Understanding individual experiences with stick-built and modular cleanrooms: Lessons learned and a call to action

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Lori T. Armistead, MA, PharmD, Division of Practice Advancement and Clinical Education (PACE), University of North Carolina at Chapel Hill Eshelman School of Pharmacy, Chapel Hill, NC, USA

Stephen F. Eckel, PharmD, MHA, Division of Practice Advancement and Clinical Education (PACE), University of North Carolina at Chapel Hill Eshelman School of Pharmacy, Chapel Hill, NC, USA and Department of Pharmacy, University of North Carolina Medical Center, Chapel Hill, NC, USA

Address correspondence to Dr. Eckel (seckel@unc.edu).

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Purpose: The purpose of this study was to assess the real-world experiences of cleanroom managers and specialists who have designed, installed, and maintained stick-built and/or modular cleanrooms, delineate the advantages and disadvantages of each type of cleanroom, and gather sterile compounding cleanroom design and installation advice and lessons learned.

Methods: This study was conducted via surveys and semistructured interviews of individuals with cleanroom experience in the previous 5 years. Qualitative analyses were conducted on participants' survey and interview responses to assess their satisfaction with each type of cleanroom and to determine what they perceive to be the pros and cons of each type based on their own experiences. Key lessons learned and advice from these individuals were also extracted from their survey and interview responses.

Results: Fourteen individuals from 13 US states completed the survey; 12 participated in follow-up interviews. Fifty percent of the participants (n = 7) had installed 5 or more cleanrooms in the previous 5 years and over half (n = 8; 57%) had 7 or more years of cleanroom experience. The average satisfaction scores for each type of cleanroom, on a 1 to 10 scale, was 5.3 for stick-built (n = 11) and 9.3 for modular (n = 4). The pros of stick-built cleanrooms included greater design and material flexibility and lower up-front costs. The pros of modular cleanrooms included the cleanroom experience and expertise of modular vendors, quick and easy installations, guaranteed certification, and high-quality and durable design features and materials. Additionally, modular cleanrooms had fewer long-term maintenance issues, greater long-term flexibility, and lower indirect and long-term costs than stick-built cleanrooms. Key pieces of advice from the participants included the following: do your homework before beginning a cleanroom project; make sure heating, ventilation, and air conditioning system(s) and air handlers are adequate for your needs; and remember that the ultimate purpose of a quality cleanroom is patient safety. Participants also advocated for industry-wide cleanroom standards that go beyond USP regulations.

Conclusion: The findings of this study confirm many of the purported pros and cons of each type of cleanroom, with further insight gained into the relative quality and costs of each type. Modular cleanrooms were considered by most participants to be a better long-term option, based on quality and lifetime costs, if feasible to install. Study participants also emphasized that designing and installing pharmacy cleanrooms is a complex and time-intensive process that often comes with a steep learning curve. While there are federal and state cleanroom standards available and consultants for hire, a comprehensive resource or manual that could provide guidance, insight, and collective lessons learned on cleanroom design and installation is needed.

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Pharmacy cleanrooms provide hospitals and other sterile compounding facilities with environments for the safe preparation of sterile medication products. Designing and installing a cleanroom is a complex, technical, and time-intensive endeavor that requires extensive planning and oversight. Pharmacy-specific state and federal regulations provide cleanroom standards to ensure that medication admixtures compounded in these facilities can be made free from particulate matter, dust, and microbials, with the ultimate goals of ensuring patient safety and minimizing the risk of harm to employees.[1,2] Changes in the minimum United States Pharmacopeia (USP) standards for cleanrooms (updates to USP chapter <797>, "Pharmaceutical Compounding—Sterile Preparations," and the newly created USP chapter <800>, "Hazardous Drugs—Handling in Healthcare Settings") need to be considered when embarking on a new cleanroom build or renovation.

In keeping with updated USP standards, cleanroom technology has evolved over the years, providing cleanroom customers with many options for meeting those requirements. "Stick-built" cleanrooms, the traditional type of cleanroom, are constructed solely on-site using standard building materials, while modular cleanrooms are constructed off-site prior to installation.[3] Modular cleanrooms are advertised to be a more cost-effective, higher-quality, more durable, and more flexible option than stick-built cleanrooms; however, approximately 85% of all cleanrooms worldwide are stick-built.[3-5]

There are many factors to consider when evaluating whether a stick-built or modular cleanroom is best for a given sterile compounding pharmacy's needs. Features that should be evaluated for a proposed cleanroom include its physical structure, internal environment, interaction technologies, and monitoring system.[6]

For the physical structure, the materials used in construction and how these materials will be combined are important, as they will affect the cleanroom's cost, time of construction, cleanability, and durability.[6] A cleanroom's physical structure will also be dictated in part by the size and shape of the space available.

Methods of controlling the internal environment, such as how appropriate temperature and humidity will be maintained, what type of filtering system and room fixtures will be installed, and the airflow technology used are important considerations as well.[6-8] The internal environment should be engineered in such a way that staff are protected from the products and the products protected from contaminants.[8] The types of interaction technology required, such as transfer hatches, anterooms, entrance doors, and location of storage should also be assessed, as well as the technical support, in-service training, and environmental monitoring vendors can provide.[6-8]

Other factors that should be weighed when exploring cleanroom options are one's facility, state, and national regulatory requirements; the durability, functionality, and total cost of the cleanroom (including both upfront and long-term costs); and what future modifications or expansion would entail.[5-7]

Potential advantages and disadvantages for stick-built and modular cleanrooms have been described. For example, the pros touted for stick-built cleanrooms include that construction materials are readily available and cost-effective, most contractors are knowledgeable and can usually accommodate modifications during construction, and construction costs can be spread out over time.[5]

Some potential cons for stick-built cleanrooms include unforeseen time, consultant, and construction management costs; excessive particulate matter generated by on-site construction; the need for multiple teams to complete the project; construction delays with associated costs; and the reality that expansion of the cleanroom will likely necessitate the pharmacy going offline.[4,5,9]

