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INTO THE FUTURE WITH BAXTER'S DoseEDGE PHARMACY WORKFLOW MANAGER SYSTEM

INTENDED OUTCOME

The right drug with the right diluent for the right dose at the right time has been and remains the ever-present responsibility of a pharmacist. The introduction of IV Workflow Management systems (IVWFM) into the sterile compounding space has significantly reduced the effort and improved the chances of consistently meeting this responsibility. This type of quality assurance verification has been the primary use of IVWFM systems since their introduction into the United States in 2008 when DoseEdge Pharmacy Workflow Manager system (DoseEdge) was introduced.

However, the pharmacist's responsibilities continue to grow with the increasing number and ever more strict regulations and guidelines governing the processes for compounding sterile preparations and the environments they are prepared in. Therefore, pharmacists must consider how these IVWFM systems can be used to support these needs.

CHALLENGES

Accurate and consistent data from published literature on the incidence of IV compounding errors is difficult to find as most facilities and pharmacists are reluctant to share this type of information. Confounding this is the fact that there is no single recognized definition of what constitutes these types of medication errors. The relatively small number of data sets that are available for error rates at individual facilities or groups of facilities not using any type of IVWFM system (or technology-assisted workflow systems) can range from 0.22%[1] to 9%[2]. These errors can result from pharmacy staff not knowing with specificity what drugs, diluents, and volumes should be used to prepare a compounded sterile preparation (CSP).

Before automation, pharmacists had to verify every CSP dispensed from the cleanroom using manual and sometimes inexact methods. It was not always possible to determine if the correct drug and/or amount was added to an IV container. Therefore, the true number of compounding errors could not be determined.

The Institute for Safe Medication Practices (ISMP) published a survey in October of 2020 that included 634 respondents, 80% of whom were pharmacists, and another 18% were pharmacy technicians[3]. The survey results demonstrated some concerning results[3]:

- 56% of all responders (355) reported always having and following standard operating procedures for the compounding process.
- 48% of pharmacist responders (243) stated that it was always easy to identify with certainty which drugs, diluents, and volumes were used when verifying the preparation of a CSP.
- 57% of respondents (361) were using technologies to support sterile compounding.
- 47% of the 361 respondents using technology (170) were taking advantage of IVWFM systems that included both barcode scanning and image capture to help manage risks.

Additionally, on November 1, 2022, the United States Pharmacopeia (USP) published the revised General Chapter <797> Pharmaceutical Compounding — Sterile Preparations (USP <797>) which provides the new minimum acceptable standards for sterile compounding. In recent years, USP <797> requirements seem to also be garnering more attention from organizations such as The Joint Commission and other accrediting bodies which now conduct inspections according to these requirements.

Many of the updates to USP <797> are relatively minor changes, and the basic principles remain the same. Examples of this are the need to maintain acceptable levels of viable and non-viable particle counts in the classified areas. However, more detail is provided around the performance and frequency of the required sampling. These changes in testing detail don't affect the basic requirements of how many particles per cubic meter or colony forming units per cubic meter are acceptable as those limits are set by separate ISO standards.

However, as with previous revisions of the chapter, some changes in the guidelines are more significant and may require considerable

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changes to pharmacy and cleanroom operations. An example of this type of significant change would be how restricted-access barrier systems (RABS) can be used. In the 2008 version of the chapter, the ISO 5 environment that can be achieved with these systems alone was considered sufficient to apply extended Beyond-use Dates (BUDs) for CSPs regardless of where the RABS was located[4]. However, the 2023 version of USP <797> requires that the RABS be located in an ISO 7 environment to apply Category 2 or 3 beyond-use dating[5]. Essentially, a RABS in an unclassified space is now equivalent to a segregated compounding area.

In any case, whether the standards of the 2008 and 2023 versions of the chapter remain the same, or they receive minor or significant updates, history tells us that they can be challenging to consistently adhere to for many pharmacies. In the 2023 State of Pharmacy Compounding survey published in Pharmacy Purchasing and Products, only 31% of respondents indicated their facilities were in full compliance with standards that will become effective in November of 2023[6]. An even more alarming statistic is that only 76% of respondents indicated their facilities were in full compliance with the 2008 version of USP <797>[6].

