

## Review Article

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# Use and impact of technology-assisted workflow (TAWF) systems for drug compounding in pharmacy practice: a scoping literature review

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### Abstract

**Objectives:** The aim of this study was to review studies describing the use and the impact of technology-assisted workflow (TAWF) systems for drug compounding in hospital pharmacy.

**Content:** This is a scoping literature review. A search was conducted on studies describing or evaluating the use of TAWF published from January 1st, 2015 to July 31st, 2021. Two databases were searched (PubMed and Embase), followed by a search on Google Scholar.

**Summary:** 218 articles were screened and 17 were identified as meeting the inclusion criteria. TAWFs all included preparation assistance software (17/17), barcode reader (17/17), photo or video taking (17/17), and some included gravimetric systems (8/17), and the use of robots (2/17). A majority of the studies included used technology for parenteral preparations (15/17, one for oral preparations only (1/17), and one used technology for both types of preparations (1/17). Most of the articles selected presented drugs prepared for adults (10/17), the others presented drugs intended for children (4/17) or for a mix of adults and children (3/17). Four parameters were evaluated: error detection rate (n=15), preparation and validation time (n=7), and costs generated or saved (n=7). Ten studies evaluated the pre-post impact of implantation of a TAWF (10/17).

**Outlook:** Given the heterogeneity of the data available, the use of TAWF was associated with an increased ability to

detect preparation errors, a reduction in preparation time and costs, and increased satisfaction of pharmacy technicians and pharmacists. However, better quality studies are needed to confirm the positive impacts studied.

**Keywords:** barcode readers; cameras; compounding; gravimetry; impact; technology-assisted workflow systems (TAWF).

## Introduction

Drug compounding is defined as the “process of combining, mixing, or altering ingredients to create a medication tailored to the needs of an individual patient. Compounding includes the combining of two or more drugs” [1].

The Food and Drug administration insists that “compounded drugs can serve an important medical need for patients, but they do not have the same safety, quality, and effectiveness assurances as approved drugs. Unnecessary use of compounded drugs unnecessarily exposes patients to potentially serious health risks.” [1]. Several authors have identified the risks associated with drug compounding, such as microbial contamination to patients, wrong manipulation or overdose [2–5].

Unlike the pharmaceutical industry, which must comply with good manufacturing practices to commercialize approved drugs in a given country, most countries and professional regulatory authorities supervise drug compounding produced by pharmacists with less demanding professional standards [6].

In hospitals, the compounding process is part of a complex drug circuit that includes more than 120 steps [7]. In order to reduce the risks associated with drug compounding, several regulatory authorities and professional associations regulate this activity, notably the United States Pharmacopeia [8–10], the Agence nationale de s curit  du m dicament et des produits de sant  (a French National Security Agency of Medicines and Health Products) [11] and two European directives. This directives are on quality and safety assurance requirements for medicinal products prepared in pharmacies

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and on good reconstitution practices in hospitals for medicinal products for parenteral use [12, 13].

Moreover, in European Pharmacopoeia (Ph. Eur), there is a monograph for pharmaceutical preparations. This monograph provides guidance as to which specific monographs are applicable to active pharmaceutical ingredients, excipients and dosage forms [14].

At the same time, several technologies, known as technology-assisted workflow (TAWF) systems for drug compounding, have been developed.

A TAWF is generally based on a software capable of supporting and documenting the different steps of the preparation. This software can use various technologies to acquire useful data for verifying the conformity of the preparation, including gravimetric systems with high precision scales, barcode readers to verify the identity of the ingredients/supplies used, and cameras to document the process as well as allow asynchronous verification by a pharmacist and robots that assist or performs specific compounding steps. The Institute for safe medication practices (ISMP) regularly publishes best practices for hospital. *ISMP Targeted medication Safety Practices for Hospitals* aims to identify, inspire, and mobilize widespread, national adoption of consensus-based best practices for specific medication safety issues that continue to cause fatal and harmful errors in patients [15]. The best practice 11 mentioned that for compounding sterile preparations the use of technology is essential to assist in the verification process.

The White paper of the American Society of Health-System Pharmacists (ASHP) also describes two primary types of automation: IV robotics and IV room workflow systems [16]. Moreover, THRIV is a coalition of healthcare providers and consumers and focuses on improving IV accuracy [17].

