LYOhub

LYOPHILIZATION TECHNOLOGY ROADMAP

www.lyohub.org

University of Connecticut

PURDUE UNIVERSITY

NIST

Welcome To Our Roadmap

To learn more about LyoHUB, our partners, and our research visit us online.

Online: www.lyohub.org

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Introduction

Who We Are & What We Do

Lyophilization (freeze-drying) removes water by sublimation at low temperature and pressure, and it is used in the food and pharmaceutical industries to preserve sensitive materials such as protein drugs, vaccines, fruits, and probiotic cultures.

The worldwide market for lyophilized foods and pharmaceuticals is approximately
$16 billion per year, a value equaled by the market for lyophilization equipment and services. Many food and pharmaceutical products could not be commercially viable without lyophilization. However, lyophilization is among the most time-consuming and expensive unit operations, with an energy efficiency of less than 5%, batch mode operation, open-loop processing, and lack of in-line quality monitoring.

> Working to transform and improve lyophilization.

To address these issues and to develop improved drying technologies for current and future products, an industry-led consortium—LyoHUB—was formed in 2014. LyoHUB's member companies span the value chain for lyophilization and include manufacturers of lyophilization equipment, instrument manufacturers, software providers, and end users in the food and pharmaceutical industries. The long-term goals of LyoHUB are to advance lyophilization technology through workforce training and industry-led precompetitive research and development. LyoHUB's current activities include writing and disseminating "best practices" papers on various aspects of lyophilization technology, hosting meetings and training

workshops on topics of interest to the members, providing online access to information and simulation tools through an interactive website, and maintaining a pilot-scale “demonstration center” in which the latest lyophilization technologies are presented and innovative new technologies are tested and developed.

A critical activity in the early years of LyoHUB has been the development of a technology roadmap for lyophilization. Generally speaking, a technology roadmap is a planning tool that connects the societal trends and pressures facing a product or industry with the technologies needed to address them. Technology roadmapping can identify gaps in broad areas such as fundamental science, technology, communication, logistics, and regulatory interactions, pointing a group toward their most impactful efforts over a particular time horizon. For LyoHUB, technology roadmapping has involved conducting a comprehensive survey of the current uses of lyophilization, projecting future needs and new product types, identifying critical gaps in current lyophilization practices and barriers to implementation of new technologies, and defining goals for the development of new lyophilization methods. The LyoHUB roadmap addresses a 20 year timeframe, embracing both current and projected needs.

5%

Lyophilization has an energy efficiency of less than 5%.

This report presents a summary of the LyoHUB technology roadmap. We first describe the process used to construct the roadmap and present the resulting roadmap in overview form. Subsequent sections then describe the five major areas of the roadmap in greater detail, identifying the advances that are needed in (1) lyophilized products, (2) lyophilization processes, (3) lyophilization equipment, (4) the regulatory interface, and (5) workforce training and education. While the roadmap is focused on lyophilization and related technologies, we hope that the needs identified will be broadly applicable to other drying technologies as well.

Overview

of the Roadmapping Process

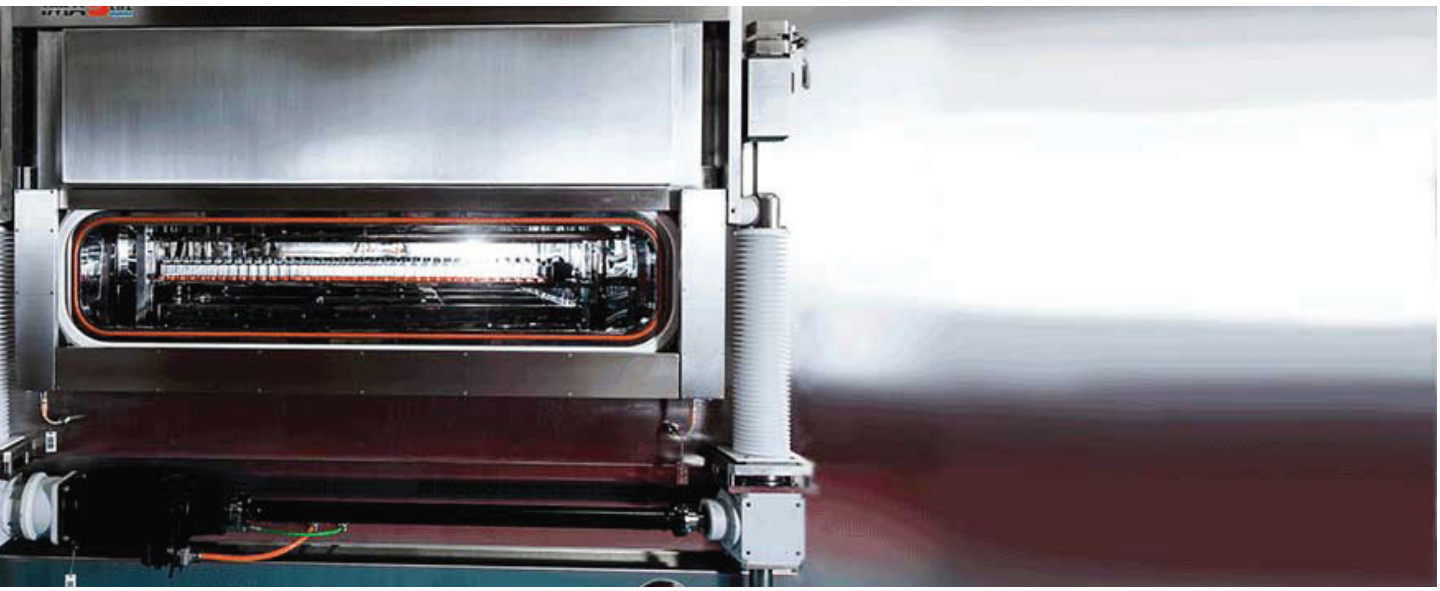
The process to develop the initial LyoHUB technology roadmap began with a structured workshop, and the roadmap proceeded to refine and focus industry feedback through a series of meetings, workshops, and discussions. The efforts progressed through three broadly defined stages as summarized below:

#01

Roadmap Framework and Initial Development

The original roadmap format included long-term, broad strategic objectives (key area topics) that would be achieved via medium-term research actions. In turn, the medium-term research actions would consist of short-term focused projects. These efforts would be guided by an impact matrix intended to capture roadmap stakeholder expectations.

A core team, consisting of industry and academic members, was formed to develop the roadmap taxonomy. To help guide the early efforts, the team engaged the Institute for Manufacturing (IfM) at the University of Cambridge for assistance in developing the roadmap structure and to facilitate the first workshop. The workshop followed IfM's S-Plan process, a well-established process to collect information covering a broad scope of topics that were defined through a series of core team meetings prior to the workshop. Topics were grouped in three interconnected layers: (1) Trends and Drivers, (2) Product Families, and (3) Technologies and Other Capabilities. Participants were invited to provide their input on the predefined layer topics, which were then aggregated into topical groups. Approximately 350 issues formed the basis for 20 Trend and Driver groups, 15 Product Family groups, and 15 Technologies and Other Capabilities groups. Multi-voting was used to prioritize the groups, and in-turn, the prioritized groups were subsequently revised and refined in Stage 2 and 3 activities.



