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Digital Twins Part 2: Enabling Technologies and Challenges

Introduction

Part 1 of this article series, published last month, briefly introduced the concept of digital twin technology, along with its background and application. In this month's continuation, we will discuss various enabling technologies for digital twins and the challenges associated with them.

Enabling Technologies

Artificial Intelligence (AI) and Machine Learning (ML): Today's virtual representations of the real world have shifted from analytical modeling to data-driven modeling due to the rapid advancement of AI/ML techniques. Compared to scientific theory-based analytical modeling, which describes specific physical processes in explicit mathematical equations, AI/ML applies general mathematical models to solve a wide range of problems. For example, AI/ML modeling can fit an artificial neural network to a specific physical process by adjusting the model parameters through training data sets. AI/ML techniques provide effective data-driven tools for quick modeling of complicated physical processes and are well suited for creating digital twins of real world, complicated processes.

Cloud Computing: Cloud computing is the delivery of IT resources, such as data storage, computing power, networking, or software, over the internet, which allows access to these resources at a reduced cost. This enables digital twin systems to be implemented more economically and without the delays typically incurred by building such infrastructure within an organization.

Internet of Things (IoT) and Smart Sensor: The advancement of microchips and communication technology has enabled various physical devices to exchange data directly through internet, which now constitutes an IoT that connects billions of devices. IoT significantly simplifies the connection between physical entities and their virtual representations. Smart sensors are an important IoT component that integrate conventional sensor technology with microprocessor(s) and/or a wireless communication unit(s) within the sensor; this enables accurate and automated collection of environmental data.

Virtual Reality (VR) and Augmented Reality (AR): VR enables human interaction with a computer-generated 3-D visual environment. AR overlays computer-generated data and images over real-time captured video or images. When used together, VR and AR provide a powerful human interface for physical-virtual twins. VR/AR technology allows users to monitor critical data and operate equipment using virtual interfaces.

Challenges

As innovative and promising as the available technologies are, there are several challenges that those looking to implement them should know about. It is critical to try and counteract these issues for digital twins to be robust and beneficial. The following include some notable challenges as well as ways to try and address them.

Robustness of AI/ML models: There is a lack of effective guidance on selecting AI/ML models and determining the model's structure (e.g., the number of layers of a neural network). The best way to address this is conducting a thorough search for the best solution out of multiple options; techniques like Bayesian optimization can improve the efficiency of the search process. The performance of a trained AI/ML model could also be highly dependent on the training data and changes in the real world, such as device upgrades or seasonal weather changes. Furthermore, AI/ML models could be sensitive to missing data or outliers, which would further affect the generation of reasonable output. Applying reinforcement learning can improve a model's adaptability and the employment of ensemble methods will enhance the resistance to partial data loss.

Reliability and Security of IT Infrastructure: IT infrastructure could become vulnerable to failures and external attacks as it scales up in users, connected computers, and distribution across geographical areas. Both administrative policies and technical measurements, such as firewalls and failover systems, must be implemented to secure the entire IT system.

VR/AR Errors: Technical glitches are inevitable with VR/AR technology, since it heavily depends on image recognition and other enabling AI technologies. VR/AR errors may take a longer time to notice because of confusion between the real-world status and the VR/AR-generated virtual effect. Implementing state-of-the-art image recognition technology, additional checks of critical operations, user training, and test performance would help reduce error rates.

Software/Hardware Upgrade: As a digital twin system integrates software and hardware developed by different parties, component upgrades may affect the entire system. For instance, a software application could stop working after an upgrade to a third-party package. Reducing the number of service providers and the frequency of software/hardware updates and performing rigorous testing after each upgrade are practical solutions.

Conclusion

A variety of computational solutions and hardware technologies are available to support robust digital twin development. However, users who are looking into enabling technology should be conscientious about what technology they implement and thorough in their research, system design, and management. While digital twins can lead to significant improvements in performance and productivity, successful implementation must consider reliability, safety, security, and other management issues.

Additional Reading

David Jones, Chris Snider, et. al., Characterizing the digital twin: a systematic literature review, CIRP Journal of manufacturing science and technology, 29(2020) 36-52 (DOI: 10.1016/j.cirpj.2020.02.002).

Aiden Fuller, Zhong Fan, et. al., Digital Twin: Enabling Technologies, Challenges and Open Research, IEEE Access, Aug. 2020 (DOI: 10.1109/ACCESS.2020.2998358).

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Digital Twins Part 1: Introduction

Introduction

A digital twin is a virtual representation of a physical product that is paired with that physical product over the course of life-cycle management to help it develop from a concept to a prototype to its final version. The term was coined by Michael Grieves and John Vickers in 2003; since then, the concept has been broadly accepted and applied in many fields, to the point that it was listed as a key strategic technology trend in 2019 by Gartner, a technology research and consulting company.* This development is largely driven by advances in technologies such as Internet-of-Things (IoT), multi-physical simulation, real-time sensors and sensor networks, machine learning, artificial intelligence, big data, data management, and data processing. This article is an introduction to the concept of digital twins. A follow-up article will explore challenges and technologies that enable digital twins in greater detail.

Background

A complete digital twin consists of a physical entity, its virtual representation, and the bi-directional information flow between the two. The physical entity sends its operation status to the virtual representation, which evaluates the status and sends operation adjustment requests back to the physical entity. The bi-directional information flow that bonds the physical and the virtual entity distinguish digital twin technology from traditional computational modeling and simulation, which only create virtual representations of the real world. More hardware and software technologies are required for a digital twin system, especially when it is applied to a complex facility comprised of multiple interrelated physical entities. All components in the real world and in the virtual world need to accommodate information flow through the entire system. The following elements are all necessary for digital twins:

Real world: Distributed sensors should be installed in the real world to continuously collect data for all physical entities, and these physical entities be controlled remotely by commands sent by computational models in the virtual world. Real-world sensor health should be monitored to assure the accuracy of collected data.

Virtual world: In addition to acting as a virtual simulation of the real world, the virtual world should be able to "understand" the status of the real world and provide executable solutions to optimize its real-world counterpart.