The interest in new technologies is growing. Indeed, the risk of error in sterile hospital preparations is important and can lead to fatal errors. It is shown in that 9% of IV preparations may involve errors (the leading issue being wrong ingredients and/or volumes)—too many of which cause patient harm and death [18].

Furthermore, in addition to assisting the different steps of preparation, the evolution of these technologies is fast and requires monitoring and adaptation to hospital pharmacy environment.

The aim of this study was to review the studies describing the use and the impact of TAWF systems used for drug compounding in hospital pharmacy.

## Materials and methods

### Study type

This is a scoping literature review.

### Data sources and selection of studies

A search was conducted on studies describing or evaluating the use of TAWF published from January 1, 2015 to July 31, 2021. Two databases were searched (i.e., PubMed and Embase), followed by a search on Google Scholar.

In PubMed, the following search strategies were used: (“compounded” [All Fields] OR “compounder” [All Fields] OR “compounders” [All Fields] OR “compounding” [All Fields] OR “compounding s” [All Fields]) AND (“workflow” [MeSH Terms] OR “workflows” [All Fields] OR “workflows” [All Fields] OR “workflows” [All Fields]) AND (“pharmacie” [All Fields] OR “pharmacies” [MeSH Terms] OR “pharmacies” [All Fields] OR “pharmacy” [MeSH Terms] OR “pharmacy” [All Fields] OR “pharmacy s” [All Fields])

In Embase, a search was carried out with two key words “drug formulation” and “workflow” in the advanced search tool.

In Google Scholar, the following search strategy was used: “drug compounding pharmacy workflow”. Manual selection was made on the first pages of search results.

For each search strategy, articles were selected based on title, then abstract, then full text. The selection was made by two research assistants and a pharmacist. Differences were resolved by consensus.

Articles describing or evaluating the use of TAWF in hospital pharmacy practice were included. Abstracts, thesis, descriptive articles without original data and articles not related to pharmacy hospital practice, were excluded. In addition, articles describing or evaluating a technology (e.g., balance, camera or robot) without sufficient details about the characteristics of TAWFs were excluded.

### Data extraction and analysis

Data relating to TAWFs was extracted from the articles included. The impact of the TAWF was assessed on four parameters when applicable: error capture rate, preparation time, validation time by the pharmacist and costs generated or saved. The impact was rated as positive, negative or uninterpretable. Descriptive statistics were produced.

## Results

From the search strategies performed, 218 articles were screened and 17 articles were identified as meeting the inclusion criteria (Figure 1) [19–35].

## Profile of studies

A majority of the studies were from the United States (12/17). The studies evaluated commercial products (16/17) or locally developed products (1/17). TAWFs all included preparation assistance software (17/17), barcode reader (17/17), photo or video taking (17/17), some included gravimetric systems (9/17), and others used robots (2/17). Most of the studies used technology for parenteral preparations (15/17), one used technology for oral preparations only (1/17), and one used technology for both types of preparations (1/17). Most of the articles selected prepared these drugs for adults (10/17), the others were intended for children (4/17) or mixed (3/17).

Four studies assessed staff satisfaction (4/17). The perceptions that emerged were that TAWFs were perceived to be more secure and accurate than the non-TAWF approach. Three studies evaluated the accuracy of TAWFs (3/17).

Eight studies declared conflicts of interest, either in fees paid to authors (5/8) or funding by the company that marketed the TAWF (3/8).

## Description of the use of TAWF

Seven descriptive studies described the systems implemented in their pharmacy (Table 1). One study compared two TAWFs. Three parameters were evaluated among these studies: error detection rate (n=6), preparation time (n=2), and costs generated or saved (n=2).

## Impact of TAWF

Ten studies evaluated the pre-post impact of the implementation of a TAWF (Table 2). Four parameters were evaluated: error capture rate (n=10), preparation time (n=6), validation time (n=6), and costs (n=6).

## Discussion

A total of 17 articles assessing or describing TAWF systems were published between 2015 and 2021. In healthcare technologies, products evolve rapidly and the study period chosen aims to take into account only the most recent data that incorporates the improvements made to the TAWF.