#02

Roadmap Refinement and Development

Input from LyoHUB members and other subject matter experts was solicited through subsequent meetings, conference participation, and calls. That input ultimately led to a roadmap framework with two overarching focus areas with associated categories and subcategories. The focus areas and categories are:

1. Advancing Lyophilization Technologies and Techniques
    a. Products
    b. Process
    c. Equipment
2. Strengthening the Industry Foundation
    a. Regulatory Interface
    b. Workforce Development

#03

Roadmap Review and Publication

A concluding series of webinars with accompanying surveys was held to finalize the content and timelines for the initial roadmap. The webinars focused on a single category with in-depth discussions on each topic and its corresponding timeline.

Roadmap Summary Table

High Quality, Lower Cost, and More Readily Available Lyophilized Products

Advancing Lyophilization Technologies and Techniques

Products

- New, Improved Analytical Methods
- Product Design, Modeling, and Simulation Tools
- Improved Container/Closure
- Adaptability to new Lyo products

Process

- Process Instrumentation
- Process Modeling and Simulation
- Process Control and Automation

Equipment

- Equipment Harmonization for Accelerated Scale-Up and Technology Transfer
- Improved Lyo Technologies & Equipment for Existing & New Products
- Disruptive Lyo Technologies & Equipment for Accelerated and Continuous Processes

Strengthening the Industry Foundation

Regulatory Interface

- Agency - Industry Communication
- Dissemination of Best Practices

Workforce Development

- Higher Education
- Workforce Training

Roadmap Summary

Chapter 3

The technology roadmap for advancing lyophilization is summarized in the Roadmap Summary Table. The overall goal of innovation in lyophilization is high quality, lower cost, and more readily available lyophilized products. The roadmap identifies two broad areas of effort needed to move toward this goal: (1) advancing lyophilization technologies and techniques and (2) strengthening the industry foundation. Technical innovations will be required in areas related to lyophilized products, the lyophilization process, and lyophilization equipment. The full implementation of these technical innovations will depend on a strong industry foundation. This in turn will require that the interface between the industry and regulatory agencies be strengthened and that a well-trained workforce be developed and maintained.

overall goals

quality	cost	available
high quality	lower cost	readily available products

3.1 Product Lifetime Stages

The remainder of this report provides additional details in each of the five key areas of the roadmap: lyophilized products, the lyophilization process, lyophilization equipment, the regulatory interface and workforce development (Overview Table). Tables for each area expand on the bulleted items listed in the Overview Table, giving specific objectives as well as the aniticipated timeframe for their completion (short, medium and/or long term).

Lyophilization can be applied to a number of different types of products, and not all of the innovations are expected to be useful for all product types. Accordingly, icons in the area tables identify the lyophilized products most likely to be affected by achieving each objective. The product types are: cells (including cell-based therapies), small molecule drugs, diagnostics, biologics (including peptides, recombinant proteins and vaccines) and foods. Each of the roadmap tables also indicates the lyophilized product development lifetime stage that the specific technology topic is relevant to. Drug product development stages are summarized in the figure below. The pre-clinical stage spans from the initial investigation of promising agents to in vivo animal testing and results in Investigational New Drug Application which requires a) animal pharmacology and toxicology studies; b) manufacturing information related to composition, stability and controls of drug substance and the drug product; c) clinical protocols and investigator information for proposed clinical studies with a rationale for testing a new compound in humans, strategies for protection of human volunteers, and a clinical testing plan. Phase 1 clinical studies focus on the safety, pharmacology, and involve the compound being administered initially at very low doses to a few dozen healthy volunteers. Phase 2 studies consider efficacy and typically involve a few hundred patients suffering from the condition the new drug is designed to treat. Effective dosage, delivery method and additional product safety issues are further addressed in this stage. Phase 3 studies are designed to test previous findings on larger populations often involving thousands of patients and multiple sites. After successful completion of Phase 3 studies, a New Drug Application can be filed. Upon NDA approval, the marketing and production of the new pharmaceutical product commences. Some of the technological topics are relevant to all five stages as reflected in the roadmap tables.