Bi-directional communication: Depending on the application, near real-time data collection and transmission and online data quality control and quality assurance should be established so that any data quality issues can be identified and solved quickly.

Data storage: Although not a required component for a digital twin system, a database of historical real-world sensor data is beneficial, as it helps reveal the root cause of malfunctions in physical entities and predict the system's future health.

Applications

Digital twin applications in industries such as aerospace, medical, oil and gas, and electric power include:

- **Asset Performance Management,** which evaluates assets that age over time due to operation and fatigue, stress, chemical oxidation, and other factors. A digital twin uses a collection of high-fidelity, physics-based computational models and advanced analytics to transform asset data into actionable intelligence to identify issues before they occur and increase service availability. This helps reduce downtime and extend asset life while still balancing maintenance costs with lower operational risk.
- **Operations Optimization,** which delivers enterprise data visibility across the board and provides a holistic understanding of operational decisions that can expand capabilities and lower production costs. A digital twin will empower operators and plant managers with Key Performance Indicator (KPI)-driven insights to raise overall productivity.
- **Business Optimization,** which reduces financial risk and maximizes the potential for greater profitability using intelligent forecasting for smarter business decisions.

Conclusion

Over the past twenty years, the digital twin has evolved from a product life-cycle management concept into a variety of well-developed technologies that benefit many industries through applications like intelligent asset performance management and operations optimization. Current applications of digital twins are replacing humans in the traditional human-machine model with a data-driven self-learning intelligent system. By leveraging machine learning, artificial intelligence, big data technologies, and advanced sensor technologies, digital twins will likely become key technology for many industries to increase system performance and operational optimization.

Additional Reading

David Jones, Chris Snider, et. al., Characterizing the digital twin: a systematic literature review, CIRP Journal of manufacturing science and technology, 29(2020) 36-52 (DOI: 10.1016/j.cirpj.2020.02.002).

Aiden Fuller, Zhong Fan, et. al., Digital Twin: Enabling Technologies, Challenges and Open Research, IEEE Access, Aug. 2020 (DOI: 10.1109/ACCESS.2020.2998358).

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HVAC Considerations for Converting Patient Rooms to Infection Isolation Rooms or Protective Environmental Rooms

Introduction

The COVID-19 pandemic has shown the need for flexibility in hospitals to address an increased patient population with suspected airborne-transmissible diseases while protecting immunosuppressed patients who are especially susceptible those diseases. The Facility Guidelines Institute (FGI) *Guidelines for the Design and Construction of Hospitals*, inclusive of ASHRAE Standard 170, provides requirements for Protective Environment (P.E.) rooms, Airborne Infection Isolation (A.I.I.) rooms, and combined A.I.I./P.E. rooms. P.E. rooms are intended for immunosuppressed patients, and A.I.I. rooms are intended for infectious patients (primarily those with infections spread through airborne transmission). The differences between P.E. rooms, A.I.I. rooms, and other patient rooms are the requirements for filtration and positive or negative air pressure relative to adjoining spaces. This paper will discuss some of the HVAC challenges associated with converting a standard patient room to an A.I.I., P.E. or A.I.I./P.E. room.

Conversion Design Considerations

The first step is developing an Infection Control Risk Assessment (ICRA) which assesses the risk of surface, air, and waterborne infection and the effectiveness of controls for reducing that risk. The ICRA addresses infection control of the patient room(s) to be converted and other areas impacted by that construction.

Next, the mechanical engineering team must perform a complete analysis of the existing HVAC system serving the room to be converted to ensure all issues noted in the ICRA and requirements of the FGI *Guidelines* are addressed. Analysis of the new application should review sufficiency of outdoor air; supply air capacity; exhaust air capacity and discharge conditions; cooling capacity; heating capacity; humidification/dehumidification; and control systems. Table 7.1 of ASHRAE Standard 170 requires patient rooms have a minimum of 4 total air changes per hour (ACH) with 2 ACH being outdoor air; A.I.I., P.E. and A.I.I./P.E. rooms require a minimum of 12 total ACH with 2 ACH being outdoor air. Where the total ACH cannot be achieved from the central system for converted rooms, HEPA-filtered recirculated air may be used. The outdoor air changes are still required in these applications.

Anterooms provided at A.I.I., P.E., and A.I.I./P.E. suites must have appropriate pressure relationships to both the patient room and the corridor as defined in ASHRAE 170 Chapter 8. Differential pressure between the A.I.I. room and adjacent non-A.I.I. rooms must be a minimum of -0.01 in. WC (-2.5 Pa). Differential pressure between P.E. rooms and adjacent non-P.E. rooms must be a minimum of +0.01 in. WC (+2.5 Pa). Anterooms serving A.I.I., P.E., or A.I.I./P.E. rooms must have their own air terminal units for both supply and exhaust for reliable control of differential pressure relationships (see NIH DRM 6.1.15). Differential pressure conditions must be controlled and monitored, including visual displays at each door with magnehelic gauges, or digital readout.

Diffusers for P.E. and A.I.I./P.E. rooms must be a non-aspirating type and located directly over the patient bed to wash the patient area with air and minimize entrainment of other air within the space, which reduces potential cross-contamination between a patient and caregiver. Providing non-aspirating diffusers directly above the patient bed can direct high velocity air onto a patient, though, resulting in discomfort; as a result, air velocity and temperature must be carefully analyzed/controlled by the design using ASHRAE Standard 55 and good engineering practice. This may include high accuracy sensors, larger diffusers, and fast-acting air valves and coil actuators to maintain a comfortable patient environment.

Exhaust air from the A.I.I., P.E., and A.I.I./P.E. suites, toilet room air, and anterooms must be exhausted directly outdoors. In converted P.E. and A.I.I./P.E. rooms, the exhaust grilles or registers shall be located near the patient room door. A.I.I rooms shall have the exhaust grille directly above the patient bed or at the headwall.

Requirements for commissioning, testing, and certification must be included in the design documents to ensure the facility functions as intended and provides a safe environment for patients and caregivers. Architectural aspects of conversion of patient rooms to P.E., A.I.I. and A.I.I./P.E. rooms will be addressed in a future article.