In contrast, due to manufacturing and assembly steps that occur off-site, modular cleanrooms are typically installed over a shorter timeframe, thus minimizing on-site disruptions.[4,5] Other potential pros for modular units are that they are built with interlocking panels, reducing the potential for air leakage or infiltration; no sanding or painting is required during their construction, reducing the risk of extra particulate matter and vapors in the environment; they can have walkable ceilings, allowing for ease of ongoing maintenance; and they tend to have lower construction management and life-cycle costs due to specialty installation teams, fewer long-term maintenance needs, and durable building materials.[4,5]

KEY POINTS

- Individuals with real-world experience designing, installing, and maintaining stick-built and modular cleanrooms were surveyed and interviewed to provide their perspectives on the pros and cons of each type of cleanroom as well as to provide advice and lessons learned on pharmacy cleanroom design and installation.
- The pros of stick-built cleanrooms included greater design and material flexibility and lower up-front costs, and the pros of modular cleanrooms included quick and easy installations, guaranteed certification, higher-quality materials, greater long-term flexibility, and lower indirect and long-term costs.
- A comprehensive industry-wide resource or manual that can provide guidance, insight, best practices, and collective lessons learned on pharmacy cleanroom design and installation is needed.

Some of the negatives associated with modular cleanrooms include large upfront costs, less flexibility for design changes during installation, and limitations due to existing building codes and/or dimensions of the available space.[5] Additionally, while the installation timeframe may be shorter for a modular cleanroom, the time required for the total build may be as long as for a stick-built cleanroom since each panel must be built to specification.[5,9]

Any sterile compounding pharmacy managers planning to renovate the current cleanroom or install a new one should assess these pros and cons considering their needs, financial constraints, and other parameters. Exploration of indirect or hidden costs of a proposed cleanroom project is also important. These tasks are difficult though, as "potential" pros and cons and estimating potential indirect costs provide limited insight.

Over the past 15 years, with the initial implementation of USP <797> and introduction of new USP <797> and <800> standards, published articles have offered advice and recommendations on how to comply with these standards, regardless of cleanroom type (stick-built or modular).[1,2,10-15] These articles often give suggestions on cleanroom design features, materials to use, and other considerations that are not specified or described in cleanroom standards that impact a cleanroom's cleanliness, workflow, and durability.[13-15]

In one such article from 2019, pharmacy leaders from 4 US hospitals provided insight on cleanroom design considerations based on their collective experiences and within the context of the proposed USP <797> and <800> updates.[2] They recommended what to consider when selecting cleanroom building materials (eg, floors, walls, ceilings) and equipment (eg, cleanroom doors, sinks, carts, pass-throughs). They also provided a generalized timeline for designing and building a cleanroom efficiently and advice on ways to design a cleanroom for the future.

The insight offered in these publications is useful for identifying some best practices in cleanroom design and installation, all within the context of complying with, and in some instances exceeding, cleanroom standards. However, the advice presented in current literature has thus far been from a select number of pharmacy cleanroom experts from a select number of healthcare institutions.

One purpose of this study was to delineate the advantages and disadvantages of stick-built and modular cleanrooms as described by individuals with real-world experience designing, installing, and maintaining cleanrooms. A second purpose of this study was to gather cleanroom design and installation advice and lessons learned from sterile compounding cleanroom managers and specialists from different types of healthcare organizations across the US. Such insight can be used to build upon the advice and best practices that have already been published.

With the publication of these findings, we are also issuing a call to action for the development of industry-wide standards that delve deeper into the decision points, details, and issues that face those undergoing a cleanroom design and installation project, thus providing comprehensive guidance and a delineation of pharmacy cleanroom best practices that can be applied to any type of cleanroom.

Methods

To gather information from pharmacy cleanroom experts on their experiences designing, installing, and maintaining pharmacy cleanrooms—and to garner from them key lessons learned—an online survey was sent to participants and follow-up semistructured interviews performed.

Inclusion criteria. The inclusion criteria were experience as a compounding pharmacy manager or specialist and participation in the installation and maintenance of at least one modular or stick-built cleanroom in the past 5 years, with at least one having been completed over a year previously. Participants were recruited through a posting in an ASHP Connect online community and by personal invitation. Eighteen individuals responded to the call to participate, and survey invitations were sent out to them via email. Fourteen survey responses were received, and 12 follow-up interviews were conducted. Prespecified minimums of 5 participants with stick-built cleanroom experience and 5 with modular cleanroom experience were met.

Methodology. A web-based survey consisting of 58 questions was developed by the research team based on a list of general topics of query. Follow-up interview questions were then developed on the basis of the content of the survey questions and a few additional avenues of inquiry. The research team was comprised of individuals with pharmacy cleanroom, survey development, and qualitative interview experience.

The survey included a mix of open-ended and multiple-choice questions that were designed to assess the factors that went into the participants' cleanroom design and decision-making processes, their experiences during their cleanroom installation(s), and their postinstallation maintenance experiences.

Once they completed the survey, all participants were invited to participate in a follow-up interview conducted virtually. The interview questions were designed to probe more deeply into the participants' survey responses and to further assess and understand their cleanroom design, installation, and maintenance experiences. Additional questions (eg, What do you wish you had known prior to selecting, designing, and installing your cleanroom? What would you have done differently with this installation if you could go back in time? What advice you would give to someone else who was about to embark on designing and installing a pharmacy cleanroom?) were also asked of the participants to elicit additional advice and key lessons learned.

Survey responses were collected from August through October 2022, and interviews were conducted virtually via Zoom (Zoom Video Communications, San Jose, CA) from September through November 2022. Each interview lasted 35 to 50 minutes and was audio recorded, and interview participants received a gift card as compensation for their time. The survey questions and interview guide are provided in eAppendixes A and B.

The study was reviewed and exempted by the University of North Carolina at Chapel Hill Institutional Review Board for Research (IRB #22-1803).

Analysis. All survey data were collected via Qualtrics software (Qualtrics XM 2022; Qualtrics, Provo, UT) and downloaded to a Microsoft Excel file prior to analysis. Demographic data and select survey questions were analyzed using descriptive statistics.