*IND = Investigational New Drug

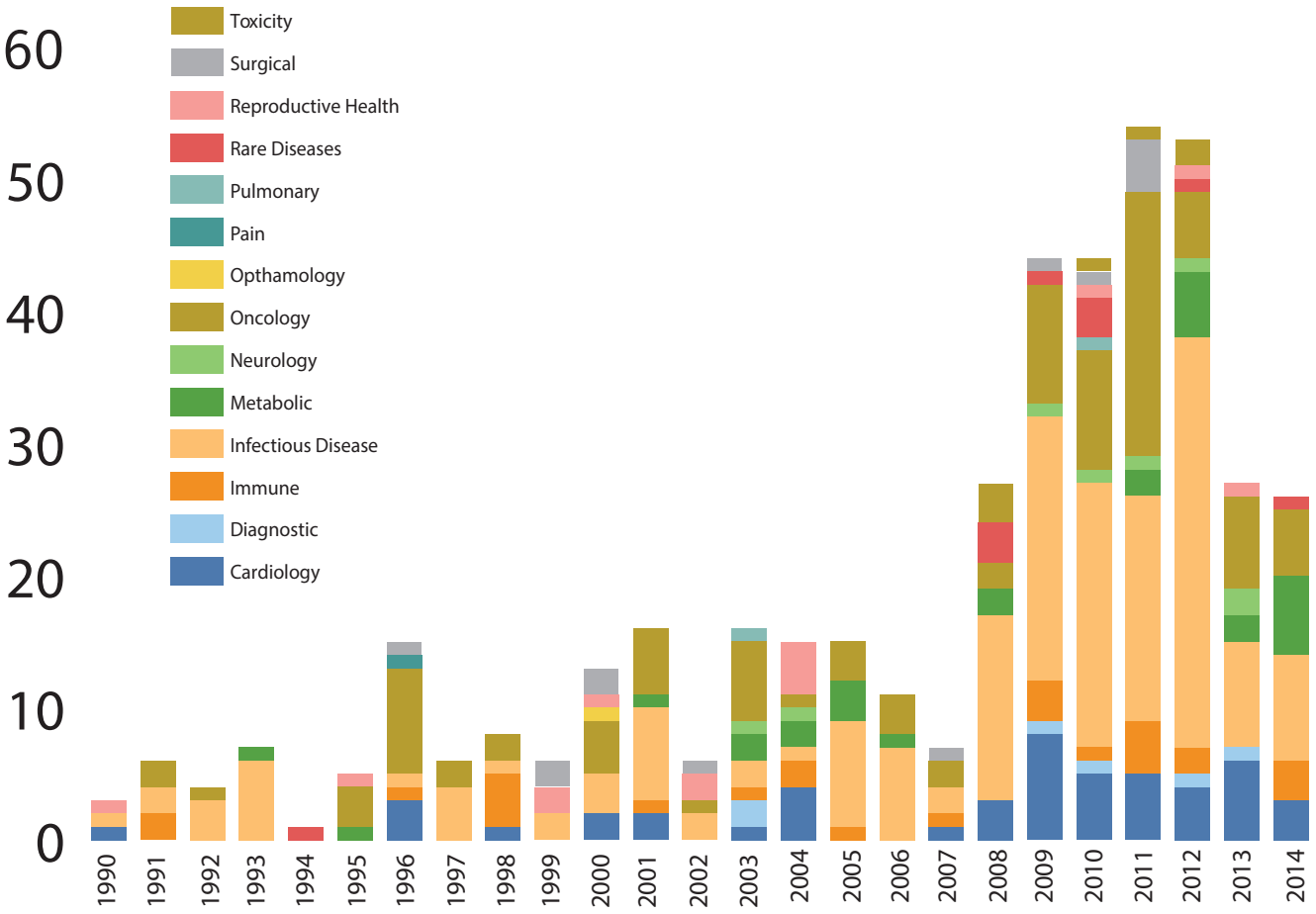
*NDA = New Drug Application

3.2 Trends and Drivers

Drug Approval Data

The lyophilized pharmaceutical sector is encountering and will need to continue adapting to an increasing number of patient-driven trends and drivers. These factors include single-use technologies, self-administered medical devices, and an increased globalization of manufacturing facilities to decrease the time and distance to end consumers. In turn, more indirect trends and drivers (viewed from a patient perspective) include reducing manufacturing process time, simplifying changes to processes, and increasing process efficiency. All of these trends and drivers, when addressed will enable manufacturers to provide patients with cost effective, efficacious treatments.

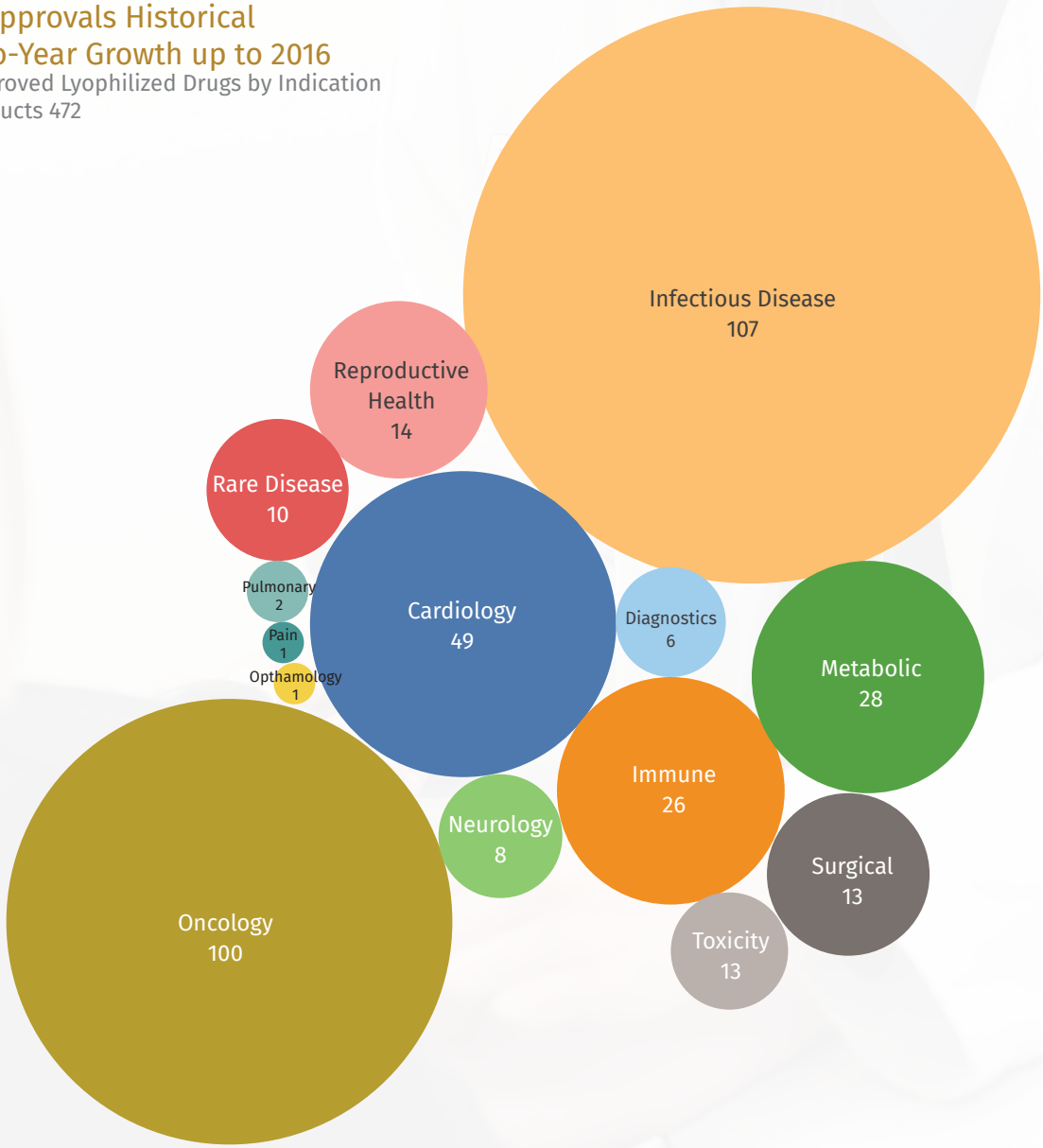
From 1990 to 1998 the share of newly approved lyophilized drugs as a share of all injectable/infusible drugs was 11.9%. In 2011, it was 41%, and in 2013-2015 injectable/infusible drugs requiring reconstitution made up half of all new approvals.



Source: Arduini, M. (2016, September). Freeze Drying Market Analysis. Presentation at IMA Aseptic Processing Symposium, Amherst, New York.

Drug Approvals Historical Year-to-Year Growth up to 2016

FDA-Approved Lyophilized Drugs by Indication
Tot. Products 472



Products

Chapter 4

Foods and pharmaceuticals together account for more than 95% of the global market for lyophilized end products, strong justification for a focus on these industries. While the largest end-product market is lyophilized foods, the greatest compound annual growth rate (CAGR) (11–13%) among all lyophilized products is for lyophilized biologics, the sector of the pharmaceutical industry that includes recombinant protein drugs, vaccines, and blood products.