Additional Reference

1. Guidelines for the Design and Construction of Hospitals, by The Facility Guidelines Institute. 2018 Edition
2. ANSI/ASHRAE/ASHE Standard 170-2017, Ventilation of Health Care Facilities

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FMC Daily Reporting and Oversight of APF Critical Parameters

Introduction

The Division of Technical Resources (DTR) / Facility Compliance Inspection Section (FCIS) generates daily reports of Facility Monitoring of Critical parameters (FMC) in Aseptic Processing Facilities (APFs) and distributes them via email to user groups and select personnel. Critical parameters include room temperature (TEMP), relative humidity (HUM), differential pressure (dP), and Air Changes per Hour (ACH); the set points for these parameters and their associated alarms are derived from the User Requirement Specification (URS) and detailed in a Critical Environment Parameter Worksheet (CEPW). Reports generated by the APF Daily Report application include an overview of all critical parameter alarm conditions (Incident Reports) from the previous day and are meant to provide review and oversight of key facility parameters and ensure the APFs are operating in a "state of control" in accordance with current Good Manufacturing Practice (cGMP) regulations and established criteria.

Data Collection

Data associated with incidents is collected from the following sources for the coverage date (normally the previous day):

- Division of Facilities Operation & Maintenance (DFOM) Building Automation System (BAS) – such as System Activity Log (SAL – logged activities including alarm acknowledgement, object changes, and data uploads and downloads) and trending data derived from the BAS (raw data sets collected per pre-defined trend configuration). Trending data configuration is normally interval collection (at a defined interval period) or Change of Value (COV – when a data point deviates from the previous set of data more than a defined value).
- DTR/FCIS APF Dashboards – such as trending graphics and raw trending data (see Figure 1).

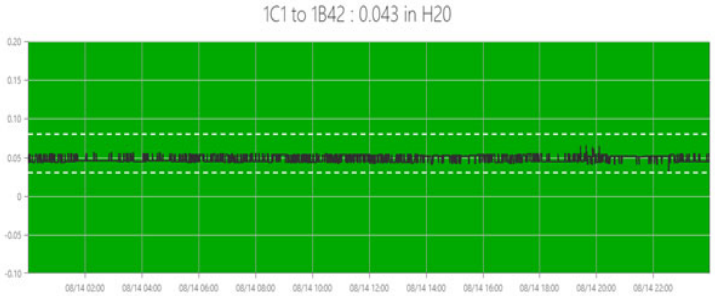

Figure 1: Example of APF Dashboard Trending Graphic

- DFOM Computerized Maintenance Management System (CMMS) – such as the cGMP LogBook Report and Work Plans/Work Orders.
- Environmental Monitoring System (EMS) data, if available (the EMS is generally a qualified user system which monitors critical environmental parameters of the facility without controlling them; it may monitor other user-specific parameters).
- Other planned activities – such as the End User's cleaning schedule, emergency generator testing, and BAS server maintenance activities.

Data Analysis/Findings

The reporter analyzes data for the following:

1. Out Of Specification (OOS) or Alarm Conditions – This is the main incident type related directly to Critical Parameters, indicating whether the space environment was out of the control range per the URS. The application creates an incident report with any related information, i.e., start/clear time, planned activities, and any LogBook notes such as findings/cause or immediate action taken.
2. Missing Trending Data – The reporter generates an Incident Report for any missing data (data gap).
3. Safety Incident – The reporter generates an Incident Report for safety device alarms such as oxygen sensor alarms.
4. Others – The reporter generates Incident Reports for any abnormal operating condition that is detected from trend analysis, such as out-of-trend values, shifting trends which are abnormal but not out of range (e.g., not in alarm), etc.

All incidents will be inputted into the application and reported. Open incidents that require further investigation will be sent via the application for feedback from DFOM and/or the End User.

Follow Up/Update on Previous Findings

Previous findings (open incidents) are tracked within the application, which documents all feedback, information, and communication between DTR/FCIS, DFOM, and the End User until the incident is resolved and closed. Some incidents may necessitate a Root Cause Analysis (RCA), Corrective Action and Preventive Action (CAPA), or System Discrepancy/Deviation (SD), which are also tracked within the application.

Conclusion

FMC daily reports help support communication among APF stakeholders and ensure that incidents are investigated, resolved, and documented in an appropriate and timely manner. These reports and associated oversight of APFs ensures compliance with regulatory requirements, including Good Manufacturing Practices (cGMPs), and supports continuous and collaborative efforts for the operation and maintenance of APFs.

Additional Reference

1. DTR-SOP-10007 Generation and Distribution of the DTR-FCIS Facility Monitoring Daily Report of APF Critical Parameters
2. DTR-SOP-1005 Corrective Action and Preventive Action (CAPA) Procedure for Maintenance of Aseptic Processing Facilities
3. DTR-SOP-1003 System Discrepancy / Deviation Management Procedure for Maintenance of Aseptic Processing Facilities
4. FCIS Facility Monitoring of Critical Parameters in APF Daily Report Application: https://dtrdata.orf.od.nih.gov/apfdaily/ (Access permission is required.)

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Standard Operating Procedures in Facilities Maintenance and Oversight of APFs

Introduction

In a current Good Manufacturing Practice (cGMP) environment, it is critical to ensure that all facility maintenance and oversight of an Aseptic Processing Facility (APF) is conducted in accordance with a multitude of regulatory requirements, good engineering practices, and manufacturer's recommendations. For instance, Section 211.68 of the Code of Federal Regulation (CFR) states that equipment "...shall be routinely calibrated, inspected, or checked according to a written program designed to assure proper performance." Establishing and implementing Standard Operating Procedures (SOPs) helps personnel keep an APF in compliance with the numerous requirements it must follow; properly developed facility SOPs provide a standard for how to perform a task or routine activity with the intent to produce consistent results and reduce mistakes.

Facility SOPs for APFs

Thorough, quality SOPs are particularly critical for APFs because there are many processes that can impact various aspects of the facility's functionality. Procedures required for APF maintenance include those impacting operations such as entry exit, preventative maintenance schedules, work order processes, calibration, emergency work, material management, and training programs. Quality Assurance (QA) oversight of the facility provides additional procedures such as compliance monitoring of cGMP facilities and processes, including continuous monitoring of critical parameters, tracking of incidents, System Discrepancy/Deviation (SD), Corrective Action Preventative Action (CAPA), Root Cause Analysis (RCA), managing change controls and facility audits.