## Impact of TAWF on error detection rate

Four studies evaluated error detection and all showing an increased rate with the TAWF systems [25, 30, 32, 33]. The error detection rate varied from 0.096 to 1.44% pre implementation vs. 1.94–42.02% post implementation.

The types of errors reported are mostly a dilution error, wrong vehicle or diluent, wrong bag type or wrong drug.

However, the results were difficult to interpret because the length of the evaluation period or the number of preparations audited differed greatly between the pre and post implementation phase of TAWF. For example, Bucci et al. [33] reported a significant increase in error detection rate, but the number of preparations was smaller in the post

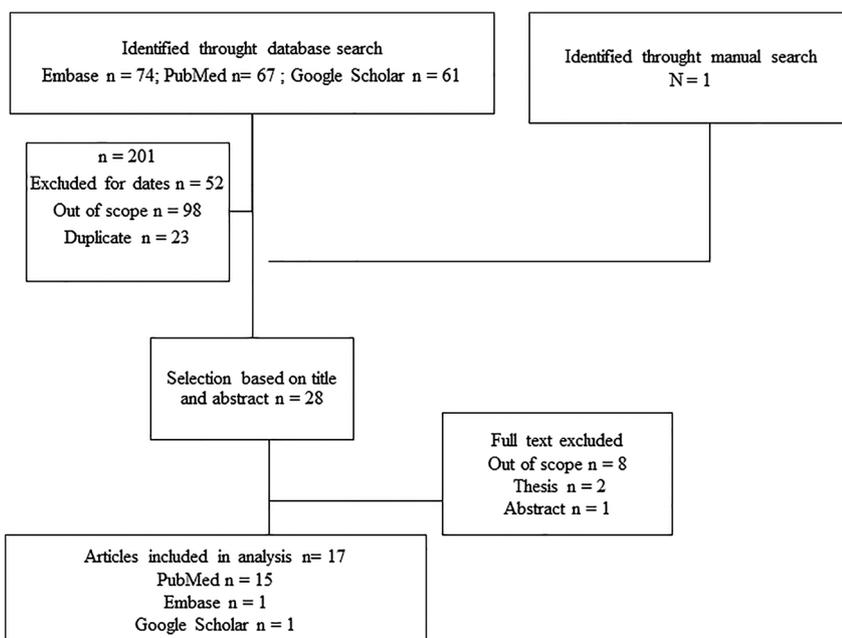


Figure 1: Flowchart of article selection.

**Table 1:** Description of the use of TAWF in hospital pharmacy (descriptive or comparative studies).

Studies	Study type	Product	TAWF <sup>a</sup>	Type of product	Preparations (n)	Description
Deng [19]	Descriptive/ single center	Baxter, dose edge™	–	Injectable	421,730	3,101 errors 72.3% (n=2,242) detected by the TAWF 27.7% (n=860) detected by the pharmacist
Terkola [20]	Descriptive/ multi center	BD, Cato®	G	Injectable	759,060	7.89% (n=59,889/759,060) errors detected by the TAWF
Benizri [21]	Descriptive/ single center	Eurekam, Drugcam®	–	Injectable	NA	Correct identification of 84.2% (n=101 preparations) by the TAWF Correct measure of the volume of 98.5% (n=118) by the TAWF
Bledsoe [22]	Descriptive/ single center	In-house	–	Per os	178,344	3,812 errors detected 1.8% (n=3,291) detected by the TAWF 0.3% (n=521) detected by the pharmacist
Marzal Alfaro [23]	Descriptive/ single center	Grifols, Phocus Rx®	–	Injectable	9,872	Error rate 0.8% (n=78/9872) – Dose-related errors (n=56) – Packaging errors (n=20) – Wrong medication (n=2) Benefit/cost ratio=€ 4.21 Return on investment = 321%
Jean [35]	Descriptive/ multi center	BD, Pyxis IV prep™	G	Injectable	2,609	Error rate: No difference in the numbers of errors detected with remote pharmacists (n=17) vs. local pharmacists (n=10) (p=0.177) Validation time: remote pharmacist 0.45 vs. 0.18 min (p<0.001) Costs: Total annual savings = \$23,770.08 Perception: optimization of workflow and sharing of workload
Pang [24]	Descriptive/ single center	Loccioni, Apoteca chemo® compared to ApoteCap®	G compared to R	Injectable	G: 18,136 R: 42,129	Error rate: G=1.58%, R=2.47%, p<0.0001 Precision: G=1.12, R=1.12, p=0.952 Time to prepare drug: G=2:39 min, R=6:07 min Total time to complete drug: G=17:49 min, R=24:45 min