All 12 interviews were transcribed verbatim using an online transcription service. Participants' responses to the open-ended survey questions and the interview transcripts were coded with in-vivo codes and grouped into emerging themes that could be categorized into pros and cons of each type of cleanroom and key lessons learned. The data was reviewed multiple times by each research team member until agreement on the key themes was reached. Example in-vivo codes for key lessons learned included "hold regular meetings," "do your homework and understand," and "overdesign your air handler."

Results

Participant demographic information. In total, 14 participants from 13 US states completed the online survey and 12 of these individuals participated in a follow-up interview. Of the 14 participants, 9 (64%) only had experience with designing, installing, and maintaining stick-built cleanrooms, one (7%) only had experience with modular cleanrooms, and 4 (29%) had experience with both types of cleanrooms. Three participants (21%) had only installed one cleanroom in the past 5 years (2 installed a stick-built cleanroom, 1 installed a modular cleanroom), while 7 (50%) had installed 5 or more cleanrooms in the past 5 years (3 installed stick-built only, 4 installed both types). The remaining participants (n = 4, 29%) installed 2 to 4 cleanrooms in the past 5 years (stick-built only). Four (29%) of the participants had more than 10 years of experience with designing and installing cleanrooms, 4 (29%) had 7 to 10 years of experience, and 6 (43%) had 3 to 6 years of experience.

The organization types represented by the participants included large healthcare systems (n = 8), pediatric hospitals (n = 2), a registered 503B outsourcing facility (n = 1), a long-term care pharmacy (n = 1), a private home care company (n = 1), and a small community hospital (n = 1). See Tables 1 and 2 for a full description of participants.

The cleanrooms installed were either replacements or brand-new builds, with no correlation observed between the type of build (replacement or brand-new) and the type of cleanroom (modular vs stick-built) (eg, replacements were not more likely to be stick-built, new builds were not more likely to be modular). Most participants indicated their organization's purpose of building or rebuilding their cleanroom was to modernize, to meet updated regulatory changes, and/or to expand to meet current and future volumes.

> *"USP 797 and 800 guidelines were being updated and implemented. To maintain compliance, if we were going to compound any hazardous drugs, we wanted to do it a in a fashion that was compliant with the regulations that were being updated."* (participant 1)

Based on the survey responses received, the installation of the participants' stick-built cleanrooms (n = 11 responses) took an average of 11.5 months (range, 4-24 months; median, 9.0 months), and the installation of their modular cleanrooms (n = 4) took an average of 11.0 months (range, 4-27 months; median, 6.5 months). Based on interview responses, factors that impacted the length of installation included size of the cleanroom, the complexity of the cleanroom, the need for contingency planning (eg, installation of a mobile cleanroom to use during construction), and preparation of the cleanroom space prior to installation.

The average size of the stick-built cleanrooms installed (n = 12) was 1,198.0 sq ft (range, 116 to 7,000 sq ft; median, 569 sq ft) and the modular cleanrooms (n = 4) were an average of 837.4 sq ft (range, 300-1,400 sq ft; median, 850 sq ft). When the 7,000–sq ft stick-built cleanroom was excluded from analysis, the average size of the stick-built cleanrooms (n = 11) was 670.5 sq ft (range, 116 to 1,600 sq ft; median, 550 sq ft)

Cleanroom satisfaction. When the participants were asked, "Overall, how satisfied are you with your cleanroom (1 = very dissatisfied, 10 = very satisfied)?", those with stick-built cleanrooms (n = 11 responses) provided an average score of 5.3 (range, 3-10; median, 6) and those with modular cleanrooms (n = 4) provided an average score of 9.3 (range, 9-10; median, 9). Of note, for those with experience with both types of cleanrooms who answered this question (n = 3 responses), their average satisfaction score was 5.3 (range, 3-7; median, 6) for stick-built and 9.3 (range 9-10; median 9) for modular—essentially the same as for all participants.

Participants were provided with an opportunity during their interviews to provide reasons for their satisfaction scores. One participant who gave their stick-built cleanroom a satisfaction score of 4 said:

> *"It's just . . . not having known everything that we could have known before we went into the*

Table 1. Participant Demographics[a]

	Survey (n = 14)	Interview (n = 12)
Male	7 (50)	6 (50)
Female	7 (50)	6 (50)
Experience installing and maintaining cleanrooms		
1-2 years	0	0
3-4 years	3 (21)	2 (17)
5-6 years	3 (21)	2 (17)
7-10 years	4 (29)	4 (33)
>10 years	4 (29)	4 (33)
No. of cleanrooms installed in last 5 years		
1	3 (21) [2 SB, 1M]	3 (25) [2 SB, 1M]
2	2 (14) [SB]	1 (8) [SB]
3	1 (7) [SB]	0
4	1 (7) [SB]	1 (8) [SB]
≥5	7 (50) [3 SB only, 4 both]	7 (58) [3 SB only, 4 both]
Type(s) of cleanrooms installed in previous 5 years		
Modular only	1 (7)	1 (8)
Stick-built only	9 (64)	7 (58)
Both modular and stick-built	4 (29)	4 (33)
Organizational role of participant		
Director of pharmacy	5 (36)	4 (33)
Pharmacy supervisor/manager	5 (36)	4 (33)
Compounding/sterile products specialist, coordinator, or manager	3 (21)	3 (25)
VP or CPO	1 (7)	1 (8)

Abbreviations: CPO, chief pharmacy officer; M, modular; SB, stick-built; VP, vice president.
[a]All data are No. (%) of respondents.

project. You know, being dissatisfied with some of the ongoing maintenance stuff. . . . We had no idea that we were going to have challenges in terms of making sure that the paint wasn't peeling. . . . When you build something, you kind of make an assumption that the paint's not going to peel, like weird stuff like that." (participant 4)

A participant with experience with both types of cleanrooms who gave their stick-built cleanroom a score of 3 and modular cleanroom a score of 10 said:

> *"When you work with the modular group on designing a cleanroom, they just have so many more reps. . . . 'So, let me ask some questions about door placement or configuration' or other stuff that's probably not a super black-and-white regulatory requirement, but they have just better insight into what they've done, what they've seen, what the feedback and customers are [saying]. . . . I think they just have more experience doing it, which is very helpful."* (participant 5)

Pros and cons of stick-built cleanrooms. All participants were asked what they perceive to be the pros and cons of stick-built and modular cleanrooms, based on their own experiences.