Development

In some cases, SOPs are specific, step-by-step technical instructions; in other cases, it may be more appropriate to use general language, or reference the User's site-specific SOPs, particularly regarding things like gowning requirements. Regardless, a well-written SOP should be clear, concise, and simple to ensure it is easily replicated every time. A consistently executed SOP contributes to product quality.

During the development of each SOP, the author collaborates with key players (e.g., end user, Subject Matter Experts (SMEs), facility QA, DFOM, etc.) to define the SOP's requirements, including execution verification. SOPs should be concise, and shall address the following:

- Objective
- Scope or purpose
- Step by step process
- Responsibilities
- Training
- Review & approval
- Management controls

In addition, SOPs often include reference documents (e.g., Work Instructions (WI), forms, and templates) to help achieve consistency and document tasks.

Training

A training program helps management identify the need for additional training, when and how often to provide refresher courses, and who requires training when there is a new or revised SOP. SOPs are used to develop and conduct the relevant training; a training coordinator shall document training on effective SOPs. Personnel must demonstrate competence by reviewing an SOP using a system which documents that the employee read and understood the procedure, or they may attend a classroom training session, which can include an exam. This process allows for management to ensure trainees have a clear understanding of the procedures and address any questions or concerns that may arise. An effective training management program should maintain auditable training records to ensure competency and compliance.

Implementation

An SOP becomes effective once it is approved and staff have received initial training; the document's effective date need not be the issue date. APF personnel shall follow the effective processes to prevent potential negative impact on the product being produced, or damage to the facility, as stated in DRM Section 13.20.1. A well written and implemented SOP can help a QA team provide compliance oversight and support for the operation and maintenance of APF facility systems and equipment.

Audits

When a facility is audited, auditors review SOPs that are in effect to ensure compliance; this review includes an inspection of training records and may include interviewing staff and/or other steps to ensure that effective SOPs are being followed. SOPs help achieve the goal of an audit by identifying if quality systems have been implemented, maintained, and remain effective. Audit observations of SOP violations require immediate action to rectify deficiencies.

Summary

SOPs play a crucial role in APF facilities by making sure the necessary maintenance, QA work, and training are performed and documented based on written procedures. As these documents are developed, reviewed, implemented, and maintained, they become an integral component of the APF's quality system. Consistent and proper use of SOPs will ensure the work performed for the maintenance and QA purposes does not alter the qualified state of the equipment and validated state of the process and/or room.

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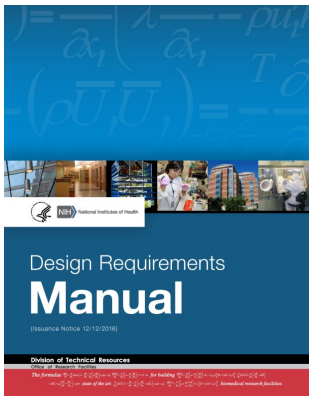
DTR Permit Review: BOD for Health Care Projects

Introduction

The National Institutes of Health (NIH) Permit Review Board[1] reviews construction, renovation, alteration, major equipment installation, or change of use projects funded by NIH. Project review occurs through the Division of Technical Resources (DTR) Permit Review Site.

The Design Requirements Manual

In addition to complying with model building codes, DTR promulgates minimum facility standards through the Design Requirements Manual (DRM).[2] Section 1.2.1 lists the codes and standards incorporated in the DRM by reference. The Facility Guidelines Institute (FGI) Guidelines for Design and Construction of Hospitals[3] is one of these referenced standards that is used in concert with other codes and standards to review health care projects.



Governing Codes and Standards

The NIH Division of the Fire Marshal (DFM) is the Authority Having Jurisdiction interpreting and enforcing Life Safety codes and standards. The Fire Protection and Life Safety Building Permit Process requires use and occupancy classification to comply with the most recent National Fire Protection Association (NFPA) 101 Life Safety Code. Most health care building renovations in the Clinical Research Center (CRC) have the occupancy classifications Health Care, Ambulatory Health Care, or Business, as described in Chapter 6 of NFPA 101. Health care projects must also meet NFPA 99 Health Care Facilities Code requirements. The Joint Commission (TJC) publishes its own hospital standards which are used to accredit hospitals in the U.S., but TJC currently utilizes a different version of NFPA 101 from NIH. If a conflict arises between the most recent version of the NFPA 101 Life Safety Code and the version required by TJC, the most stringent requirements should be used with DFM's concurrence.

Guidelines for the Design and Construction of Hospitals

The FGI Guidelines requires clinical care staff to develop and document a Functional Program during the planning and design phases of every project. The best way to create consistent documentation between FGI requirements and DTR Permit Review is to include the Functional Program developed by the Clinical Center in the Basis of Design (BOD). The BOD is a record of the design process, including all requirements, and should coordinate spaces and their technical requirements in accordance with the FGI Guidelines so that the correct codes and standards are used during development as well as review.

The elements of the FGI Functional Program are:

- the purpose of the project and services to be provided
- the project type, e.g. renovation, and size
- the existing/proposed building construction type (per the International Building Code)
- the existing/proposed occupancy classification (per NFPA 101)
- department operational adjacencies, circulation patterns, etc.

The Space Program is another document required by the FGI which is helpful to designers and reviewers. It lists each room name with the relevant Guidelines paragraph number to coordinate technical requirements with rooms. It should also be included in the BOD.

Summary

Health care projects at NIH must include the correct occupancy classification as well as documentation from the Clinical Center about the uses of rooms. The clearest way to ensure the correct engineering and architecture criteria are applied is to use the FGI Functional Program and Space Program from the start of the project. Identify the uses of spaces, room names, department affiliations, etc. according to the terms used in the FGI Guidelines to create consistent documentation between user criteria, Construction Documents, and DTR Permit Review. Additional policies, standards, and design requirements will be discussed in a forthcoming article.