The strong growth for lyophilized forms of these products is attributable to the overall rapid growth of this drug class and to the fact that lyophilized forms are frequently needed to ensure adequate shelf stability. It is estimated that, without the use of lyophilization, 60% of current pharmaceutical biologics could not be commercially viable.

Through technology roadmapping, LyoHUB participants have identified several broad areas of need for lyophilized products, including the need for new and improved analytical methods to characterize lyophilized solids, the need for modeling and simulation tools to support the design of lyophilized products, the need for improved container/closure systems, and the need to adapt lyophilization to entirely new types of end products. Each of these areas is discussed in greater detail below.

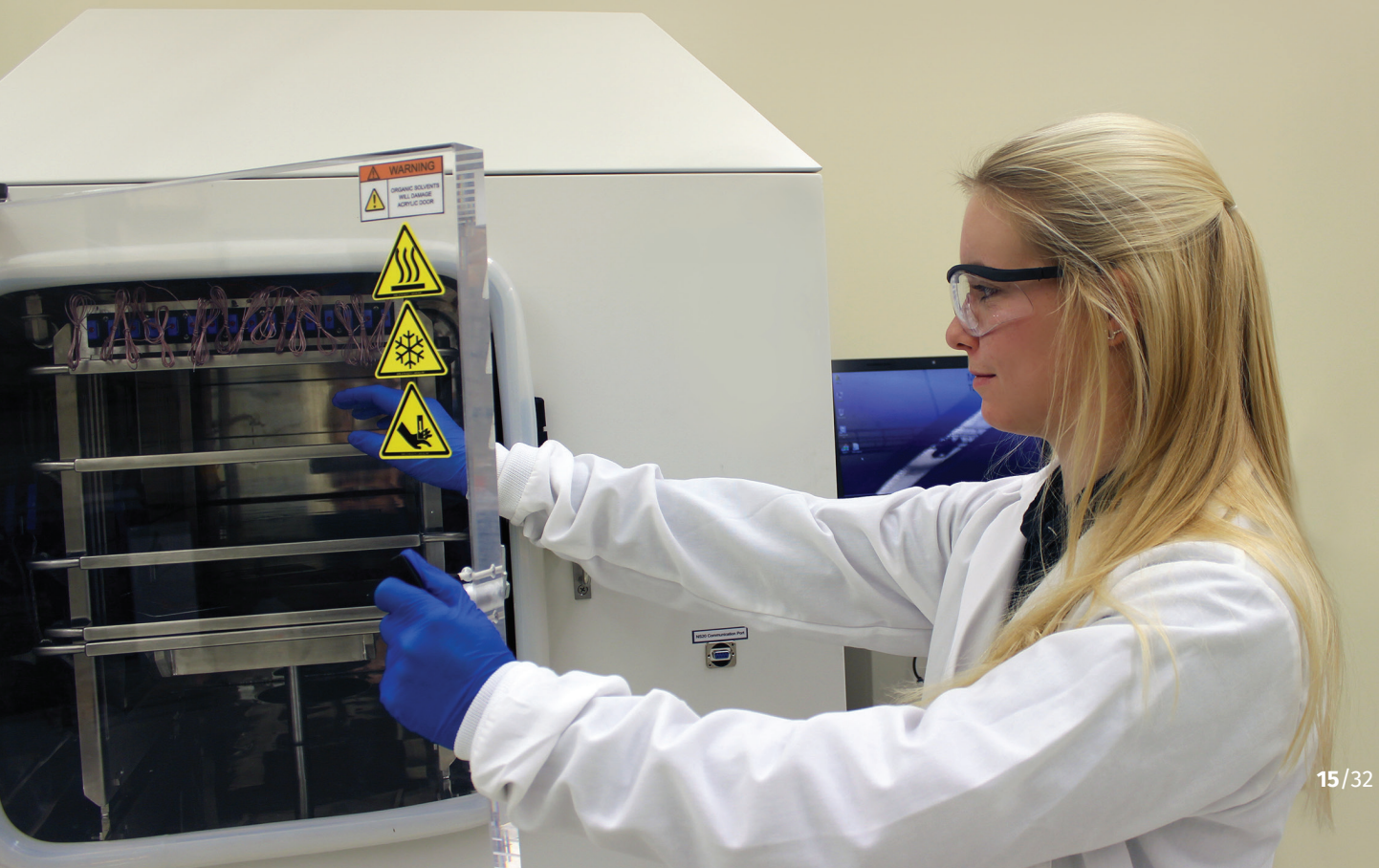
4.1 New and Improved Analytical Methods

Currently, lyophilized pharmaceuticals are characterized using a number of chemical, physical, and biophysical methods. The attributes measured include moisture content (e.g., by Karl Fisher titration), glass transition temperature (Tg, e.g., by differential scanning calorimetry), chemical integrity of the drug molecule (e.g., by high performance liquid chromatography and/or mass spectrometry), and, for proteins and other biologics, the secondary and higher order structure of the drug molecule in the solid powder (e.g., by Fourier transform infrared spectroscopy). Often, these properties are weakly correlated to the storage stability of the lyophilized product, if at all, so that the development and selection of an optimally stable formulation is largely a matter of trial and error. Roadmapping


Pre-Clinical
Clinical Phase 1
Clinical Phase 2
Clinical Phase 3
Market
Cells
Small Molecule Drugs
Diagnostics
Biologics
Foods
Short (2017-2018)
Medium (2019-2024)
Long (2025+)
Products
New & Improved Analytical Methods
Reduce formulation development time
by relating analytical attributes of lyophilized solids to formulation stability and performance
Improve measurement and characterization
of product and process performance by developing solid state characterization techniques for frozen and freeze dried states (e.g. for measuring protein tertiary structure and real time, non invasive measurement of residual moisture content.)
Product Design, Modeling and Simulation
Understand which physical properties are critical for protein stability in lyophilized solids
(e.g., molecular mobility, acid/base relationships)
Create a platform formulation
that stabilizes different classes of macro-molecules
Develop approaches to provide fast reconstitution
for high concentration protein formulations
Develop fit-for-purpose excipients
(e.g., viscosity reducers, shorter cycle times) suitable for a variety of APIs (active pharmaceutical ingredient)
Improved Container/Closure
Introduce new and easy-to-use formulations designed for self-administered medical devices
and container/closure systems to improve user convenience
Develop vial or stoppers with built-in, multi-sensor arrays
for development purposes
Develop better understanding of container/formulation interaction
(e.g. vial fogging and lyophilized cake cracking)
Develop new container/closure system for improved user convenience with low oxygen permeability
including for needle-free reconstitution and plastic vials.
Adaptability to New Lyophilization Products
Develop new lyophilization processes to handle cell & gene therapies and diagnostic agents

4.1

participants thus identified a need to reduce formulation development time by relating the analytical attributes of lyophilized solids to formulation stability and performance. Similarly, participants felt there was a need for improved solid-state analytical methods that would offer improved characterization of frozen and freeze-dried solids that better predicted storage stability and other performance attributes (e.g., reconstitution time). Since excipients are critical to the properties of lyophilized solids, participants suggested that the design, development, and clinical evaluation of new excipients could help to expand formulation options and improve product performance.