The pros of stick-built cleanrooms they highlighted were that stick-built cleanrooms offer greater control over build, size, and customization (design and material flexibility); they can

Table 2. Organization Types Represented[a]

	Survey (n = 14)	Interview (n = 12)
503B outsourcing facility	1 (7)	1 (8)
Large healthcare system or academic medical center	8 (57)	6 (50)
Long-term care pharmacy	1 (7)	1 (8)
Pediatric hospital	2 (14)	2 (17)
Private for-profit home care company	1 (7)	1 (8)
Small community hospital	1 (7)	1 (8)

[a]All data are No. (%) of respondents.

be cheaper to build than modular cleanrooms; they can be completed faster (from start to finish) than modular cleanrooms; and most contractors can do the work.

> *"You get to pick your fit and finishes . . . whatever the building likes or whatever you prefer."* (participant 1)

The cons of stick-built cleanrooms, on the other hand, are that they can, conversely, be *more* expensive and time consuming to build than modular ones, and there is inconsistent cleanroom experience among general contractors (GCs) and architects. In fact, many participants with experience installing stick-built cleanrooms stated that significant quality assurance, communication, and oversight is often required of stick-built cleanrooms during the installation process.

> *"Using a stick-built construction requires significant coordination with not only the project GC but also the subcontracted trades to ensure the equipment and finishes meet the user requirements and specifications. There can often be a disconnect between what the owner thinks they are getting and what the actual finished product is, and the owner must be very involved and specify materials of construction, finish details, HVAC requirements, etc."* (participant 11)

> *"[Managing a stick-built cleanroom installation] requires a lot of time. . . . I had many other responsibilities at the time, and I don't think anybody knew how much time it was going to take going behind the barricade to make sure things were going okay, talking to the construction people. [It required] a minimum of twenty hours a week. I was living and breathing work for a long time."* (participant 6)

Additionally, ideal finishes are difficult to achieve in stick-built cleanrooms, there can be difficulties with certification, and stick-built cleanrooms come with potential long-term challenges (ie, higher long-term costs, more maintenance issues, less flexibility).

> *"We had metal grates on our HEPA filters, and we had a bunch of mold after they built it. . . . When we did the investigation, the duct work was dirty. There was an actual fingerprint through one of my filters. My ducts and my metal plates weren't cleared. . . . When you look at that kind of stuff, you're like, 'You should not be building an expensive pharmacy and then having to remediate it before you even open it.'"* (participant 3)

For a list of issues participants had with their stick-built installations, see eAppendix C. Many of these issues contributed to delays and/or unanticipated costs.

See Box 1 for a full list of stick-built cleanroom pros and cons.

Pros and cons of modular cleanrooms. When asked about pros of modular cleanrooms, participants stated that modular vendors have significant cleanroom experience and expertise (more than most GCs), the installation process is quick and easy, and modular cleanroom materials and design features are high-quality and durable. They also said that the certification process is smooth, in part because modular companies guarantee certification. Finally, in contrast to stick-built cleanrooms, modular ones come with significant long-term benefits (ie, lower long-term costs, fewer maintenance issues, more flexibility to adapt to future growth and/or regulatory changes).

> *"For the modular one, we've not had any issues from a compliance standpoint. It's just so well built and easy to clean and easy to work in. Well designed."* (participant 5)

> *"They come in at least once a year to do our maintenance and stuff, which is great. That's proactive. If something needs to change, then and there, they'll do it."* (participant 1)

On the flip side, modular cleanrooms typically have higher up-front, direct costs and may offer less design flexibility than stick-built cleanrooms (eg, they may not always fit the appropriated space, they are less customizable).

> *"We are challenged here with real estate. We're challenged with being able to do modular, and so we end up sticking [cleanrooms] wherever we can. And that's probably the circumstances that influence most builds—feasibility. The availability of space is the deciding factor."* (participant 8)

Additionally, some participants said that their organizational leadership was not aware of the benefits of modular cleanrooms, so going modular was not seriously considered by the leadership, especially in light of perceived higher costs. A few participants with modular cleanroom experience also noted the additional time needed to prepare a space for a modular cleanroom prior to installation.

Box 1. Pros and Cons of Stick-Built Cleanrooms

Pros of stick-built cleanrooms

- Stick-built cleanrooms offer greater control over build, size, and customization.
- Initial costs of stick-built cleanrooms are less than for modular cleanrooms.
- Stick-built cleanrooms can be completed faster (from start to finish) than modular cleanrooms.
- Most contractors can do the work.

Cons of stick-built cleanrooms

- Ideal finishes are difficult to achieve in stick-built cleanrooms.
- Stick-built cleanrooms may have greater indirect and long-term costs than modular cleanrooms.
- The installation process for stick-built cleanrooms is typically longer than for modular cleanrooms.
- There is inconsistent cleanroom experience among general contractors and architects.
- There can be difficulties with initial and ongoing certification of stick-built cleanrooms.
- Stick-built cleanrooms come with potential long-term challenges (ie, higher long-term costs, more maintenance issues, less flexibility).

Box 2. Pros and Cons of Modular Cleanrooms

Pros of modular cleanrooms

- Modular vendors have cleanroom experience and expertise.
- The installation process of modular cleanrooms is quick and easy.
- Modular cleanroom materials and design features are high-quality and durable.
- The certification process with modular cleanrooms is smooth.
- Modular cleanrooms come with long-term benefits (ie, lower long-term costs, fewer maintenance issues, more flexibility to adapt to future growth and/or regulatory changes).
- Modular cleanrooms typically have fewer indirect costs.

Cons of modular cleanrooms

- Modular cleanrooms provide less design flexibility than stick-built cleanrooms do.
- Modular cleanrooms may not always suit the appropriated space.
- Modular cleanrooms typically have higher up-front costs than stick-built cleanrooms.
- Modular cleanrooms are perceived by some to be more expensive than stick-built cleanrooms.