Additional Reading

1. News to Use: The Design Review Process https://www.orf.od.nih.gov/TechnicalResources/Documents/News%20to%20Use%20PDF%20Files/2017%20NTU/The%20Design%20Review%20Process%20-%20November%202017_508_508.pdf

2. The National Institutes of Health (NIH). Design Requirements Manual, (Issuance Notice 12/12/2016) Rev. 1.5: 03/5/2020 https://www.orf.od.nih.gov/TechnicalResources/Pages/DesignRequirementsManual2016.aspx

3. The Facility Guidelines Institute. Guidelines for Design and Construction of Hospitals and Outpatient Facilities, 2018 ed. Chicago: American Society for Healthcare Engineering, 2018 https://fgiguidelines.org/guidelines/2018-fgi-guidelines/

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Lighting Design Considerations in Biomedical Research Facilities

Introduction

Lighting in biomedical laboratories has evolved over the years to meet energy code requirements and to accommodate flexible lab designs with advanced digital capabilities. A laboratory might need different types of spaces such as collaboration and innovation spaces, data analysis and documentation spaces, and typical wet and dry lab spaces. Lab lighting design must therefore address the various illuminance levels needed for all these spaces while also addressing important visual factors. A layered lighting system approach can meet these needs and align with the architectural design, while advancements in energy efficient technology such as Light Emitting Diode (LED) fixtures and integrated lighting controls aid in meeting energy codes.

Visual Factors

The primary factor in lab design is typically illuminance. However, difficult visual tasks are performed in biomedical labs, and failing to account for this in lighting design can lead to eye fatigue, poor visibility, and an uncomfortable working environment. Designers must therefore also consider the following visuals factors:

1. Uniformity
2. Glare
3. Shadows
4. Surface Brightness
5. Vertical Surface Illumination

Appropriate fixture placement that accounts for these factors will result in improved lighting and productivity of lab personnel.

Additional Factors

Another important factor for successful lighting design is the selection of appropriate finish colors for the floors, walls, and ceiling. The lighting designer must work closely with the architects and interior designers to provide a workspace that facilitates innovation and collaboration while reducing eye fatigue.

Color temperature of lamps should be chosen based on the type of work performed. A future article will explore various color temperatures and their application.

The lighting quality perceived by individuals is very subjective based on their preferences and age. As humans age, most need higher light levels to perform visual tasks. The lighting designer should seek information about the occupants in the lab space and the types of visual tasks to be performed there.

Layered Lighting Design

As the name implies, a layered lighting design approach uses overhead lights combined with task lights to meet required lighting levels while addressing the visual factors. In this approach, the ambient lighting from ceiling mounted (direct, indirect, or combination) light fixtures provides lighting levels adequate for circulation within the lab. Energy efficient task light(s) integrated with casework can provide higher illuminance levels required on the bench top, where difficult visual tasks are performed. If flexible casework is planned, lighting power sources should have flexible connectors while meeting National Electrical Code requirements; many casework vendors incorporate task lighting in their modular design, which enables changes to lab layout without intrusive major renovation.

Integrated Lighting Controls

Lighting control technology has improved significantly with the development of occupancy sensors, daylight sensors, and centralized controls. Occupancy sensors played a major role in energy savings during the pandemic since occupancy in most spaces dropped to as low as 25%. Systems using occupancy sensors can be standalone or integrated with building controls; whichever is chosen for the project, the designer must ensure the system is user-friendly so that lights are controlled per design intent and planned energy savings can be realized. Lighting controls and systems should be commissioned to ensure they perform as designed, and users and maintenance personnel should be trained in proper operation and maintenance.

Summary

Thoughtfully designed, layered lighting systems in laboratory spaces can support research needs and a flexible architectural design. In addition, properly commissioned lighting control systems, paired with daylighting (when appropriate), can increase researchers' eye comfort and productivity. Effective, efficient lighting design will account for a variety of factors and make best use of available technology to support the activities that take place in a space.

Additional Reading

1. NIH Design Requirements Manual - Chapter 10 Section 10.7
2. Lighting laboratories: Design Challenges https://www.labmanager.com/lab-design-and-furnishings/lighting-laboratories-design-challenges-23433
3. Thoughtful Lighting for modern labs https://www.arup.com/perspectives/lighting-in-extreme-laboratory-environments

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Specific Pathogen-Free Animal Research Facilities

Introduction

Specific pathogen-free (SPF) animal research facilities provide breeding, housing, and procedural space for animals free of a defined list of pathogens. SPF animals are distinct from gnotobiotic animals, which are completely germ free and require sterile facilities.

SPF facilities must be designed and operated to provide pathogen-free (though not sterile) environments to protect the health of the animals and the veracity of the research conducted within. An SPF facility can be as small as a microisolator housing a few animals, but a more typical facility is a dedicated suite consisting of one or more procedure rooms and holding rooms that is located within a larger general-purpose vivarium. Animals are either bred within the SPF facilities or introduced after quarantine and rigorous testing to confirm they are pathogen-free.

Strategies for Containment

Traditional biocontainment facilities maintain isolation with a tightly sealed perimeter envelope and mechanical systems that create cascading negative pressurization to prevent pathogens from exiting the containment barrier. SPF facilities utilize an analogous design strategy, but instead use cascading positive pressurization to prevent pathogens from entering the containment barrier. At the entrance to the SPF facility, there may be one anteroom or a series of anterooms serving as pressurized 'sinks' or 'bubbles' to prevent pathogens from entering or exiting the facility.

Similarly, SPF facility entry and exit protocols are designed to prevent pathogens from entering the facility. Sterilization is required for all personnel and all materials entering the facility. An entry sequence may include an anteroom, change area, PPE storage and disposal space, and autoclave, all appropriately pressurized with spaces becoming increasingly positive within the facility. Holding rooms are typically the most positively pressurized to maximize isolation.

The location of an SPF facility can enhance its operation and function. Location within a general-purpose vivarium provides a level of security, control, and proximity to support functions and personnel. Location in the interior of a building (i.e. not on a perimeter wall) will isolate the facility from wind, humidity, and temperature variations which reduces the burden on the mechanical system and segregate the facility from potential environmental contaminants.