DISCUSSION

The compounded sterile preparation goals of ISMP and USP are both rooted in ensuring that safe medications are available to patients when they are needed, ISMP with the Guidelines for Sterile Compounding and the Safe Use of Sterile Compounding Technology, and USP with General Chapter <797>. Although, in some ways, the two organizations approach the goals differently, there is overlap in that they both focus on processes to achieve the goals. It's this process overlap that can allow IVWFM systems with broad functionality such as the DoseEdge system to support the needs of pharmacies in their pursuit of compliance with both organizations' guidelines.

From an ISMP perspective, the use of technology such as an IVWFM system to improve the safety, efficiency, and prioritization of compounding within the cleanroom is a well-known and frequent topic of discussion. In fact, ISMP includes this in their 2022-2023 Targeted Medication Safety Best Practices for Hospitals and has done so since 2016[7]. These improvements can be achieved by automating potentially error-prone processes that have traditionally been performed manually. These error-prone processes can include researching and following the correct and complete compounding process, manually performing dose calculations and determining appropriate BUDs, prioritizing urgently needed products and using the 'syringe pull-back' or 'proxy' method for indicating volumes of drugs injected into final containers.

Additionally, in 2022, "ISMP Guidelines for Sterile Compounding and the Safe Use of Sterile Compounding Technology" was published. It contains essential technology attributes, safe pharmacy processes, safety gaps, and associated best practices for various technologies such as automated compounding systems, IV robotics and IVWFM systems.

The ISMP essential attributes for IVWFM systems are listed below. Many align nicely to address the gaps or issues associated with CSP preparation[8].

ISMP Essential Technology Attributes	DoseEdge System Functionality
IV workflow management systems are interfaced with the electronic health record to eliminate order transcription from one system into another. If a compounded sterile preparation has been discontinued before initiation of the compounding process, the system interface allows for the removal of these products from the queue.	✓
IV workflow management systems allow users to create a master formulation record for non-patient specific batch, stock solution, and patient-specific compounded sterile preparations.	✓ A
When master formulation records are created, the IV workflow management system prompts for an independent double check, which is documented in the system.	
Master formulation record changes are timestamped, saved, and identify the user who made the modification.	
IV workflow management systems provide an electronic log of changes made to the database by users.	✓
IV workflow management systems allow users to customize the incoming order queue to prioritize work.	✓
Machine-readable coding (e.g., barcode, RFID) is used to verify source products, including diluents, during the compounding process.	✓
IV workflow management systems automatically perform calculations or conversions.	✓
IV workflow management systems guide users through essential steps in the compounding process including which steps require video or still images or gravimetric analysis.	✓
Image-capture pictures are clear such that syringe graduation marks, drug and/or diluent names, lot numbers, and expiration dates are easily visible.	✓

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IV workflow management systems that use gravimetric analysis prevent users from creating master formulation records for preparations that are outside the system's tolerance limits, and if staff attempt to weigh a volume outside the integrated scale's tolerance limit the IV workflow management system alerts the user.	
IV workflow management systems document all steps and components of the compounding process (e.g., products used, the practitioner who performed the compounding, the primary engineering control, machine readable code scans, date and time of preparation, alerts or warnings presented during the process, the practitioner who verified the preparation), and the information is available to users in a log and/or report.	✓
IV workflow management systems allow for remote verification using video or image capture, and, when used, gravimetric analysis.	✓
IV workflow management systems track beyond-use dating of opened or reconstituted products to warn practitioners and prevent use of an expired product.	✓
IV workflow management systems allow for customization of labels (e.g., tall man lettering, color print, reverse print, electronic health record compatible barcode).	✓
IV workflow management systems limit the printing of the dispensing label until the compounding process is complete.	✓
Workload (e.g., incoming load) is documented by the technology and captured in a report to inform and facilitate operational improvement.	✓
Close-call compounding events (e.g., wrong drug scans) intercepted by the technology are captured in a report to facilitate compounding error analysis and process improvement. Data in vendor reports are provided in a useful format and do not require significant manipulation by the end user.	✓
When a system update is available, IV workflow management system vendors ensure all customers receive and install the update in a reasonable timeframe.	

2022 ISwMP Guidelines for Sterile Compounding and the Safe Use of Sterile Compounding Technology

A - Can be obtained from DoseEdge Technical Support

The use of IVWFM systems to help meet the Chapter <797> standards is discussed far less, if at all. However, given the broad functionality of some of these systems, such as the DoseEdge system, they can influence pharmacy procedures and documentation practices etc. which can directly or indirectly support these requirements.

The following are many of the standards from the 2023 version of USP <797> that could potentially be supported by using IVWFM systems[5].