4.2 Improved container/closure systems

Roadmapping participants also identified a need for new and improved container/closure systems. Currently, most lyophilized pharmaceuticals undergo lyophilization in individual glass vials with rubber stoppers, which also serve as the container/closure system for the final product, although some are supplied in dual-chamber syringes.

Participants identified the need for new and easy-to-use container/closure systems, perhaps involving needle-free systems. The possible advantages of replacing glass containers with plastics were also discussed, together with the need to better characterize chemical and physical interactions between the formulation and the container. **Participants also identified a need for lyophilization vials or stoppers with built-in multisensor arrays,** which would allow the conditions experienced by an individual vial (e.g., temperature, pressure) to be monitored during lyophilization, shipping and storage. Vials with built-in sensors would enable out-of-range conditions to be identified for single vials. As a result, lyophilization cycles could be better controlled, valuable information could be provided to inform lyophilizer design, and, in production, out-of-range vials could be discarded without compromising all of the vials in the lot.

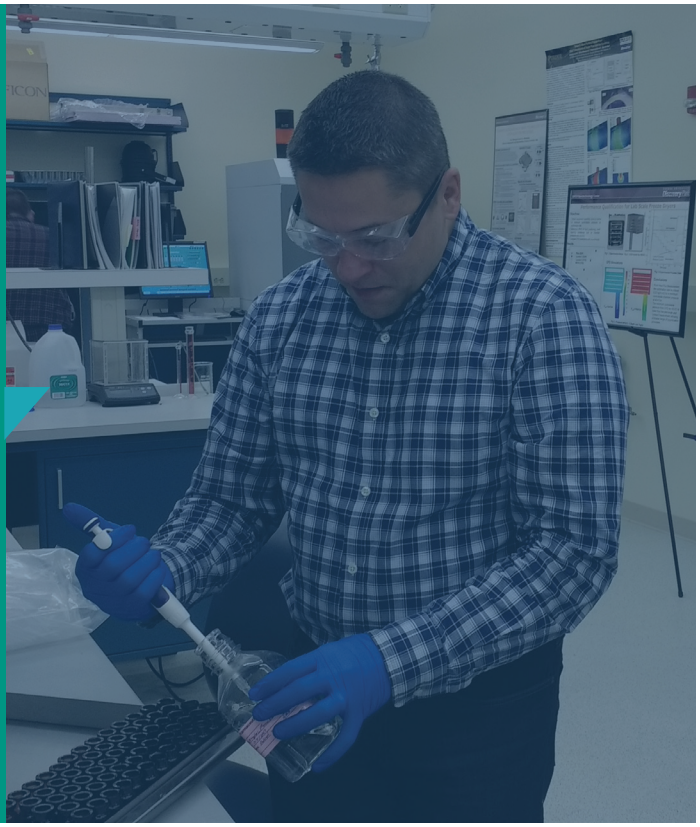
4.3 Adapt lyophilization to new product types

As noted above, foods and pharmaceuticals account for more than 95% of current lyophilized end products. During technology roadmapping, participants identified a need for new lyophilization processes that can handle the entirely different types of products now entering the marketplace. These products include gene therapies, cell-based therapies, and diagnostics, all of which may require dried forms produced without heating to ensure shelf stability. Participants noted that there is little to no information on lyophilizing these materials in the open literature.

Process

Chapter 5

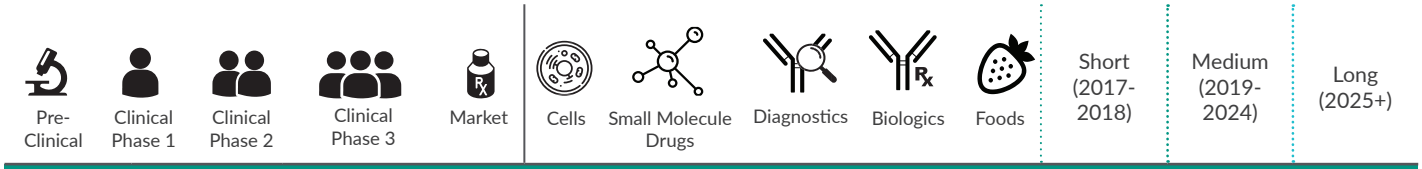
Current lyophilization practice uses open-loop controls with predetermined settings for process input parameters, such as heat transfer fluid temperature and chamber pressure, with some monitoring of process output parameters. Product attributes such as product temperature, drying rate, and residual moisture content are rarely monitored directly in the manufacturing setting. Process deviations from the approved settings require evaluation, investigation, and response according to regulatory agency requirements.



Process automation, on the other hand, uses a network of process sensors and actuators which are analyzed and controlled by computerized process software.

Similar to its effect in the chemical industry, process automation is likely to bring about a significant increase in productivity and efficiency of lyophilization processes. For example, monitoring both heat flow to the product and product temperature while varying heat transfer fluid input has been shown to accelerate primary drying by 50%. [1]

[1] LyoPAT™: Real-Time Monitoring and Control of the Freezing and Primary Drying Stages During Freeze-drying for Improved Product Quality and Reduced Cycle Times. Millrock, 2016.



Process

Process Instrumentation

Develop in-line, in-process spectroscopic techniques
for moisture content and product temperature determination

Develop wireless and/or wired distributed sensors
for continuous measurement of temperature and other process variables

Develop TDLAS
(tunable diode laser absorption spectroscopy) and other tools for in situ sublimation rate measurements

Develop technologies for 100-percent, automatic inspection
(residual water content, visual appearance) of lyophilized products

Process Modeling and Simulation Tools

Develop models and simulations
to characterize the impact of process variations on product quality using physics-based and statistical approaches

Primary Drying

Secondary Drying/Freezing

Provide models which are user friendly
and supported by ongoing training and updates

Develop and use computer models
to estimate manufacturing process costs

Process Control Tools

Develop closed loop process controls
with integrated PAT (process analytical technology) and process monitoring tools

Improve control of the freezing process
to increase consistency and quality and reduce cycle times

Three major areas for future technology development

The transition from the current open-loop processes to more efficient automated closed-loop control in lyophilization will require better scientific understanding of the process as well as technology development.

The LyoHUB roadmapping participants identified three major areas for future technology development related to lyophilization process: (1) process monitoring instrumentation, (2) process modeling and simulation, and (3) process control and automation.