Physical and Operational Considerations

As with any vivarium, an SPF facility should consider the physical, programmatic, and operational requirements of its specialized function, all of which should be documented in the project Basis of Design. Considerations include:

- Access control, which should be tightly restricted.
- Travel paths of materials, animals, and personnel, which should be carefully planned to minimized exposure to contaminants, conflicts, and travel distances.
- The entry sequence for personnel, which includes gowning and PPE that is sterile and appropriate for working with the animal species in the facility. Requirements may include lockers, changing rooms, and an air or water shower.
- The entry sequence for materials, which may include an autoclave, fumigation chambers, UV chambers, and other methods of sterilization.
- The number, size, and adjacencies of rooms, which may include one or more holding rooms, procedure rooms, storage areas, and rooms for support functions and equipment.
- Husbandry requirements, including noise, vibration, temperature, humidity, and lighting for all species under consideration.
- Decontamination or sterilization needs for individual rooms or the entire facility. Methods, agents, procedures, and impact on continuous operations must all be considered.
- The design of walls and ceilings, which must withstand the pressure differential, prevent pathogen transmission, facilitate decontamination, and resist degradation from exposure to chemical disinfectants and other cleaning materials and methods.
- The design of floors, which must be monolithic, slip resistant, and resistant to chemical disinfectants. Floor drains, if required and used, should be capped and include deep seal traps filled with chemical disinfectant.

Summary

SPF animals are valuable research models which require specifically designed facilities. These facilities should provide environments which protect the health and pathogen-free status of the animals and the integrity of the research conducted within.

Additional Reading

Guide for the Care and Use of Laboratory Animals, Eighth Edition (2011), The National Academic Press

Biosafety in Microbiological and Biomedical Laboratories (BMBL) 6th Edition, https://www.cdc.gov/labs/BMBL.html

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Cold Weather Concreting

Introduction

According to the American Concrete Institute (ACI), "the conditions of cold weather concreting exist when the air temperature has fallen to, or is expected to fall below, 40°F (4°C) during the protection period"; the protection period is "the amount of time recommended to prevent concrete from being adversely affected by exposure to cold weather during construction" (ACI 306R-16). This definition streamlines an older, more complicated definition which included factors such as consecutive days and average daily temperature; the new definition focuses more directly on keeping concrete from being damaged by cold weather.

Damage Caused by Cold Weather

Concrete must be protected in cold weather until it can handle the cold on its own. The setting time of concrete increases significantly in colder weather because low concrete temperature has a major impact on the rate of cement hydration. Below 40°F, the hydration reaction slows and the concrete stops gaining strength. Early-age freezing (when the concrete is still saturated) may also cause permanent damage; concrete can lose up to 50% of its ultimate strength when it freezes at an early age. It is important to note that these are concrete temperatures, not air temperatures (concrete temperature is measured in accordance with ASTM C1064/C106M). Refer to Table 5.1 of (ACI 306R-16) for recommended concrete temperatures during placement.

Considerations and Precautions

Successful concrete work can be accomplished during the coldest weather if the appropriate precautions are taken. Critically, concrete should be protected from freezing until it attains a minimum compressive strength of 500 psi (3.5 MPa), which is about two days (48 hours) after placement for most concrete that is maintained at 50°F. Once concrete has reached at least 500 psi, it will not be damaged by exposure to a single freezing cycle (Powers, 1962). Per (ACI), correctly proportioned, produced, and protected concrete placed during cold weather will develop satisfactory strength and durability to meet the proposed service recommendations; the necessary degree of protection is inversely proportional to the ambient temperature. If cured properly, concrete placed in cold weather "has the potential to develop higher ultimate strength…and greater durability than concrete placed at higher temperatures…[and] is susceptible to less thermal cracking than similar concrete placed at higher temperatures" (ACI 306R-16).

The following are some of the best practices of cold weather concreting:

- Plan adequately (anticipate weather conditions prior to the placement of concrete; necessary equipment and materials should be on site before the cold weather is likely to occur).
- Keep surfaces in contact with concrete free of ice and snow and at a temperature above freezing.
- Use cold weather mix concrete (discuss the appropriate mix design and delivery temperature of the concrete with the concrete ready-mix producer).
- Use non-chloride accelerators to increase the rate of the hydration.
- Avoid the use of fly ash or slag cement, as they set slowly.
- Insulate subgrade with insulated blankets few days prior to pouring.
- Schedule concrete pouring for the warmest part of the day.
- Use insulation blankets or heated enclosures to protect the concrete from freezing.
- Use air-entrained concrete if the concrete will be exposed to freeze-thaw conditions during and/or after placement.
- Monitor and record the concrete surface temperature (the surface temperature reflects the effectiveness of protection, regardless of ambient temperature).
- Limit rapid temperature change of concrete when protective measures are removed.
- Ensure on-site management of concrete test cylinders agrees with the expectation of the project officer and the testing agency.

References

ACI 306R-16: Guide to Cold Weather Concreting.

Powers, T.C. 1962. Prevention of frost damage to green concrete.

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Metrics and KPIs in Aseptic Processing Facility Operations

Introduction

A Key Performance Indicator (KPI) is a quantifiable measure that characterizes a metric, or group of metrics, over time to demonstrate health, stability, and control. KPIs support the regulatory requirement to operate facilities in a state of control; they are derived from critical parameter metrics (Temperature (TEMP), Relative Humidity (RH), Differential Pressure (dP), and Air Changes per Hour (ACH)) used for reporting the health of individual rooms, whole facilities, and the entire Aseptic Processing Facility (APF) Portfolio. Critical environmental parameters are the most important metrics to report, as they have defined regulatory requirements and can directly impact the product being produced in the APF.

Facility-level KPI acceptance criteria are often recorded in the User Requirement Specification (URS), which provides traceability to the performance required to conform to regulatory, equipment, process, or material-related limits. Other KPIs that are reported on specific systems and utilities, include the health of specific utilities, calibrations, and O&M Performance, with several others currently in development.

APF KPIs are established using SMART criteria, which involves asking: Is the objective **Specific**? Can you **Measure** progress towards that objective? Is the goal realistically **Attainable**? Is it **Relevant** to the operation of the APF and program objectives? Finally, does the KPI fulfill the **Timeframe** requirements of the objective?