"For the modular, I didn't have as much appreciation for what additional infrastructure needed to be in place for the cleanroom to operate. It's a little bit more complex because it has a hazardous room that requires exhausting. But there's still a fair amount of water and electricity and other things that have to get to the room. It wasn't difficult, it's just something that I hadn't anticipated. . . . Actually installing [the modular cleanroom only] took a few weeks, maybe 6 at the most, [but] there was a lot of work to prep the space, especially in our instance—pipes and ducts and everything else that needed to move to get the cleanroom to fit." (participant 5)

"It's like a house on wheels, right? Plug and play, like you just stick it in, but it's more complicated than that because you need to make sure [everything] lines up. . . . And you need to make sure they're on the same page with facilities or the general contractor as it's being built." (participant 1)

For a full list of modular cleanroom pros and cons, see Box 2.

The cost question. Since the cost of a cleanroom—including both initial costs and total lifetime costs—is a very important consideration, the interviews further explored the key factors that impacted the total cost of their cleanrooms. These factors included both direct and indirect costs. Direct costs mentioned by participants included the cost of building materials used, number and type of consultants hired, and type of equipment and automation installed. Indirect costs included time involved for personnel to monitor installation, costs required to fix errors made during the construction process, costs resulting from construction delays, and unexpected repair and maintenance costs (after certification) due to poor quality of materials and/or construction. A list of direct and indirect costs mentioned in this study can be found in Box 3.

Box 3. Direct and Indirect Cleanroom Costs

Direct costs

- Cost of construction materials (which are dependent on the quality of materials and the size of the cleanroom)
- Costs of hiring general contractors, subcontractors, architects, and/or modular vendors
- Number of consultants hired
- Amount and type(s) of automation and other equipment installed
- Existence of concurrent construction projects (eg, adjacent pharmacy space, a new hospital building)

Indirect costs[a]

- Time required for staff to oversee the construction process
- Time needed for staff to communicate cleanroom requirements to inexperienced contractors and architects
- Costs required to fix errors made during the construction process
- Delays caused by errors made during the construction process
- Unexpected repair and maintenance costs (after certification) due to poor quality of materials and/or construction
- Unanticipated challenges with the existing HVAC equipment and/or other infrastructure

[a]These indirect costs are typically significantly higher for stick-built cleanrooms.

Considering all these factors, most participants thought the total cost difference between the two types of cleanrooms was minimal, with differences in when costs are incurred and the type of costs incurred—more up-front, direct costs for modular cleanrooms versus more indirect and long-term costs for stick-built ones.

> *"What I find from my history and working with modular cleanrooms, I don't ever remember having maintenance and facility repair work that was [very] invasive. . . . I think modulars are going to be the cheapest route for the long haul, even though it's more cost more up front and it takes more of a footprint to put it in."* (participant 8)

> *"If you just do a very basic, traditional cleanroom with metal studs and drywalls with epoxy paint, vinyl flooring, and a lay-in ceiling, your delta in initial capital investment between that and a modular cleanroom is going to be much bigger. . . . [But if you] work with your GC, use some different materials for construction, and really come up with a design that approaches a modular-type finish, that delta will be less. . . . It just depends on how particular you are in your finishes and design selections."* (participant 11)

Lessons learned/advice from participants. The advice and lessons learned garnered from the participants on the design and installation of cleanrooms, regardless of cleanroom type, were categorized into the following themes.

Do your homework before beginning a cleanroom project. Preparation is key. One key piece of advice proffered by the participants is to learn what you can about cleanrooms before you get started. Read articles, research different design and material options, and talk to as many people as you can to learn from their experiences. Understanding workflows, researching how ergonomics can benefit you operationally, and vetting contractors, mechanical engineers, and other vendors you hire are key for an efficient and smooth cleanroom installation.

> *"Conduct site visits. Talk to as many people who are in a similar type of environment, from a volume perspective, type of department (eg, cancer center versus non–cancer center), 24-hour versus not 24-hour, etc. Talk to other people and learn from their experience."* (participant 4)

> *"Pharmacists were not educated on this stuff. I have had to learn this by on-the-job-training. Go to trainings, talk to people. Ask questions about engineering stuff and everything. . . . Learn how to calculate air changes per hour based on how many HEPA filters you have, how many square feet you have, and the air per hour. . . . Learn how to read construction schedules and be sure things align as they should. . . . Be patient. Be willing to learn what you don't know."* (participant 6)

Additionally, once you have researched information and your cleanroom design is complete, it is critical to plan thoroughly for each step of the installation process, including the installation of equipment.

> *"Plan for all lead times. Have a Gantt chart of not just what the install is going look like but . . . what is the lead time for when your fridge is going to be inside your cleanroom? Because that changes the number of particles in there. When is your printer going to be in there, and what supplies do you need inside? Because you've got to get those in."* (participant 1)

> *"Be prepared for the possibility that nothing will go right or anything that could go wrong, probably will. Plan for the worst."* (participant 3)

Ensure you have someone with cleanroom expertise on your team. Cleanrooms are complex and specialized projects that require significant expertise to complete efficiently and economically. The cleanroom project manager must fully understand the federal, state, and organizational requirements for cleanrooms as well as ensure those regulations are met. They must also understand what their facility's structural requirements and capabilities are. Several participants emphasized the importance of understanding the minimum USP requirements but also realizing when you need to go above those requirements (eg, air changes).

Since not all construction companies, architects, and subcontractors fully understand cleanroom requirements and regulations, the duty to communicate these regulations to the contractors lies with the person in charge of the installation process. When you look at your cleanroom designs, make sure you understand them on multiple levels, since the designs include not just the room's floor plan but other details as well. This person must ensure the correct materials of construction are being used, the finish details are as designed, and heating, ventilation, and air conditioning (HVAC) requirements are met.

