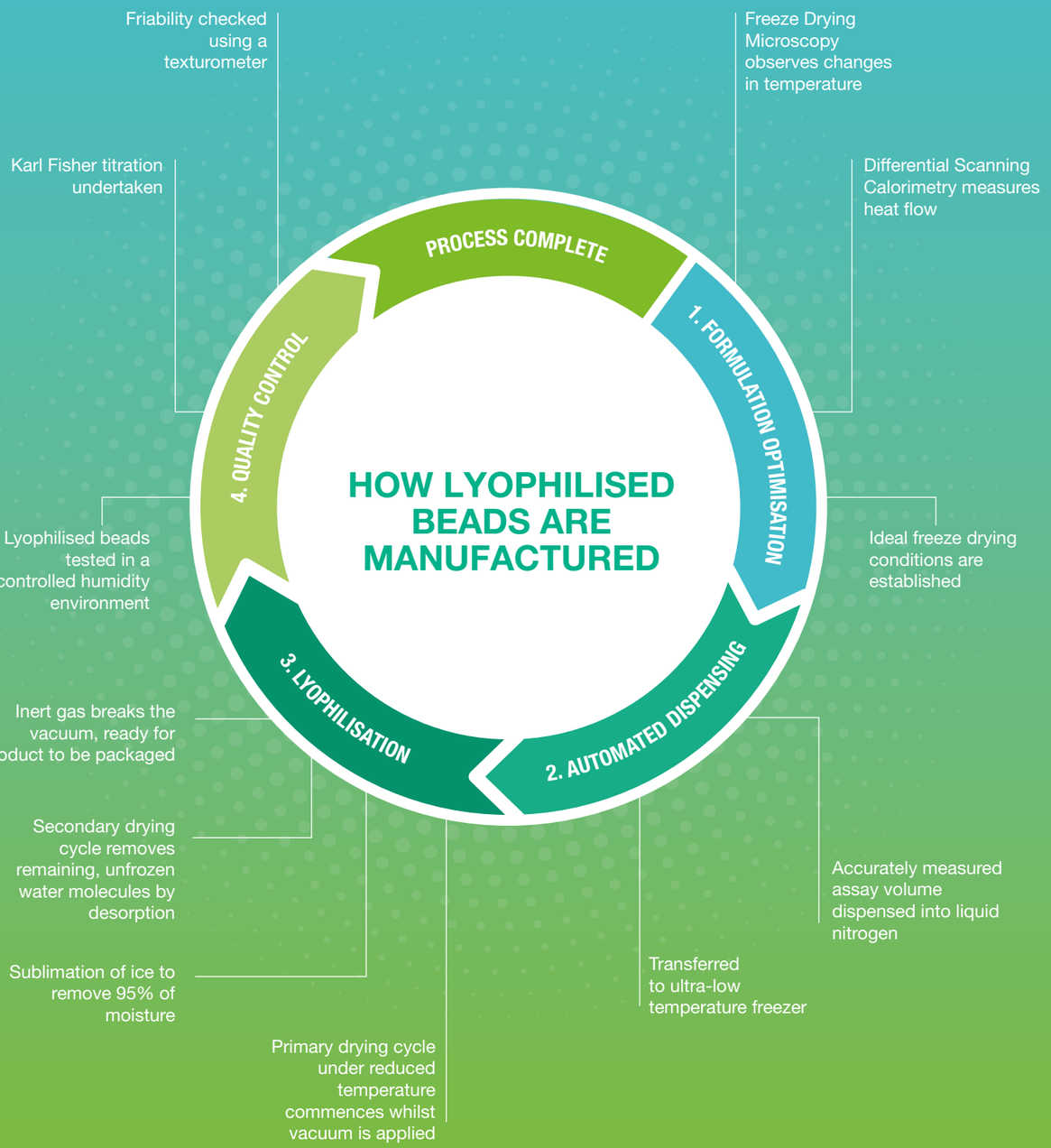
Point of Care testing offers the accuracy of laboratory-based testing but delivers results in minutes or hours rather than days. Reagents in Point of Care devices must be stabilised as cold chain transportation and storage is not an option in remote or challenging locations.