USP Chapter <797> Standards	How DoseEdge Functionality Could Provide Support
3. PERSONAL HYGIENE AND GARBING Personal hygiene and garbing are essential to maintain microbial control of the environment. Most microorganisms detected in cleanrooms are transferred from individuals. Squamous cells are normally shed from the human body at a rate of 10^6 or more per hour, and those skin particles are covered with microorganisms. Individuals entering a compounding area must be properly garbed and must maintain proper personal hygiene to minimize the risk of contamination to the environment and/or CSPs. Individuals that may have a higher risk of contaminating the CSP and the environment (e.g., personnel with rashes, recent tattoos, oozing sores, conjunctivitis, or active respiratory infections) must report these conditions to the designated person(s). The designated person(s) is responsible for evaluating whether these individuals should be excluded from working in compounding areas before their conditions have resolved because of the risk of contaminating the CSPs and the environment.	Remote verification could help decrease the number of pharmacists required to enter the cleanroom to verify doses including in-process and final checks. This can be especially beneficial on off-shifts when staffing may be lower or when pharmacist verifiers with higher risks for contamination may be the only pharmacist on duty.
4. FACILITIES AND ENGINEERING CONTROLS The design of the facility should take into account the number of personnel and their movements. 4.1 Protection from Airborne Contaminants Proper design and controls are required to minimize the risk of exposure of CSPs to airborne contaminants. Total airborne particle counts by ISO classification must not be exceeded: ISO 5 = 3520 particles/m^3 ISO 7 = 352,000 particles/m^3	Remote verification can help minimize the number of pharmacist verifiers needing to enter the cleanroom which may be able to affect the overall design. This decrease in staff needing to enter the cleanroom can also be used as a control mechanism to decrease airborne contaminants.

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6. MICROBIOLOGICAL AIR AND SURFACE MONITORING 6.2.3 Viable air sampling data evaluation and action levels Viable airborne particle counts by ISO classification must not exceed actionable levels: ISO 5 > 1 cfu/m^3 ISO 7 > 10 cfu/m^3 6.3.3 Surface sampling data evaluation and action levels: ISO 5 > 1 cfu/media device ISO 7 > 10 cfu/media device	The decrease in staff needing to enter the cleanroom associated with remote verification can also be used as a control mechanism to decrease viable air and surface contaminants.
11. MASTER FORMULATION AND COMPOUNDING RECORDS 11.1 Creating Master Formulation Records (MFR) An MFR is a detailed record of procedures that describes how the CSP is to be prepared. An MFR must be created for all CSPs prepared from nonsterile ingredient(s) or CSPs prepared for more than one patient. 11.2 Creating Compounding Records (CR) CR documents the compounding of each CSP. A CR must be created for all Category 1, Category 2, and Category 3 CSPs. A CR must also be created for immediate-use CSPs prepared for more than one patient. The CR must be created to document the compounding process. A prescription or medication order or label may serve as the CR. If an ACD, workflow management system, or other similar equipment is used, the required information in the CR may be stored electronically as long as it is retrievable and retains the required information.	The following DoseEdge functionality can be used in aggregate to support most/all the requirements for the contents of an MFR and CR, and help ensure that the MFRs and CRs are followed: • Customizable Drug Formulary • Customizable Product Formulary • Customizable Actions • Customizable Procedures • Customizable Scan Events • Storage capabilities • Customizable product-specific information fields
12. RELEASE INSPECTIONS AND TESTING 12.2 Sterility Testing For Category 2 CSPs assigned a BUD that requires sterility testing (see Table 13) and all Category 3 CSPs, the testing must be performed. 12.3 Bacterial Endotoxins Testing Category 2 injectable CSPs compounded from one or more nonsterile component(s) and assigned a BUD that requires sterility testing and Category 3 injectable CSPs compounded from one or more nonsterile component(s) must be tested to ensure that they do not contain excessive bacterial endotoxins.	Customizable Actions and/or Procedures can be used to remind compounders when sterility and/or bacterial endotoxin testing (or other requirements) needs to be completed.

