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SIMPLIFIED WORKFLOW

Ready-to-Use (RTU) parenteral packaging components & kits

Operational and development benefits

DWK LIFE SCIENCES
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When DWK Life Sciences first introduced a Ready-to-Use (RTU) primary packaging system for parenteral drug content, we committed to a single goal: to simplify sourcing and derisk drug development, including clinical packaging and small batch commercial packaging with a container closure system conforming to the most demanding USP / EP / JP standards for RTU pharmaceutical injectable applications.

The offering was thoughtfully designed with clinical insights collected from Drug Developers, Compounding Agencies, and Contract Service Providers seeking opportunities to single-source certified RTU components that could directly enter the aseptic fill area, provided in inventory-matched quantities, accompanied by lot traceability documentation and available off-the-shelf for immediate consumption.

The product has evolved since introducing **WHEATON® COMPLETEPAK** with vials packaged in glass-to-glass configurations to Stevanato Group **EZ-fill®** with vials packaged in non-glass-to-glass nest & tub and partitioned tray configurations. This allows DWK to offer the broadest range of RTU container closure system solutions that meet industry standards and are most widely adopted and compatible with global fill operations.

This whitepaper overviews injectable drug manufacturing using RTU and traditional inline processing, the role of RTU components, and secondary packaging considerations, and highlights benefits associated with workflow and total cost of ownership (TCO).

Parenteral drug manufacturing: a new paradigm

Parenteral drug products are manufactured to **strict sterility guidelines** using well-documented and validated aseptic processes and quality controls executed by highly trained personnel. Approaches for large batch, high throughput injectable drug production are often associated with traditional inline cleaning and sterilization of packaging components requiring complex facility design and site management, capital equipment investment, incoming raw material controls and process validations, and specialized operators[1].

The recent growth of precision, complex, and high-value biologics drug development and manufacturing, the adoption of small batch RABS/Isolator lines, and advancements in robotic filling equipment have presented a new fill & finish workflow paradigm. These factors drive interest in replacing in-house washing, depyrogenation, and sterilization with ready-to-use (RTU) container closure systems (CCS)[2]. The range of RTU solutions requires a consultative approach between the packaging supplier, drug developer, and manufacturer to ensure operational fit and achievement of their workflow objectives.

1 > Cynthia A. Challener, Prepping Fill/Finish Systems to Ensure Quality Output, BioPharm International, Vol. 33, Issue 12, Pg. 13-20, Dec. 2020
2 > Jennifer Markarian, Filling Small Batches, Pharmaceutical Technology, Vol. 2021 eBook, Issue 2, Pg. 14-17

In-line processing challenge

Regulatory agencies expect drug manufacturers to demonstrate compliance with global sterile manufacturing controls and their ability to deliver injectable drug products to the medical marketplace meeting patient safety, drug efficacy, and shelf-life claims. Pharma company developers and packagers that choose to process primary packaging components in-house face challenges associated with sterility assurance and burden significant upfront and operational costs.

Challenges exist with developing and producing highly complex biologics and other specialty and small-batch drugs when attempting to accelerate development timelines, improve workflows and ensure clinical and commercial drug products are particulate clean, non-pyrogenic, and sterile[3].

Costs associated with inhouse and inline component processing include substantial capital investments into processing equipment, physical plant, cleanroom space, expenses related to processing equipment operation, routine maintenance, quality control (personnel and environmental testing), and component processing personnel. Implementing and maintaining such an inline processing program can drive a higher total cost of ownership (TCO), increase compliance risks, impact timelines, and reduce workflow, leaving drug manufacturers with less time and resources that otherwise could be used for other value-added development, clinical, and commercial operations.

3 > Kristin Brooks, Pharmaceutical Packaging Market Report Digital Edition Contract Pharma, June 2019

RTU adoption & cost benefits

RTU CCS used for the packaging of injectable drug products typically consists of serum vials, stoppers, and aluminum seals or pre-assembled snap caps having been pre-processed remotely, resulting in the delivery of a completely sterile packaging system. Thus, RTU components are prepared for direct entry into the aseptic core and are accompanied by lot-controlled documentation certifying processing methods, critical thresholds, and reference to associated international standards for aseptic pharmaceutical packaging.