But until now, lyophilising reagents for Point of Care devices has been at best inefficient. That is because the traditional method requires them to be dispensed within the device and then lyophilised in situ. This requires a freeze-drying capacity significantly larger than necessary, simply to accommodate the volume of cartridges.

It slows down the manufacturing process, delaying the launch and roll-out of life-changing concepts. These inefficiencies also lead to significant increases in cost, time and batch variability across multiple production runs.

But beads do not have to be lyophilised in situ. They can be manufactured in far more economical quantities and then sub-assembled into the cartridges later, resulting in a throughput uplift of up to 1,000 times greater than the traditional method.

“Lyophilised beads have revolutionised the manufacturing process. They provide a far more efficient and cost-effective use of freeze-drying capacity, resulting in a throughput uplift of up to 1,000 times the volumes achieved by lyophilising in situ.”



HOW LYOPHILISED BEADS ARE MANUFACTURED

STAGE 1 – FORMULATION OPTIMISATION

The process starts in the same way as any lyophilisation project, with a detailed analysis of the formulation. This means establishing the ideal freeze-drying conditions of the assay before lyophilisation begins. This is usually achieved by using the combination of Freeze-Drying Microscopy (FDM) and Differential Scanning Calorimetry (DSC).

FDM uses a miniscule amount of a formulation. The sample is frozen and placed in the chamber under vacuum. These conditions are accurately controlled, reproducing those of a manufacturing freeze dryer.

Observing the crystallisation, freezing and collapse temperature of the sample can help to identify:

- optimal temperatures
- reagents which are likely to be challenging
- the effect that varying concentrations of the excipients can have on the final conditions.

DSC calculates how the Glass Transition Temperature (Tg') – the temperature at which the formulation changes from a brittle 'glassy' state into a viscous 'rubbery' state – will be affected under different heating rates of the product. This provides an indication of the duration of the lyophilisation cycle and helps to calculate the benefit that annealing (thermal treatment) could have on the final conditions.

DSC can also be used to analyse dry, post-lyophilisation samples.

This helps to:

- determine the residual moisture content
- establish recommended storage temperatures to maximise stability.

Both FDM and DSC help to identify challenging components and the most promising excipient combinations in varying concentrations. This provides a good understanding of the conditions to be applied on a larger scale with a minimum reagent cost to the client.

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STAGE 2 - AUTOMATED DISPENSING

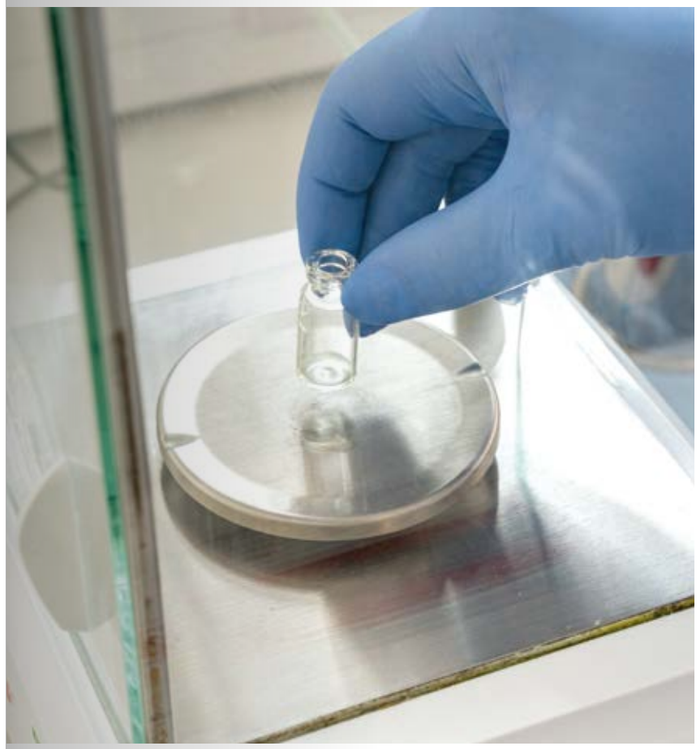
Once the ideal freeze-drying conditions of the assay are established, accurately measured droplets of this formulation are dispensed into liquid nitrogen. This accuracy will ensure that each bead contains a precise dose for its application.