G, use of gravimetric system; NA, not applicable; R, use of a robot; TAWF, technology-assisted workflow systems. <sup>a</sup>All TAWF included software to help with preparation, use of a barcode reader and taking photos or videos.

implementation phase (0.47% (n=116,686 preparations) vs. 42.02% (n=5,195 preparations), p<0.0001). The large difference is explained by the fact that the system alerts on all types of errors, including errors within the tolerance threshold. Considering that the expected error rate is often low, it is preferable to target similar and sufficiently long observation periods.

A systematic review by Batson et al. [36] highlighted the impact of automated compounding technology for the preparation of chemotherapy. They demonstrated that compounding technologies improved accuracy in dose preparations and reduced dose errors compared with manual compounding. Flanagan et al. [37], reported a low proportion of error detected with the use of a TAWF, both with one that was not integrated with patients electronic medical files and with one that was integrated (0.72 and 0.88%, respectively).

The definition of an error varied from one study to another (wrong dose errors, wrong drug/diluent errors, wrong concentration errors ...). Also, TAWF systems allowed the detection of errors that were not detectable by human (e.g., too small discrepancy to detect) and possibly not clinically significant. Further studies should use a detailed definition of error including all types encountered and their level of clinical significance.

### Impact of TAWF on preparation and validation time

Six studies evaluated the impact of TAWF on preparation and validation time [25, 27, 28, 31–33]. Four studies have documented a reduction in preparation time of 9.2–34.8% [27, 29, 30, 34] and five in validation time [23, 27, 29, 34, 36]. One

**Table 2:** Assessment of the impact of the use of TAWFs in hospital pharmacy.

Studies	Study type	Product	TAWF <sup>a</sup>	Preparations (n)	Impacts			
					Errors	Preparation	Validation	Costs
Reece [25]	Pre-post single center	BD, Cato <sup>®</sup>	G	Pre: 51,037 Post: 15,843	↑	↓	↓	↓
Davis [26]	Pre-post single center	Locally developed	–	Pre: 680,000 Post: 826,220	NI	NA	NA	↑
Bhakta [27]	Pre-post single center	OmniceII™, IV station onco™	G, R	Pre: 509 Post: 944	NI	↓	↓	↓
Roberts [28]	Pre-post single center	BD, Pyxis IV prep™	G	Pre: 643 Post: 748	NI	↓	↓	NA
Lin [29]	Pre-post single center	Baxter, dose edge™	–	Pre: 110,963 Post: 101,765	NI	NA	NA	↓
Wright [30]	Pre-post single center	Baxter, dose edge™	–	Pre: 1530 Post: 85,869	↑	NA	NA	NA
Achey [31]	Pre-post single center	Grifols, MedKeeper, Pharmacykeeper <sup>®</sup>	–	Pre: 680,000 Post: 826,220	NI	↑ <sup>b</sup>	↑ <sup>b</sup>	NA
Eckel [32]	Pre-post multi center	Baxter, dose edge™	–	Pre: 244,273 Post: 96,865	↑	↓	↓	↓
Bucci [33]	Pre-post single center	BD, Pyxis, IV Prep <sup>®</sup>	G	Pre: 116,686 Post: 5,195	↑	↑	↓	NA
Marzal-Alfaro [34]	Pre-post single center	Grifols, Phocus Rx <sup>®</sup>	–	Pre: 51,589 Post: 54,430	NI	NA	NA	↓

G, use of gravimetric system; NA, not applicable; NI, not interpretable; R, use of a robot; TAWF, technology-assisted workflow systems; ↓, decrease; ↑, increase; 0, no significant change. <sup>a</sup>All TAWFs included software to help with preparation, use of a barcode reader and taking photos or videos. <sup>b</sup>Study combining preparation and validation time in the same parameter.

study had documented an increase in preparation time and in validation time of 13.2% [33]. With the use of TAWF systems, the mean preparation time per dose varied (i.e., 51 s [33] and 180 s [36]). The data presented was difficult to interpret given the variability in what was being measured (i.e., TAWF start-up time, preparation time per dose, validation time per dose, combined time, type of preparation). The measurement of the workload involving a TAWF system must take into account the start-up time required for the system implementation (e.g., installation of tubing, calibration, preparations, other requirements related to the operation of the TAWF). The higher the number of preparations, the less the weight of these steps in the calculation of the average preparation time will be. There should be a minimum threshold for the number of preparations for a TAWF to be considered cost-effective in a hospital. This threshold is currently unknown. With the current studies available, it is not possible to rule on the effect of TAWF in pharmacies on the working time.