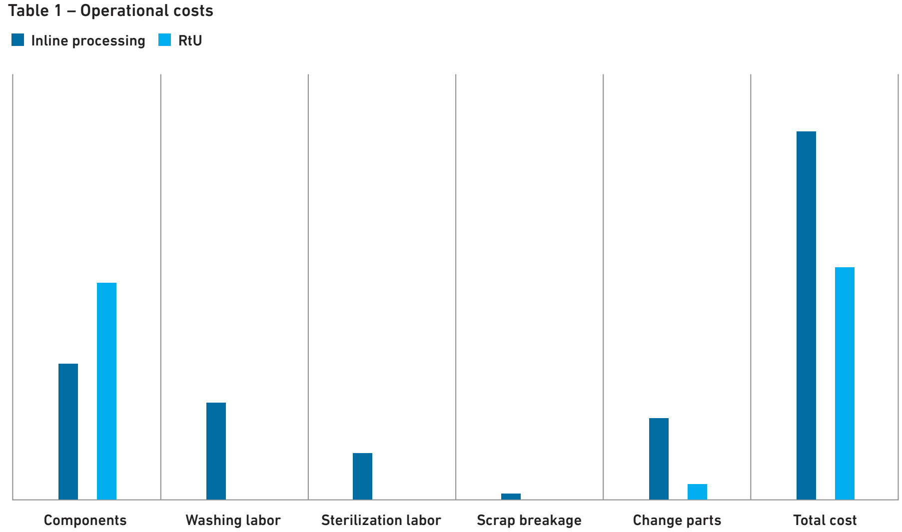
In this way, pre-sterilized components supplied directly to the filling station offer a cost- and space-saving alternative to the operation of a washing and depyrogenation line and minimize time-consuming, risk-based, and costly upstream processing steps traditionally managed by drug developers and clinical stage and commercial stage fillers. Comparably, RTU negates the investment required for processing equipment, equipment processing space, and procedural and operational personnel. This ultimately drives many drug manufacturers to rely on RTU CCS to reduce risk, lower total ownership costs, accelerate development timelines and improve workflows.

Most significant is the cost associated with the inline preparation of processed vials, which can be compared to aseptic drug filling using RTU vials configured in modules, nest & tubs, and partitioned trays. In our model, we assume the processing of approximately 250,000 vials per year[4]. The comparative analysis includes operational costs associated with the use of unprocessed vials undergoing in-house/inline processing versus RTU components. This analysis provides labor and utility costs for cleaning and sterilization, typical scrap rates, and processing equipment change parts. (Table 1).

Through RTU vials, the cost of operations alone is estimated at approximately 37% savings (year 1). When capital equipment is added to this analysis, drug developers and manufacturers who purchase RTU components as an alternative to installing and operating inline processing equipment can save an estimated 80% of total costs in year 1. This analysis is thought to provide a conservative estimation as it does not include costs associated with inline equipment commissioning, preventative maintenance, QC testing, ongoing validations, nor the lost opportunity cost associated with the space used for inline processing equipment.

4 > Prince Sterilization Services, LLC, RTU Contract Processing Workflow 2021

Table 1 – Operational costs



RTU beyond cost benefits

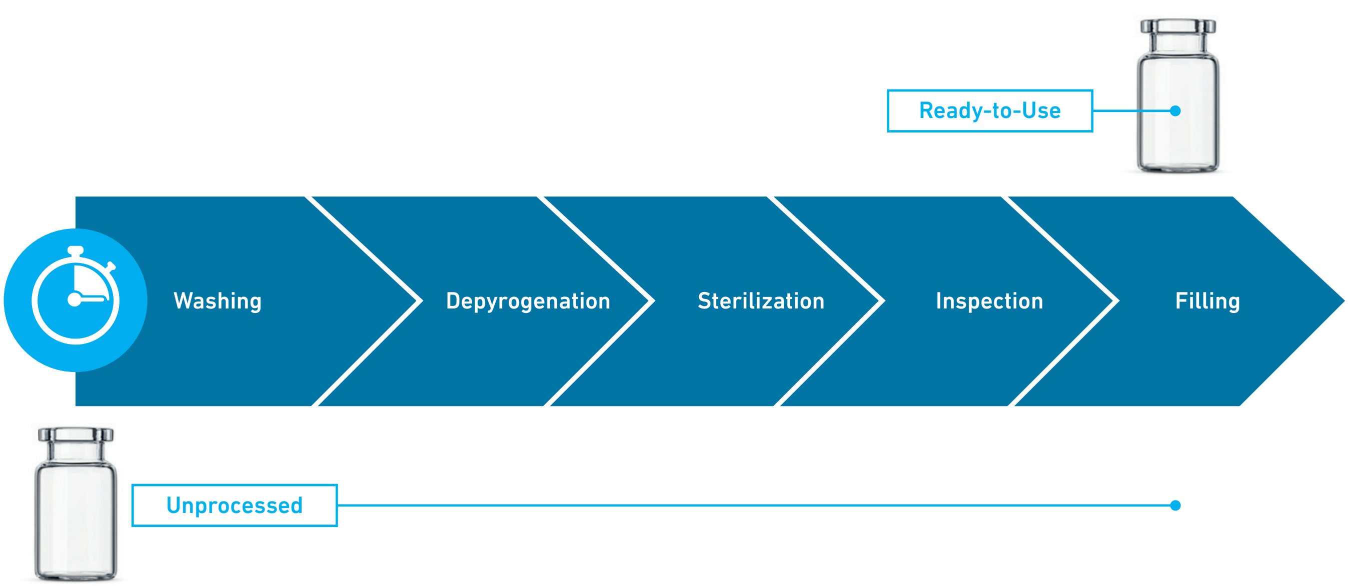
Beyond cost, many drug manufacturers seek to reduce risks associated with the implementation of inline process controls and the execution of validations required by international regulatory bodies to demonstrate conformance to sterility standards. In addition, many drug manufacturers are adopting Isolators and Restricted Access Barrier Systems (RABS), supporting small-batch clinical and commercial drug manufacturing increasingly reliant upon RTU components and RTU secondary packaging such as nest & tub and partitioned tray configurations. Many developers and packagers have limited component processing experience and use RTU components to reduce compliance risk and eliminate processing effort.