> *"Make sure that you have someone on your project that's knowledgeable in this field and they understand what your specifications are and can outline them to your vendor. I would encourage everybody to really go through internally and identify someone who can work with your design and architecture firm or your [modular] cleanroom vendor from the outset, saying, 'We expect that where the floor goes up to the wall, that'll be a flush transition. We expect that the ceiling will be monolithic and smooth and will not be a drop-type or lay-in ceiling.'"* (participant 11)

"If you don't have an internal expert, go and find one" [participant 2]. Since not all contractors are experts in pharmacy compliance and the effort and time required to design and install a cleanroom can be daunting, many participants advocated hiring a consultant (or several consultants) to aid in the design process.

> *"Hiring a consultant was a big thing for us, so I feel like we were pretty well informed [in] the decisions that we made. . . . We don't have a compounding coordinator or somebody that's super familiar with how to build a cleanroom, what all the requirements are. . . . [The consultant's recommendations were] invaluable to us."* (participant 2)

Those with experience installing modular cleanrooms highlighted the "built-in" consultancy that comes with hiring a modular vendor, a benefit of working with modular vendors described above.

Many also emphasized the importance of hiring a general contractor or vendor with specific experience installing cleanrooms, one that you can trust. Whether you are working with a general contractor to build a stick-built cleanroom or with a modular vendor, it is also important to talk with their references and fully understand what their experience is before hiring them.

Keep the future in mind as you design your cleanroom. Cleanroom installation projects are time-extensive and expensive projects, so planning for long-term growth and potential regulatory updates can save money and time down the road. Having to rebuild a cleanroom within 10 years of your original build is neither cost-effective nor simple.

Some strategies for future-proofing a cleanroom include going above and beyond current regulations where it makes sense to: building in space for additional hoods, gloveboxes, refrigerators, and/or biosafety cabinets; designing additional square footage inside the cleanroom (if possible); building in additional engineering controls, properly sizing your air handlers, and making sure your exhaust fans are sized for future growth; and adding additional rooms to help you meet probable future demands (eg, a "beta-lactam room" or a negative pressure room for hazardous drug compounding).

> *"They were designing a pediatrics cleanroom, and they specifically were like, 'We need to put in the option for an additional hood to be externally vented, and we'll just cap it.'* (participant 1)
>
> *"Our home infusion pharmacy was the one pharmacy that has a triple buffer room. . . . They built a beta-lactam room just because there was one Joint Commission surveyor or consultant, who said, 'You know, you do an awful lot of beta lactams. Why don't you have your own room for this?' And even though we know it's not a standard, they did decide [to do] that just to future-proof themselves. They built a beta-lactam room."* (participant 12)

It is also important to plan for future preventative maintenance and damage mitigation costs. Preventative maintenance and some damage mitigation is typically provided by modular vendors. However, for stick-built cleanrooms, all maintenance and repairs are typically done by internal facilities staff or external contractors once the cleanroom is complete. These costs will either show up in the total cost of a modular project or as hidden, indirect costs for stick-built cleanrooms, as described above. These costs should be an integral part of your initial cost-benefit analysis.

Involve the pharmacy staff in the cleanroom design process. Since the cleanroom staff will be working in the cleanroom daily, their input is critical. Additionally, make sure they understand why things are located where

they are (eg, pass-throughs) and what the workflow should look like once operational. You will likely need to retrain your staff before move-in day.

> *"Have your staff involved from the first step, because they're the ones that have to live in it. Everything else you can hire a contractor for. But . . . if you don't get your staff to understand the why you're doing something, it doesn't matter how sexy and how clean your cleanroom is. They have to operate it."* (participant 3)

Hold team meetings regularly. Perform site visits often. In most cleanroom building projects, there are many individuals involved, including GCs, architects, pharmacy leadership, and engineers. Establishing good communication channels will help minimize delays. Regular meetings and site visits can facilitate good communication and a smooth construction process. Being involved as the construction is going on will also allow for regular quality control checks and real-time corrections.

> *"I've learned that over time the best thing to do is to have everyone on the same page, because the GC's got subcontractors who've got subcontractors, and they're all over the place. . . . It's just important to get them on the same page as everybody else, because at the end of the day, that's your cleanroom. You have to make sure things go smoothly. . . . Get your certifier and your board of pharmacy on the same page as well, especially if you're trying to meet tight timelines, because that made a huge difference. A lot of things have to be done in a certain stepwise order."* (participant 1)

> *"Make sure you have someone who is knowledgeable and really able to check in on a daily or weekly basis during the installation, to make sure that what is being done in the field and what's being installed matches what you thought you were getting or what you specified, because that's not always the case. And sometimes it just takes somebody, you know, walking through and saying, 'Hey, that's not really what I thought that would look like. Let's talk about what's going on here.'"* (participant 11)

Make sure you have adequate HVAC system(s) and air handler(s) for the needs of your cleanroom. The importance of the quality and performance of a cleanroom's HVAC system was something just about everyone commented on. They recommended to be involved in your air handler and becoming familiar with the settings of the system and with all the people who are doing the HVAC work from the start.

Several participants also advocated overdesigning your air handler so it can exceed USP minimum air changes per hour, especially in high-volume spaces and for handling changes in seasonal weather. They emphasized the relationship between the performance of an HVAC system and the potential for contamination in a cleanroom suite (eg, multiflora, mold). Additionally, they discussed the importance of understanding how the room's HVAC duct work is connected to other space(s) and how that can impact the HVAC system's performance.

> *"I think one of our big problems is that we didn't look thoroughly enough—from a planning perspective—the impact of whether or not the existing HVAC systems were really, truly going to be able to maintain the necessary temperatures and humidities in our areas. We have very extreme weather; we have the classic four seasons. . . . The months of January and February are very, very, cold [and] in July and August [it's] horribly hot, and so as the HVAC system [for the building] continues to get older, it's having trouble keeping tabs on what's going on in those rooms."* (participant 10)

> *"Our largest problems occurred in areas where we were trying to utilize preexisting building air handlers to support our cleanroom suites. Suites with dedicated air handlers were better able to achieve above minimum standards for air changes per hour and temperature and humidity control. . . . [Also], have your conversations with the HVAC guys on the duct work. I mean that. They worked the longest—they started first and ended last. I mean, they spent a year crawling around in the space above us."* (participant 12)

Allow the individual overseeing a cleanroom project sufficient time to prioritize it. Since a lot of time and effort is required to successfully shepherd a cleanroom to completion and ultimately, certification, the individual(s) responsible for overseeing such a project should be given sufficient time to prioritize it.