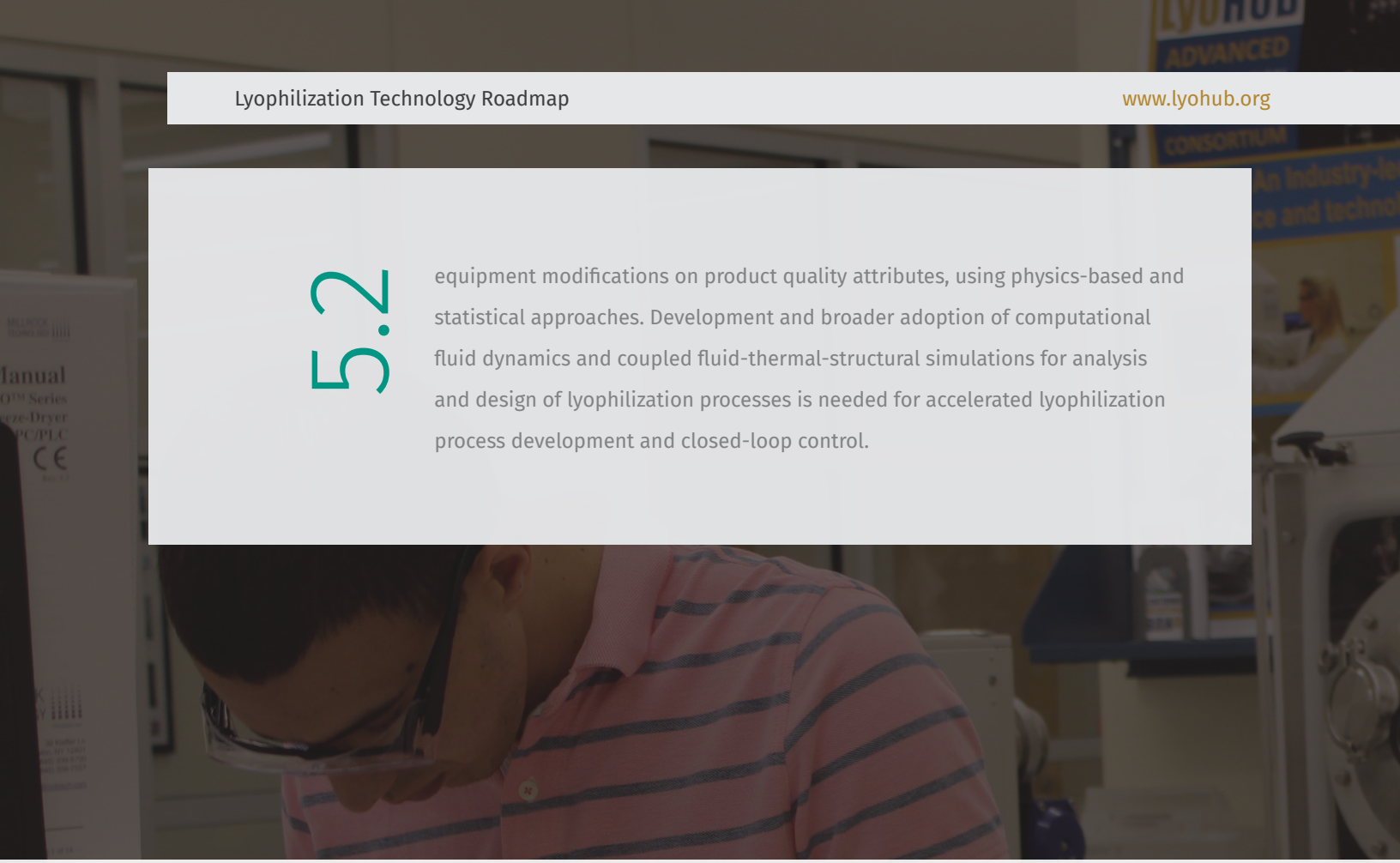
5.1 Process monitoring instrumentation

Process monitoring instrumentation during lyophilization in a GMP (good manufacturing practices) production setting is very limited due to the harsh vacuum environment and strict sterility requirements. The roadmap participants identified several areas of technology development that would have high impact for process improvement. The current practice in process development mainly involves wired temperature probes for product temperature monitoring. Whereas such wired probes are widely used in process development at laboratory and pilot scale, they are typically not compatible with the automatic loading systems used in the production environment. Wireless, non-invasive product temperature sensors that could be used in a GMP setting are a high-priority for future technology development. Real-time spectroscopic measurements of product residual moisture content and vapor flow rates are desirable technologies that would enable direct monitoring of product attributes and process uniformity.

5.2 Process modeling and simulation

Mathematical modeling of heat and mass transfer processes in freeze-drying is widely recognized as an important tool for developing robust lyophilization processes. Reliable models of quasi-steady state primary drying stage are currently widely used by the industry. The roadmapping participants recognized the need for advancing the mathematical modeling tools for freezing and secondary drying stages. Additionally, there is a need to develop models and simulations that quantify the impact of process variations, such as chamber pressure, variation in product loads, and

5.2 equipment modifications on product quality attributes, using physics-based and statistical approaches. Development and broader adoption of computational fluid dynamics and coupled fluid-thermal-structural simulations for analysis and design of lyophilization processes is needed for accelerated lyophilization process development and closed-loop control.



5.3 Process control and automation

The consensus of roadmapping participants was that there are two major areas of future technology development for process control: (1) control of the freezing process at all scales from laboratory to production and (2) closed-loop control of the primary drying stage. Controlled ice nucleation in the freezing stage is needed for consistent ice crystal structure and, as a consequence, uniform mass transfer resistance and drying rates across the product batch. The primary drying stage is typically the longest and most energy intensive stage of freeze-drying. Currently, only the end of primary drying is monitored in production by monitoring residual moisture content in the chamber through comparative pressure measurement. The closed-loop control of primary drying can bring about significant process acceleration and efficiency improvement and will require development of process analytical technologies for the monitoring and controlling of heat flow and product temperature in real time.

Equipment

Chapter 6

Because of the high capital costs for production-scale pharmaceutical lyophilization systems and the lengthy regulatory approval process, the pace of innovation in lyophilization equipment has been slow.