The beads are then transferred to lyophilisation freezers to begin the next stage.

STAGE 3 – LYOPHILISATION

Lyophilisation takes place in two cycles – primary and secondary drying.

- Primary drying cycle (sublimation): During sublimation, the pressure in the environment is lowered while a vacuum is applied. This causes the ice to sublime, removing 95% of the water.
- Secondary drying cycle (desorption): This will remove the remaining unfrozen water molecules from the formulation. An inert gas is then used to break the vacuum in the environment, ready for the product to be sealed.



STAGE 4 - QUALITY CONTROL

When the lyophilisation process is complete the beads are tested in a controlled-humidity environment. Firstly, the Karl Fischer titration technique is applied to detect the levels of residual moisture within the beads, and this is followed by a friability test using a texturometer.

Beads are also checked for their dissolution rate. This is a critical property, especially when the beads are to be used in a Point of Care device, where timing from the sample/buffer injection to the result is crucial.

The beads then undergo checks on their appearance, such as texture, roundness and consistency.

If the process is conducted by an experienced manufacturer with best-in-class facilities, it is likely to take place in a quality assured environment.

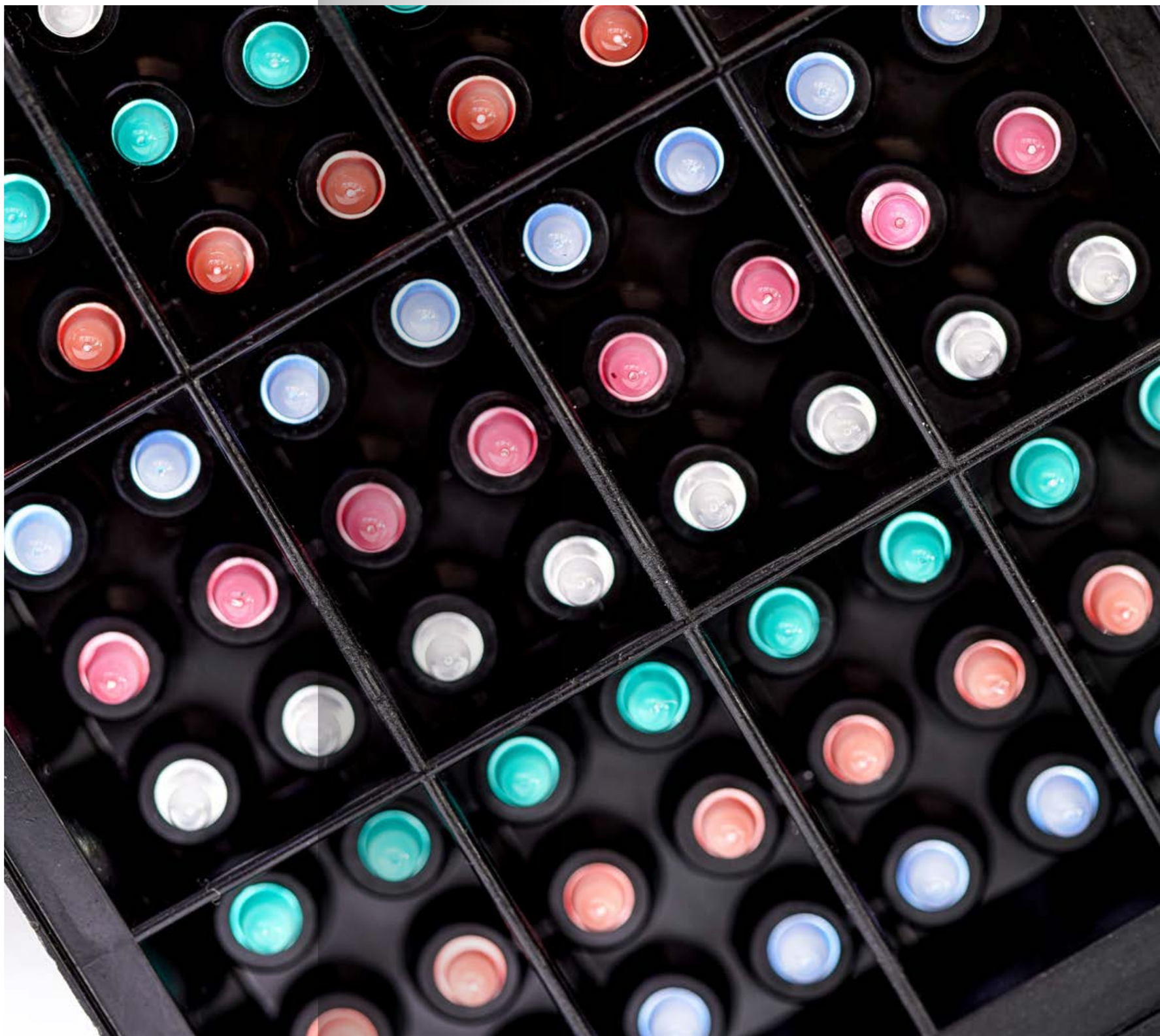
At Biofortuna, lyophilised beads are manufactured in a 450m^2 humidity controlled clean room within our ISO 13485 and ISO 17025 certified and FDA compliant manufacturing facility.