> *"[Let] the person from your staff helping with your [stick-built] cleanrooms just have that focus and not any competing responsibilities, because it really is hard when you're trying to make sure everything goes well."* (participant 6)

Don't forget the primary reason for building quality cleanrooms. All products prepared in a sterile compounding pharmacy are meant to be given to patients. Therefore, ensuring that you build a fully compliant cleanroom, thus ensuring the safe and sterile production of compounded products, is critical. Patient safety is the ultimate purpose behind building quality cleanrooms.

> *"I think the heart of pharmacy is to protect our licenses and to protect our patients and to protect*

everybody involved. But it causes us to have to work twice as hard with poor conditions and additional disinfection steps and corrective actions to get things back up to [necessary standards]." (participant 8)

"We do a lot of volume, and every patient dose has a significant liability to it that could jeopardize lots of licenses and [patient] care. So, there's just a lot on the line. But any day that you can provide patient care, and you can sleep at night the day after knowing that it was okay, that's a huge win." (participant 1)

Advocate for the establishment of industry standards; find a way to share your expertise. Participants not only recommended learning from others' experiences when embarking on a cleanroom project, they also advocated paying it forward by sharing lessons learned. There are many nuances of designing and building a cleanroom for sterile compounding that require more detailed decision-making processes than the federal and state regulations offer guidance on. Several participants thought that creating a common repository of people's experiences and developing a manual or guidebook of recommendations and industry standards would be very helpful.

"When you build a cleanroom, frankly, there needs to be a manual that just says, here's how you do it. That's where it's important to talk with people who have done this before, who have experience with building [cleanrooms]. . . . We [should] pool people's experiences." (participant 3)

"Should we require our staff to buy their own dedicated cleanroom shoes that don't leave the building? But there's no law that says you have to do that. There's no industry standard yet that says that you should be doing stuff like that. So, maybe that's something that can be added to a manual—ask [cleanroom managers] whether or not they have those kinds of requirements in place, particularly around scrubs and shoes." (participant 4)

Participants also provided some additional, specific lessons learned based on their experiences. See eAppendix D for a sample list of those lessons learned.

Discussion

We surveyed and interviewed sterile product cleanroom managers and specialists from a variety of organizations on their experiences with designing, installing, and maintaining stick-built and modular cleanrooms. Through these surveys and interviews, we were able to delineate real-world pros and cons of each type of cleanroom.

Positives of stick-built cleanrooms. A few benefits of stick-built cleanrooms over modular ones were identified. Stick-built cleanrooms, unlike modular ones, can be built to fit most any space while maximizing use of that space. Depending on the parameters and shape of a given cleanroom space, a modular cleanroom may not be a feasible option. Additionally, stick-built cleanrooms offer more design flexibility and customization options, which some customers prefer.

These benefits align with what is generally promoted for stick-built cleanrooms.[4,5,9]

Positives of modular cleanrooms. A number of positives for modular cleanrooms were also identified, including that they are more durable, easier to clean, cleaner to install, and easier to maintain and repair. Those with modular cleanroom experience also emphasized that compliance and certification were more certain and easier to obtain than for stick-built cleanrooms. The long-term flexibility to adapt to regulatory changes and future growth were also clear positives.

These benefits also align with what is generally promoted for modular cleanrooms.[4,5]

Quality. One of our biggest findings, however, offered new insight on the idea that most GCs, subcontractors, and architects are knowledgeable about cleanrooms and can do a good job.[4] While a few of our participants had reasonable or good experiences with the contractors they hired, most experienced issues with their contractors, architects, and/or subcontractors, issues that did not arise during modular installations. eAppendix C provides a sampling of some of the issues they experienced.

Related to these issues, several participants also highlighted the amount of time they, or another staff member, spent checking in with and monitoring their stick-built installation for quality assurance. These personnel costs, which were not minimal, were not accounted for in their initial cleanroom budget.

Costs. Our participants had conflicting opinions on which type of cleanroom is less expensive. However, these differing perspectives primarily boil down to differences in when costs are incurred and in the relative direct versus indirect costs.

Modular cleanrooms typically have more up-front, direct costs, as many already recognize.[5,9] However, when maintenance and repair costs—with associated cleanroom downtime—are factored in, the total costs of the two types of cleanrooms are comparable, with modular cleanrooms being considered by most to be the overall best investment, especially in the long term. Construction delays and construction errors, as well as extensive staff time needed to monitor the stick-built installation process, are additional indirect costs that are typically not considered when thinking about the costs of a stick-built cleanroom but should be. Participant quotes listed in eAppendix C highlight how inexperience and errors by contractors can impact the efficiency of installation and the overall costs of stick-built cleanrooms.

This multifactorial understanding of cleanroom costs is supported by others with extensive cleanroom experience.[9]

Time to completion. Our participants also had conflicting perspectives on which type of cleanroom is quicker to install. However, our study demonstrated that, even with space preparation included, our participants' modular cleanrooms were built and installed in comparable, if not slightly less, time than their stick-built cleanrooms (11.0 months vs 11.5 months, on average) and with less disruption. This finding is similar to a finding in another study wherein a 2,000-L stick-built cleanroom was completed in 27 months and completion of a modular one took 25 months.[9]

Advice and lessons learned. This study also compiled cleanroom design and installation advice and lessons learned from a wide variety of cleanroom managers and specialists from healthcare organizations across the US, adding to the current body of literature on the subject. These lessons learned came from a collective total of more than 92 years of experience.

Additionally, several participants highlighted the need for a collection of industry-wide cleanroom best practices for the design and installation of cleanrooms, regardless of type.

Strengths and limitations. The key strength of this study is that it included real-world customer voices speaking from their own cleanroom experiences and representing a variety of healthcare organizations in 13 states. Half of the participants were involved with designing, installing, and maintaining 5 or more cleanrooms in the previous 5 years, and most of them had 7 or more years of cleanroom experience. Additionally, a wide variety of organizations were represented, including large health systems, a small community hospital, and several outsourcing or home care facilities.