14. ESTABLISHING BEYOND-USE DATES Each CSP label must state the date, or the hour and date, beyond which the preparation must not be used and must be discarded (i.e., the BUD). The BUD is determined from the date and time that preparation of the CSP is initiated. 14.2 Parameters to Consider in Establishing a BUD When establishing a BUD for a CSP, compounders must consider parameters that may affect quality. The BUDs for CSPs are based primarily on factors that affect the achievement and maintenance of sterility, which include, but are not limited to: • Conditions of the environment in which the CSP is prepared • Aseptic processing and sterilization method • Starting components (e.g., sterile or nonsterile ingredients) • Whether or not sterility testing is performed • Storage conditions (e.g., packaging and temperature) 14.3 Establishing a BUD for a CSP The BUD must not exceed the shortest remaining expiration date of any of the commercially available starting components. 14.5 Multiple-Dose Containers The use of preservatives must be appropriate for the CSP formulation and the route of administration. For example, the preservative must not be inactivated by any ingredients in the CSP, and some preservatives are not always appropriate for the patient (e.g., neonates) or route of administration (e.g., intrathecal or ophthalmic injection). After a multiple-dose CSP container is initially entered or punctured, the multiple-dose container must not be used for longer than the assigned BUD or 28 days if supported by antimicrobial effectiveness testing results on the CSP, whichever is shorter.	BUDs are automatically calculated from the time the compounding process is initiated. They can be customized and automated to account for the many options that are available between and within the three Compounding Categories BUDs can be customized at the dose level based on: • Starting components used in the dose • Location of preparation (environmental conditions such ISO classified vs SCA/RABS) • Storage conditions • Processes used during preparation (including sterility testing) The BUD of individual doses are compared to the BUDs or expiration dates of the components used in dose to ensure they are appropriate. With 'Preservative-free" and "Route of Administration" designations in the Product Formulary, inappropriate component use can be prevented. "Work in Progress" products and labels can automate BUDs for components used during preparation

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15. USE OF CONVENTIONALLY MANUFACTURED PRODUCTS AS COMPONENTS 15.1 Use of Conventionally Manufactured Single-Dose Containers A conventionally manufactured single-dose container is a container closure system that holds a sterile product for parenteral administration (injection or infusion) that is not required to meet the antimicrobial effectiveness testing requirements. If a single-dose vial is entered or punctured only in an ISO Class 5 or cleaner air, it may be used up to 12 h after initial entry or puncture as long as the labeled storage requirements during that 12-h period are maintained. Opened single-dose ampules must not be stored for any time period. 15.3 Use of Conventionally Manufactured Pharmacy Bulk Packages A conventionally manufactured pharmacy bulk package is a container of a sterile product for parenteral use that contains many single doses. The contents are intended for use in a pharmacy admixture program and are restricted to the sterile preparation of admixtures for infusion or, through a sterile transfer device, for the filling of empty sterile containers. The pharmacy bulk package must be used according to the manufacturer's labeling (see <659>, General Definitions, Injection Packaging Systems). The pharmacy bulk package must be entered or punctured only in an ISO Class 5 PEC.	"Work in Progress" products and labels can also automate BUDs for single dose products, multiple dose products and pharmacy bulk packages used during preparation
18. QUALITY ASSURANCE AND QUALITY CONTROL 18.1 Notification About and Recall of Out-of-Specification Dispensed CSPs If a CSP is dispensed or administered before the results of release testing are known, the facility must have procedures in place to: • Immediately notify the prescriber of a failure of specifications with the potential to cause patient harm (e.g., sterility, strength, purity, bacterial endotoxin, or other quality attributes) • Recall any unused dispensed CSPs and quarantine any stock remaining in the pharmacy. • Determine the distribution of any affected CSP, including the date and quantity of distribution. • Identify patients who have received the CSP.	Lot number tracking can be used to trace products and components to individual patient doses.

CONCLUSION

The safety, efficiency, and waste-reduction benefits with the use of IVWFM systems are well-established. ISMP has put forth much effort in defining what an effective system should be capable of and recommending their use among other technologies in the cleanroom.

Although IVWFM systems are only used in a minority of facilities, that number continues to grow due to an ever-increasing focus on safety and efficiency.

With the updated version of USP <797> effective on November 1, 2023, there is also a heightened interest in what facilities need to do to become compliant before the effective date.

IVWFM systems with broad functionality such as the DoseEdge system, can help support pharmacies in their pursuit of regulatory compliance, optimized workflows, compounding efficiency, and most of all, patient safety.

The DoseEdge System is not intended to replace the knowledge, judgment or expertise of pharmacists and pharmacy technicians in the preparation of IV admixtures or oral doses.

For safe and proper use of the product mentioned herein, please refer to the appropriate Operator's Manual.

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DoseEdge System is software intended to improve & document workflow in your pharmacy, and to help reduce opportunities for error. It is not intended to replace the knowledge, judgment, or expertise of pharmacists and pharmacy technicians in the preparation of IV admixtures or oral doses.

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