Metrics

A metric is a quantifiable measure of the health of a component, system, or utility. Metrics use a variety of calibrated probes and sensors to measure characteristics of interest, which are reported to the Building Automation System (BAS) for monitoring and control or to a qualified Environmental Monitoring System (EMS) for monitoring only. For control systems, there is an established setpoint to which the BAS will control the environment. The BAS will not command the system to react to values within a dead band range above and below the setpoint, which prevents the system from "hunting" and experiencing accelerated wear. Beyond this range may be upper and lower alert limits, depending on the metric; however, there is no regulatory requirement for alert limits, and alerts may result in frequent notifications (nuisance alerts). Beyond the alerts are upper and lower alarm limits established by the URS. Delays filter transitory effects of minor/typical occurrences, such as door openings, so that systems only alarm at significant events.

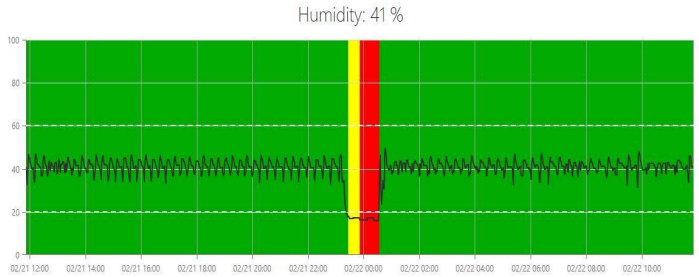
Sensors and probes must be calibrated on a regular schedule to assure reliability of the data. Trends are evaluated to assure values do not drift towards alert/alarm levels over time, which would indicate the system or component may need adjustment, maintenance, or recalibration. Trends of concern are reported in the FCIS APF Daily Report and investigative measures are initiated as a precursor to corrective actions. In the future, automated trend analyses may be featured in FCIS dashboards to track and communicate these issues more effectively.

Scales for Metrics

APF metrics are generally reported using the following scale:

GREEN	The measured value is between the upper and lower alert values, or has exceeded these alert values for less than the delay interval.
GRAY	There is data/communications loss.
YELLOW	The measured value is between the alert and alarm value for longer than the alert delay interval, or the measured value has exceeded the alarm values for less than the alarm delay interval.
RED	The measured value is at or beyond the lower or upper alarm value for a period longer than the alarm delay interval.

The metric in the example below includes dashed horizontal lines, which are the upper and lower alarm limits. There are no alert limits for this metric; note that the setpoint would generally be the midpoint between the dashed horizontal lines (alarm limits). The bold black sinusoidal line represents the data from the sensor probe, in this case tracking RH. Mid-time interval, the RH exceeded the lower alarm value for the duration of the delay interval, as depicted by the yellow band. Because the value continued to exceed the lower alarm value for longer than the delay, the sensor went into alarm, as depicted by the red band. When the probe detected that the humidity returned to within the normal operating range, the background returned to green.



Conclusion

Metrics measure the health of systems and environmental parameters. KPIs synthesize one or more metrics into more complex structures which provide insight into the health of groups of systems, entire facilities, or even the entire APF portfolio. Both metrics and KPIs are trended to analyze their performance over time and demonstrate operation in a state of control. Loss of control or trending towards a loss of control can indicate issues which need to be investigated and mitigated, including calibration, progressive failures of components, or defects in operating codes. Metrics and KPIs should be regularly reviewed against internal factors (such as changes in equipment, utilities, and operations) and externalities (such as technology, regulation, and program requirements) to provide assurance that the facility is operating within appropriate parameters and in a state of control, and that it is as ready as possible for unplanned disruptions.

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Engineering Requirements for N_2 and LN_2 Use and Storage

Introduction

Nitrogen (N_2) has many uses in laboratory operations. As an inert gas, N_2 is primarily used to control the atmosphere for sensitive equipment and experiments. At a temperature of -196° C (-320° F), nitrogen in its liquid form (LN_2) can be used in tanks or freezers for maintaining samples in a cryogenic condition. However, if not properly stored and handled, nitrogen can pose a health risk to workers; as a result, spaces where N_2 and LN_2 are present must be conscientiously designed and constructed to mitigate such risks.

Nitrogen Risks

N_2 comprises approximately 78% of standard breathing air, while oxygen (O_2) comprises only about 21%. Because of its large concentration in breathing air, most people consider N_2 to be a harmless gas. When released in a confined space such as a closed room, however, the percentage of N_2 can quickly increase to over 80%, thus reducing the percentage of O_2 to less than 19%; this is known as oxygen displacement. At O_2 levels below 19%, humans can start to experience adverse effects. At 16% O_2 levels, breathing and pulse rates can be affected, which can impact cognitive functions. As O_2 percentage levels continue to decrease, people will fall into unconsciousness, and eventually the conditions could become fatal. Because of these potentially serious risks associated with the use, storage, and generation of nitrogen, whether in a gaseous or liquid state, spaces where N_2 or LN_2 are present must be carefully evaluated during the design and construction phases of a project to ensure the appropriate safety measures are in place.

Design Guidelines and Considerations

Gaseous N_2 is usually stored in cylinders and piped to various points of use, so the storage area may be within the lab itself or a local storage room. LN_2 is usually stored in bulk containers outside the facility and piped into the lab for use in tank freezers or low temperature freezers; however, it can also be stored locally in cryogenic storage dewars within the lab or an associated storage room.

N_2 has a specific gravity just less than breathing air (0.97 compared to 1.0) so its natural tendency at standard temperature and pressure is to rise to the top of the room or space. For this reason, NFPA 55-6.17.4.3 calls for exhaust ventilation grilles no more than 12” from the ceiling in a space where N_2 or LN_2 is located. It is critical to note, though, that when N_2 is released from a high pressure cylinder through a small orifice, such as a shut off or regulator valve, the temperature of the gas will drop from expansion; similarly, when LN_2 tanks are vented to remove the fog in the tank for access to samples, the temperature of the released N_2 gas will be extremely cold. Both these scenarios cause the N_2 to fall to the lower levels of the room. As the N_2 gas quickly warms, it will rise due to its lower specific gravity, and as it rises through the breathing zone of the users, the percentage of O_2 can be reduced to an impactful level for the occupants in the space. For this reason, N_2 should also be treated as a gas that is heavier than air and should therefore also be exhausted at a point no more than 12” above the floor of the space, per NFPA 55-6.17.4.2. Simultaneously treating N_2 gas as both heavier than air and lighter than air to fully address health risks means that exhaust ventilation points should be located at both high and low levels in the space. These exhaust ventilation points should be located behind the points of potential release to draw the gas away from the breathing zone of users within the space.