LYOPHILISATION IN MOLECULAR DIAGNOSTICS: EXPERIENCE IS CRITICAL

Working with a knowledgeable and experienced beads manufacturer can significantly accelerate assay development and manufacture. It ensures a cost-effective and efficient freeze-drying process and reduces the time and overall cost of bringing an assay to market.

There are many companies with experience in lyophilised reagents and biochemical tests. But choosing a partner with a strong track record in molecular diagnostics can maximise the chances of a smooth progression from development to full scale manufacture.

Their expertise and experience will help you to identify which reagents or additives are not suitable for lyophilisation. This enables alternatives to be selected or allows the design of assay protocols that combine both lyophilised and non-lyophilised components without wasting time and resources.



WHY PARTNER WITH A CONTRACT MANUFACTURER TO PRODUCE YOUR BEAD-BASED ASSAYS?

- **Greater chance of success**
- **Faster production cycles**
- **Benefit from specialist experience**

Developing a new assay that will transform lives and be commercially successful is a notoriously slow and complex process. New formulations require expensive and time-consuming set-ups every single time. There are no shortcuts when creating an assay that is expertly developed and ready for deployment.

It is tempting to believe that managing all your manufacturing processes in-house is the most streamlined and snag-free route to success. After all, what could benefit your production cycle more than having everything under one roof, ready for immediate analysis, testing and shipping?

But in reality, overseeing every aspect of production in-house can:

- put a strain on resources
- create bottlenecks
- delay commercialisation and revenue.

Partnering with a contract manufacturer and building a long-term relationship is often the key to success. It pays to bring in the specialised bead expertise that a contract manufacturer can offer.

When formulating your assay, you may not have the expert knowledge in-house to lead the transition from assay development to manufacturing. Does your team have, for example, the intricate knowledge of stabilisation techniques and buffer reactions needed to make this process a success?

By partnering with a contract manufacturer armed with specialist bead experience, you can benefit from their years of technical expertise (which will continue to grow and evolve with each new project).

The more experience a contract manufacturer has, the quicker and smoother your route to market will be. Years of experience can equate to a reduction of months of trial and error and re-testing, with no surprise upheavals to your timescales, resource requirements or budget.

By choosing a contract manufacturer that also has development experience, you will benefit from the efficient manufacturing processes which can come only from a detailed understanding of the development process and the deployment of leading-edge equipment.

By being selective in your choice of partner, you will benefit from production cycles that may be far quicker than you would achieve in-house. As a result, you will save production time from the very start, enabling increased throughput at every stage.

HOW A CONTRACT MANUFACTURER CAN HELP YOU TO SCALE UP PRODUCTION

- **Reduced risk**
- **Lower entry and exit costs**
- **Faster return on investment**
- **Greater flexibility and agility**

A key benefit of partnering with a contract manufacturer of bead-based assays is their ability to scale quickly, smoothly and successfully.