### Impact of TAWF on costs

Six studies assessed the impact of a TAWF on costs [27–29, 31, 34, 37]. All the studies concluded on a reduction in

costs, linked either to a reduction in production costs (i.e., reduced preparation or validation time) or to a reduction in costs associated with preparation errors. Calculated savings were also difficult to interpret given the data presented. In Batson's systematic review, the compounding technologies were associated with reductions in annual costs compared with manual compounding [36].

### Staff satisfaction

Three studies assessed the satisfaction of pharmacy staff exposed to the use of a TAWF [28, 33, 34]. In general, respondents perceive TAWFs to be more secure given the increased traceability of the process and the technologies used to facilitate error detection. Regarding the speed of the systems used in Bucci et al. [33] study, staff members agreed that the volumetric method was faster than the gravimetric TAWF method. In Marzal-Alfaro 2020 [34], all employees would like the speed of compounding to be increased. This perception is not, however, a reflection of reality since four studies have shown a reduction in preparation time and five a reduction in validation time.

## Future research

It is often difficult and costly to properly assess a change in practice. A well-designed study should include a starting hypothesis, a calculation of an adequate sample size to answer the main outcome being assessed. In most of the studies consulted, it is rather a convenience sample that does not provide a robust answer to the questions asked. Hospitals should be encouraged to come together and come up with a solid study design for evaluating the integration of a new technology before generalizing it within a regulatory authority. Such evidence should also be published independently. The evaluation of the impact on productivity, risks, quality and costs remains relevant, but we must ensure to measure the effect of technology on all the tasks entrusted and not in isolation.

## Strengths

This study targeted different TAWFs concerning all types of preparations (IV and oral, hazardous and non-hazardous) with a focus on gravimetric systems. It highlighted the components of a TAWF and the main outcomes assessed. It also makes it possible to identify the limits of the studies and the improvements to be made to the estimates for the next studies. The data presented might also help pharmacists identify their local assessment criteria for a possible acquisition of a TAWF system.

## Limitations

The search strategy was limited to the period 2015–2021 due to the rapid evolution of technologies. Previous publications were not considered to avoid previous software versions or technologies. It should also be noted that only studies written in English were included in this review. A broader search strategy would provide a broader perspective on TAWF and their evolution. Six of the 17 studies selected were descriptive and did not assess the impact of implementing TAWFs. Studies that assessed the impact of TAWF used a pre/post design and were neither controlled nor randomized. In addition, there was positive publication bias in favor of technologies (e.g., negative studies are not published). TAWF change over time and the results should of these studies should be interpreted with caution considering the evaluated version of a given TAWF. It should be noted that the different studies included often had a different definition of medication preparation (e.g., Achey's study was the only one to consider loading

up the medication on a cart as part of the medication preparation process [31]). This had an impact on the comparison and analysis of the temporal impact of TAWFs. There is a learning curve when implementing a new system, so the duration of the post implementation period must be considered. Most studies did not have a comparable duration of study for the pre and the post phase. Finally, several of the studies published included (8/17) a declaration of conflicts of interest involving TAWF manufacturers.

## Conclusions

Given the heterogeneity of the data available, the use of TAWF was associated with an increased ability to detect preparation errors, a reduction in preparation time and costs, and increased satisfaction of pharmacy technicians and pharmacists. However, better quality studies are needed to confirm the positive impacts studied.

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**Competing interests:** Authors state no conflict of interest.

**Informed consent:** Informed consent was not needed for this literature review.

**Ethical approval:** The conducted research is not related to either human or animal use.

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- Supplementary Material:** The online version of this article offers supplementary material (<https://doi.org/10.1515/pthp-2021-0009>).