Oxygen monitoring is required to protect personnel in the event of a situation where oxygen displacement reaches hazardous levels. The intent of the monitor is to warn occupants of low oxygen levels so they can immediately vacate the area and contact authorities to address the emergency condition. NFPA 55-6.9 requires an Employee Alarm System is required to warn users and occupants in the event of an emergency, and DRM Chapter 12.3: Compressed Gas and Cryogenic Systems provides control and alarm requirements specific to NIH facilities in concert with NFPA 55. In particular, DRM Section 12.3.1.J calls for the use of oxygen monitoring specific to the gas to be detected. The OSHA Respiratory Protection Standard (29 CFR 1910.134) also requires oxygen monitoring for any place oxygen percentages could potentially fall to less than 19.5%. As noted above, the use or storage of N_2 and LN_2 can reduce oxygen percentages below the OSHA threshold, so oxygen monitors should be included in the design and construction of spaces containing N_2 or LN_2.

Monitors should be equipped with at least two sensors located in the breathing zone, approximately 4’ above the floor, and should also provide both audible and visual notification of an alarm. A remote audible and visual alarm should be provided directly outside the space to provide notification to anyone outside the space to not enter the area. Additional guidance and requirements for the use of oxygen monitoring in NIH aseptic production facilities can be found in DRM Section 13.10.7. Information on oxygen monitoring for the use of LN_2 in BSL-3 laboratories can be found in DRM Section 8.6.10.B.

Additional Information

1. NFPA 55, Compressed Gases and Cryogenic Fluids Code, 2020
2. The OSHA Respiratory Protection Standard (29 CFR 1910.134)
3. NIH Design Requirements Manual Sections: 6.17.4, 8.6.10, 12.3, 13.10.7

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Vapor Pressure and Flooring Installation

Introduction

A major cause of flooring failure is excessive moisture in the underlying slab. Moisture can migrate through the slab as water vapor can become trapped between the slab and impervious flooring. The trapped vapor can condense, causing flooring to cup, buckle, and blister, leading to adhesive failure and mold growth. Before flooring is installed, it is necessary to understand the causes of vapor migration and confirm acceptable slab conditions.

Vapor Pressure

Vapor pressure is the natural tendency of moisture to seek equilibrium by migrating from areas of high concentration to areas of low concentration in the form of water vapor. The vapor emission rate is the rate at which water is released from a slab via vapor pressure.

Reducing Moisture in Slabs

Moisture in slabs should be controlled to below the levels the flooring manufacturer indicates as acceptable for installation of their products. This can be achieved by:

- Using appropriate concrete mixes with the minimum water necessary for placement. Admixtures can be used to increase workability and reduce the amount of water used.
- Providing sufficient curing time. Over time, the water in a concrete mix reacts with cement and admixtures, resulting in less free internal moisture.
- Completing the building enclosure to provide protection from the elements. Concrete is porous, and environmental water will penetrate and raise the internal moisture level.
- Operating the HVAC systems. Temperature and humidity control can reduce moisture content.
- Providing well-designed grading and landscaping, which can divert surface water and groundwater from slabs.
- Installing vapor barriers that block the movement of moisture from the soils below slabs installed on grade. To be effective, a vapor barrier must be a continuous, impermeable system, installed with sealed joints, and free of damage and penetrations.
- Providing dewatering measures below slabs as required in areas with high, seasonally high, or perched water tables.

Testing

It is important to determine the moisture content of a slab to identify it is appropriate for the installation of a new flooring. Two of the more common moisture testing methods are the calcium chloride test and the internal relative humidity probe.

The calcium chloride test measures the vapor emission rate of the slab. This is done by placing a test kit containing a quantity of calcium chloride ion on a slab to measure moisture near the surface. After a determined time, the kit is retrieved and weighed, and the weight gain is attributed to moisture from the concrete. The results can be used to calculate the estimated vapor emission rate of the slab.

The advantages of this test are that it is widely accepted by flooring manufacturers and relatively easy to perform, and it does not require testing equipment. The disadvantages are that it only measures the free moisture near the surface of a slab, and that both the test and the analysis take time.

The relative humidity probe measures the internal relative humidity of the slab. The test requires drilling holes to a depth of 40% of the slab's thickness and inserting capped plastic sleeves. After waiting for a duration defined by the test, a probe is placed in the sleeve and reads the humidity at the bottom of the hole.

The advantages of this test are that the humidity is measured near the center of the slab, the instruments can be independently calibrated, and the results are acquired quicker than with the calcium chloride test. The disadvantages are that it is less widely accepted by flooring manufacturers, and that the probe and calibration require more financial investment.

Conclusion

It is important to avoid excess moisture in slabs and to test them to ensure acceptable conditions prior to flooring installations; both the calcium chloride test and the relative humidity probe provide the necessary data. Tests should be conducted after HVAC systems are operating and the slab has been acclimated to final environmental conditions. It is important that tests be conducted in accordance with their respective ASTM test method (see Additional Information, below). This will include such factors as proper temperature and humidity, the proper number of tests and test locations, and proper subfloor preparation. If these conditions and recommendations are not strictly adhered to, then no test method will ever present an accurate assessment of the concrete's vapor emission rate.

Additional Information

ASTM F-1869-10, *Standard Test Method for Measuring Moisture Vapor Emission Rate of Concrete Subfloor Using Anhydrous Calcium Chloride*
ASTM F-2170-11, *Standard Test Method for Determining Relative Humidity in Concrete Floor Slabs using in situ Probes*
ASTM F-710 *Standard Practice for Preparing Concrete Floors to Receive Resilient Flooring.*