An experienced contract manufacturer will be able to accommodate demand spikes easily. This means you can approach every step in your production cycle stage-by-stage, without needing to forecast your requirements prematurely.

The right contract manufacturer can take you to small, mid- and large-scale output, with the capability to flex these requirements. This freedom to adjust manufacturing output, even late into the production cycle, offers significant benefits to developers wishing to be flexible without suffering operational consequences.

This flexibility reduces the overall risk to your investment.

Any new product development will have a factor of risk. Your assay must be tested, assessed and managed throughout every stage of the manufacturing process. To do all of this in-house, you will need to contend with significant knowledge, time and resource barriers. It means a sizeable investment in all three upfront.

An expert contract manufacturer will be well-versed in risk management and will ensure that the best possible steps are taken to deliver a successful product launch. In addition, working with a contract manufacturer will allow you to benefit from smaller entry and exit costs – ideal for fast-paced markets where deployment must be achieved quickly, before the next development comes along.

Of course, flexibility isn't just about managing risk. It's about reacting to sudden opportunities and being fleet of foot enough to exit declining technologies and take advantage of new ones such as Point of Care testing.

This agility will empower you to respond to volatile and unpredictable market forces, rapidly increasing demand and evolving biological threats.

"Working with a contract manufacturer will allow you to benefit from smaller entry and exit costs – ideal for fast-paced markets where ROI must be achieved quickly."

SELECTING THE RIGHT LYOPHILISED BEADS PARTNER: 6 QUESTIONS TO ASK

A good lyophilised bead manufacturer will help you turn life-changing concepts into reality.

Advanced lyophilisation expertise can overcome your freeze-drying stabilisation issues and accelerate your projects to the next level, overcoming barriers to scaling up. They can also help you to avoid expensive mistakes.

Here are six questions you should ask when choosing a lyophilised beads contract manufacturer:

1	Do they provide turnkey solutions that meet your specific requirements for bead development and production?
2	Can they support you through the regulatory approval process?
3	Can they handle cold chain and dry ice incoming shipments of reagents?
4	Do they provide detailed analytical reports and rapid proof-of-concept prototypes?
5	Do they offer the flexibility and capacity you need?
6	Are they open and transparent, with a partnership approach to developing mutually beneficial relationships?

WHY OUTSOURCE YOUR LYOPHILISED BEADS PRODUCTION TO BIOFORTUNA?

Assay developers outsource their projects to Biofortuna because we are an experienced and trusted custom development and contract manufacturing partner.

Assay developers outsource their projects to Biofortuna as a trusted partner for custom development, contract manufacturing and genomic services. We can develop PCR assays in lyophilised, air-dried and liquid formats, using a range of different technologies.

We support diagnostic product and platform developers, research groups and not-for-profit organisations, providing custom services and turnkey solutions.

Our experienced lyophilisation experts will:

- ensure your formulation is suitable for lyophilisation
- oversee a flexible, quality assured manufacturing process
- reduce the overall time and cost of bringing an assay to market

Our support is tailored around your exact requirements and is defined by a problem-solving mentality. We listen to precisely what you need and utilise our experience, expertise, and resources to deliver the solution.

We partner with some of the world's most innovative in-vitro diagnostic and point of care assay developers, supporting them to take their assays from concept through to commercialisation.

A combination of technical expertese, state-of-the-art facilities, FDA registration and ISO 13485 and ISO 17025 accreditation means that our customers can rely on the highest scientific standards when bringing their products to market.

GET EXPERT TECHNICAL ADVICE

Biofortuna is a specialist contract development and manufacturing organisation providing genomic services, custom development and manufacturing support to the In-vitro diagnostic, consumer health, life sciences and pharma biotech sectors.

As an FDA registered, ISO 13485 and ISO 17025 accredited provider, we integrate our quality management system and design control standards within all our assay design, development and production projects.

Contact us today for an informal discussion around how we can help you bring your assays to market faster.

E&OE excepted: 01/22

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