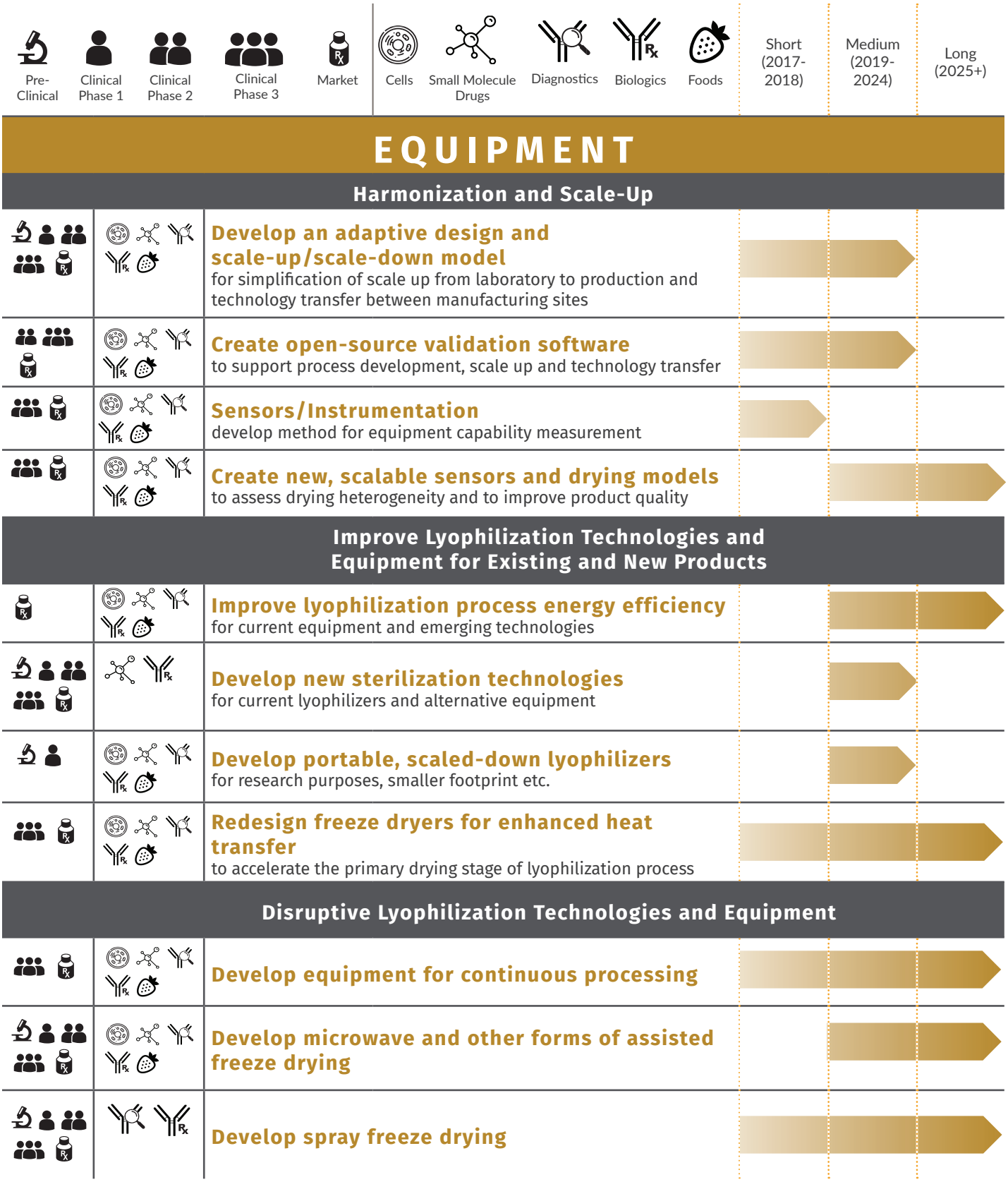
Design of lyophilizers has not changed.

The essential design of lyophilizers has not changed appreciably in the decades since the first tray-style lyophilizers were introduced. However, changes in the design of lyophilizer components, such as the size and location of the duct between the product chamber and condenser, can increase vapor removal capacity, shorten cycle times, and increase overall energy efficiency. LyoHUB roadmap participants have identified several technologies that are likely to improve current lyophilization equipment and may lead to disruptive new technological alternatives to lyophilization.

> The pace of innovation in lyophilization equipment has been slow.

6.1 Equipment harmonization and scale-up

There is consensus in the lyophilization community regarding the need for harmonization of performance characterization of lyophilization equipment. Such harmonization can significantly shorten the equipment and installation validation time and accelerate processes development and technology transfer between different lyophilizer systems. As an initial step in this direction, LyoHUB is preparing a publication of recommended best practices in lyophilization equipment performance characterization. A unified approach for testing and reporting is needed for equipment characteristics, such as minimum controllable pressure, temperature, and pressure uniformity under various loads.


Pre-Clinical
Clinical Phase 1
Clinical Phase 2
Clinical Phase 3
Market
Cells
Small Molecule Drugs
Diagnostics
Biologics
Foods
Short (2017-2018)
Medium (2019-2024)
Long (2025+)
EQUIPMENT
Harmonization and Scale-Up
Develop an adaptive design and scale-up/scale-down model
for simplification of scale up from laboratory to production and technology transfer between manufacturing sites
Create open-source validation software
to support process development, scale up and technology transfer
Sensors/Instrumentation
develop method for equipment capability measurement
Create new, scalable sensors and drying models
to assess drying heterogeneity and to improve product quality
Improve Lyophilization Technologies and Equipment for Existing and New Products
Improve lyophilization process energy efficiency
for current equipment and emerging technologies
Develop new sterilization technologies
for current lyophilizers and alternative equipment
Develop portable, scaled-down lyophilizers
for research purposes, smaller footprint etc.
Redesign freeze dryers for enhanced heat transfer
to accelerate the primary drying stage of lyophilization process
Disruptive Lyophilization Technologies and Equipment
Develop equipment for continuous processing
Develop microwave and other forms of assisted freeze drying
Develop spray freeze drying

6.2 Improve lyophilized technologies and equipment for existing and new products

Sterilization Process

Areas of Improvement

Current production lyophilizers have very low-energy efficiency. Improvement of both process and equipment is needed to achieve highly efficient and robust lyophilization. The major directions for current equipment improvement include:

- More efficient heat transfer to the product
- Improved transport of sublimed vapor from chamber to condenser through changes in the design of chamber-to-condenser interface and valves
- Optimized configuration and operating conditions of icing condensers.

An additional area of major improvement for current lyophilization equipment is the sterilization methods. Pharmaceutical lyophilization systems are sterilized to eliminate microorganisms and inactivate viruses, and typically a sterility assurance level of 10-6 needs to be demonstrated. The current sterilization methods are time consuming and costly. The most widely used sterilization is achieved by exposure to saturated steam at a temperature of 121–125 C. Steam sterilization involves heating and recooling the entire lyophilization system, producing undesirable thermal stresses that accelerate equipment wear and aging. Due to the large thermal mass of production-scale equipment, a typical sterilization cycle takes more than six hours. There is a need for low-temperature sterilization methods and associated technologies. Alternatives to steam sterilization include vaporized hydrogen peroxide (VHP) sterilization and cold plasma sterilization.

10-6	121° C	6 hrs
Assurance Levels	Sterilization Temperature	Sterilization Cycle

6.3 Disruptive lyophilization/drying technologies and equipment

Electromagnetic Heating in Freeze-Drying

The use of electromagnetic radiation in the form of infrared (IR) heaters or volumetric heating by microwave- or radio-frequency dielectric heating can significantly accelerate the freeze-drying process.

Technology development is needed to adapt electromagnetic heating methods to the scale and operating requirements of pharmaceutical lyophilization systems. The main advantages of electromagnetic heating are the extremely fast response and greater tunability, including local temperature control, as compared to the currently used heating methods based on circulating heat transfer fluids. Such highly tunable and responsive heat inputs are advantageous for closed-loop, automated lyophilization processes.