Despite the diversity of participants, this study only included 14 participants, a key limitation. These results may not represent the full spectrum of pharmacy managers with cleanroom installation experience. Additionally, selection bias likely played a role in the results, as each participant volunteered to share their experiences. The recruitment process may have drawn individuals who felt they had particularly compelling positive or negative experiences to share, thus skewing our findings. Response bias may have also impacted the results if participants felt compelled to give more extreme responses or examples than they might have otherwise done due to perceived expectations. Finally, participation in this study was limited to compounding pharmacy managers and specialists. Therefore, these results may not represent the full spectrum of those with cleanroom experience. Additional insights, lessons learned, and best practices could be culled from many others with cleanroom experience, including certifiers, facility maintenance departments, cleanroom staff, and other cleanroom managers.

Conclusion

The pros and cons of stick-built and modular cleanrooms, as expressed by individuals with real-world experience designing, installing, and maintaining pharmacy cleanrooms, have been described. Stick-built cleanrooms were preferred when fit was important and/or customization of design elements was desired. Modular cleanrooms, on the other hand, were considered the better option with regards to durability; cleanliness; ease of installation, certification, maintenance, and repair; and long-term flexibility.

While stick-built cleanrooms can be built to achieve the same quality as modular cleanrooms, it may be difficult to do so with ease and speed. Many participants in this study emphasized the difficulties and the extra, indirect costs they have experienced when installing and maintaining stick-built cleanrooms, challenges that aren't commonly or widely recognized.

With regards to costs, the larger up-front, direct costs of modular cleanrooms versus stick-built cleanrooms were acknowledged, while most participants agreed that modular cleanrooms are a better long-term option costwise if feasible to install.

Regardless of the type of cleanroom, designing and installing a pharmacy cleanroom is a complex and time-intensive process that often comes with a steep learning curve. While there are federal and state cleanroom standards available and consultants for hire, a comprehensive resource or manual that can provide guidance, insight, and collective lessons learned on pharmacy cleanroom design and installation is not yet available.

This study highlights some important lessons learned by cleanroom managers and specialists who have recently designed, built, and maintained pharmacy cleanrooms. Their collective experience and insight can provide guidance, as can other sources. However, these lessons learned can and should be developed into a more comprehensive compendium, with more detailed industry standards and best practices for pharmacy cleanroom design and installation with USP <797> and <800> standards compliance in mind.

Disclosures

The study was sponsored by QleanAir Scandinavia. The sponsor did not participate in the conduct or reporting of the study. The authors have declared no potential conflicts of interest.

Additional information

The authors provided the following CRediT statement. Lori Armistead: Conceptualization, Methodology, Investigation, Writing - Original draft, Writing - Revision and Editing; Stephen Eckel: Conceptualization, Methodology, Writing - Revision and Editing, Supervision.

References

1. United States Pharmacopeial Convention. *USP Compounding Compendium*. Accessed August 7, 2023. www.usp.org/compounding
2. Hansen KN, Mehta A, O'Neil DP, Wolf M. Designing the pharmacy cleanroom of the future. *Pharmacy Purchasing & Products*. Published July 2019. Accessed August 7, 2023. www.pppmag.com/article/2411.

3. Rader RA. The next decade of cleanrooms. *Pharma Manufacturing*. Published 2019. Accessed May 9, 2023. www.pharmamanufacturing.com/articles/2019/the-next-decade-of-cleanrooms.
4. AES Clean Technology. Stick built vs modular. Accessed May 9, 2023. https://www.aesclean.com/stick-built-vs-modular/.
5. Bodnar M. Choosing the right cleanroom construction approach. *Pharmacy Purchasing & Products*. Published November 2021. Accessed May 9, 2023. www.pppmag.com/article/2839/?search=clean%20rooms.
6. Rahe H. Understanding the critical components of a successful cleanroom and barrier isolation project. *Am J Health-Syst Pharm*. 2000;57:346-50. doi:10.1093/ajhp/57.4.346
7. Pharmacy and cleanroom design/renovation buyer's guide. *Pharmacy Purchasing & Products*. Published March 2022. Accessed May 9, 2023. www.pppmag.com/article/2889/?search=clean%20rooms.
8. Jackson CA, Wilson DA. World at work: hospital pharmacy clean-rooms. *Occup Environ Med*. 2006;63:68-70. doi:10.1136/oem.2005.020719
9. Backstrom S, Makowenskyj P, Jornitz M. Second level thinking in cleanroom decision making. *American Pharmaceutical Review*. Published October 15, 2017. Accessed May 11, 2023. https://www.americanpharmaceuticalreview.com/Featured-Articles/343693-Second-Level-Thinking-in-Cleanroom-Decision-Making/
10. Bodnar M. Choosing the right cleanroom construction approach. *Pharmacy Purchasing & Products*. Published November 2021. Accessed August 7, 2023. www.pppmag.com/article/2839.
11. Rahe H. Understanding the critical components of a successful cleanroom and barrier isolation project. *Am J Health-Syst Pharm*. 2000;57:346-350.
12. Pharmacy and cleanroom design/renovation buyer's guide. *Pharmacy Purchasing & Products*. Published March 2022. Accessed August 7, 2023. www.pppmag.com/article/2889
13. Robert PA, Kroon L. Expecting the expected: planning considerations for cleanroom construction. *Int J Pharm Compd*. 2021;21(4):276-281.
14. Medrano J, Yamamoto T. Clean room design: achieving pharmacy flow with USP 797 and USP 800 standards. Dekker Perich Sabini. Accessed August 7, 2023. www.dpsdesign.org/insights/clean-room-design-achieving-pharmacy-flow-with-usp-797-and-usp-800-standards/.
15. Wagner JT, Kastango ES. Understanding pharmacy cleanroom design requirements. *Pharmacy Purchasing & Products*. Published February 2005. Accessed August 7, 2023. www.pppmag.com/documents/V2N1/pp16Cleanrooms.pdf