Spray Freeze-Drying

Spray freeze-drying can be used to produce bulk lyophilized drug substance much faster than freeze-drying in trays and vials. This is due to:

- The large surface area available for sublimation because of small particle size, and
- Faster heat transfer by forced convection or high-temperature radiant heating instead of low-temperature conduction and radiation in traditional freeze-drying.

A critical step in advancing spray freeze-drying technology for pharmaceutical manufacturing is achieving better process understanding and development of mathematical models of spray freeze-drying that could be used for process design. Additionally, sterile powder filling technology needs to be more readily available for spray freeze-drying to be applicable for manufacturing unit dosage forms of lyophilized products.

Equipment for Continuous and Semi-Continuous Lyophilization

In current practice, the lyophilization of pharmaceutical and biological products is performed as a batch-type operation. The starting liquid solutions are filled in vials, syringes, or trays and then lyophilized as a single batch. Batch uniformity remains a serious issue, especially for large-scale production lyophilizers. Food freeze-drying has seen a shift over the last few decades to semicontinuous and even completely continuous operations. The progression from batch to continuous processing typically brings about increased productivity and uniformity in product attributes. Various approaches for semicontinuous and continuous lyophilization are being explored by industry and academic researchers. Examples include semicontinuous processes based on spray freezing and agitated vacuum drying, atmospheric spray freeze-drying, foam drying, rotary shell freeze-drying in vials and electrospinning. The roadmapping participants identified continuous lyophilization as a high-priority technology development area for pharmaceutical manufacturing.

Regulatory Interface

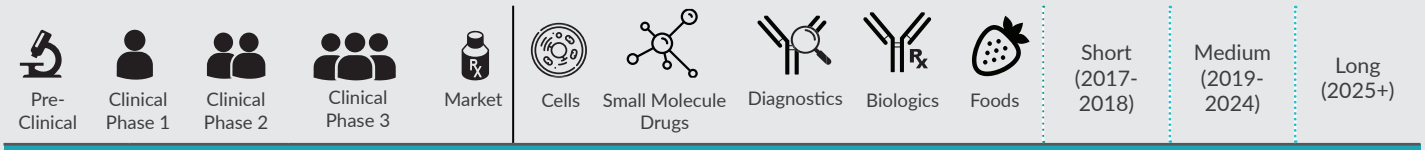
Chapter 7

In addition to the technical innovations described above, progress in lyophilization is critically dependent on the interface between the industry and various regulatory agencies, including the U.S. Food and Drug Administration. Together with workforce education and training, the regulatory interface provides the foundation on which any technical innovations must rest.

Participants in technology roadmapping identified several strategies for improving the regulatory interface for lyophilization and related technologies. At a broad level, they saw opportunities to improve communication between regulatory agencies and the industry. Specific strategies suggested by the participants included developing a systematic approach to setting inspection expectations to ensure consistency and compliance and improving the industry's ability to change validated lyophilization processes to accommodate new technologies. Similarly, participants felt that improving the receptivity of regulatory agencies to new technologies through various means of communication would help reduce the barriers to implementation of new technologies.

Together with workforce education and training, the regulatory interface provides the foundation on which any technical innovations must rest.

A specific form of communication embraced by the roadmapping participants is the creation and dissemination of "best practices" papers. A best practices paper summarizes the views of industry and academic researchers at a given time regarding the most preferred and/or accepted methods or techniques, as well as identifying areas for improvement. In the pharmaceutical industry, best practices papers serve as a form of communication among industry members and with regulatory agencies. For lyophilization, participants in technology roadmapping felt that best practices papers on equipment qualification, platform lyophilization process development, instrumentation, and other topics were needed. They recommended that the documents be disseminated via open access, though they did not preclude publication in scientific or trade journals. The participants further recommended that best practices information be shared between the food and pharmaceutical industries, and that a framework or set of criteria for updating best practices be established.



Strengthening the Industry Foundation

Agency – Industry Communication

Develop a systematic approach
to enforce inspection expectation for consistency and compliance

Improve ability to change validated lyophilization
processes to accommodate new technologies

Improve receptivity and remove barriers
to new technology implementation

Publish Best Practices Papers

Publish best practices papers
on equipment qualifications, platform lyophilization process development, instrumentation, and other topics

Disseminate best practices via open access

Share best practices and other information
between pharmaceutical industry and food industry

Establish framework for updating best practices

Higher Education

Develop new biotech processing education programs
at universities to meet industry shortages of skilled workers

Add educational programs in universities
to train new workforce on lyophilization technologies

Certification/assessment tools

Workforce Training

Develop and deploy workforce distance learning programs
on practical considerations for formulation and process development

Host workshops to educate industry
about current and emerging technologies, measurement techniques/technologies, and process and formulation topics

Need to increase the educational role
of equipment manufacturers in order to avoid manufacturing disruptions

Need to address the shortage
of adequate technical training to decrease operational impacts

Workforce Development

Chapter 8

Effective implementation of new and existing lyophilization technologies will require a skilled workforce across all education levels. In technology roadmapping, participants identified a need for new educational programs in biotechnology processing at the university level to meet the industry shortages of skilled workers. They suggested that content related to lyophilization technologies be included in such programs and that universities develop certification and assessment tools that would be recognized by the industry. For continuing education of both technical and operational workers, roadmapping participants felt that distance learning programs related to practical considerations for lyophilization formulation and process development should be developed and deployed. Similarly, participants also recognized the need for workshops to educate industry about current and emerging lyophilization technologies, process and formulation topics, and measurement techniques. A need to expand the educational role of equipment manufacturers was also identified and thought to be important in avoiding manufacturing disruptions. At the operator level, there is a need to address the shortage of technical training in lyophilization to decrease operational impacts.

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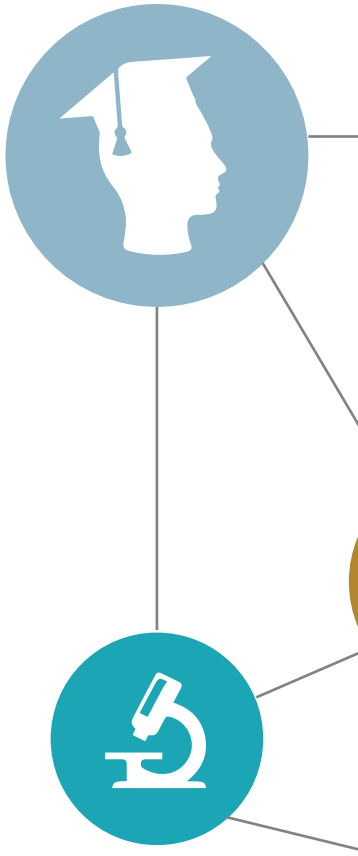

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