For developers, RTU products allow them to simultaneously identify promising injectable proteins and targets using primary packaging components and secondary packaging most likely to be used in subsequent development and commercial stages - ultimately accelerating and derisking the development cycle and technology transfer.

The need to streamline downtime between batch runs exists for packagers supporting small batch fills reliant upon a range of vial capacities. When packaged in industry standard secondary packaging formats such as nest & tub and partitioned trays, RTU components facilitate rapid changeovers to improve workflows.

DWK Life Sciences RTU components directly enter the filling environment to streamline workflow and negate the need for time-consuming, risk-based, and costly in-house/inline processing steps for both developers and packagers; this results in developers and packagers having more time for primary development and manufacturing efforts and relying on DWK to meet their RTU primary packaging needs.[5]

5 > Marga Vines, Parenteral Manufacturing Market Trends, Contract Pharma Digital Edition March 2015



Delivering to industry standards

At DWK, we recognize the dynamic nature of today's drug development and packaging markets and their need to meet validated aseptic operational requirements. Our RTU portfolio is designed to maximize the selection of certified choices, assuring workflow efficiencies and alignment to development, clinical, and commercial packaging processes.

DWK Life Sciences manufactures and distributes RTU CCS designed to industry standards for parenteral packaging components. RTU components conform to standards for Particulate Matter in Injections (USP <788>/EP 2.9.19), Bacterial Endotoxins Test (USP <85>/EP 2.6.1), and sterility standards inclusive of Sterility Assurance Level (SAL) ≤10-6 and ethylene oxide Residuals (EMA/CHMP/CVMP/QWP/85037 4/2015).

Our RTU vials also meet machinability standards and are available in three configurations: non-glass-to-glass nested, non-glass-to-glass partitioned trays, and non-partitioned tray packs. All RTU glass vials meet the pharmaceutical-use glass containers (USP <660>/EP 3.2.1) and ship with a Certificate of Analysis or Certificate of Conformity detailing lot control, processing standards, and shelf life.

DWK RTU portfolio – vials

RTU nested & partitioned

DWK offers Stevanato Group EZ-fill® vial systems consisting of ISO standard glass vials having been cleanroom packed in industry standard nested tubs and trays partitioned with non-glass-to-glass (NGtG) contact and affixed with floating Tyvek® inlay and Tyvek® lid cover, then placed inside double Tyvek® bags for EtO sterilization

Stevanato Group EZ-fill®is the market reference platform for pre-sterilized vials, which helps to ensure flexible and streamlined processability. The secondary packaging configurations allow CRO, CDMO, CMO, and Biopharma companies to maximize flexibility in aseptic filling using a common vial platform that can be integrated seamlessly across a broad range of parenteral filling capacities and formats. EZ-fill® significantly improves drug packaging quality, reduces Total Cost of Ownership (TCO), and accelerates development and time to market.

Stevanato Group EZ-fill® vials / Courtesy of Stevanato Group

RTU non-partitioned

DWK non-partitioned tray packs consist of RTU glass vials packed in polypropylene trays. These RTU vials meet the same standard for particulates, endotoxins, and sterility and are cleanroom-processed and packaged. However, vials are packed in polypropylene trays having a fold-down transition flap, then inside double layers of permeable and non-permeable vacuum-sealed bags instead of partition packaging, allowing streamlined entry into aseptic cores using conveyance feed systems.

While offered in validated configurations, non-partitioned vials can be custom-prepared to specific cleanliness and sterility levels and to secondary packaging requirements best aligned to operational workflows. This provides drug developers and manufacturers additional flexibility in aligning operating and process controls to RTU packaging configurations. The elimination of rigid secondary packaging makes RTU non-partitioned vials ideally suited for bench and convenience-fed filling processes.

Conversely, RTU vials configured in partitioned nest & tub and partitioned trays eliminate glass-to-glass contact during transport and filling, providing added cosmetic and safety benefits by eliminating potential glass surface blemishing or fracture sources. Furthermore, the secondary packaging associated with nest & tubs and partitioned trays conforms to industry dimensional standards, making it a first choice for small-batch operations using robotic, combi, and flex fill systems requiring change-over flexibility.

RTU Non-partitioned vials

DWK RTU portfolio – sealing components & kits

RTU stoppers & aluminum seals

Stoppers and aluminum seals undergo similar validated RTU processing followed by cleanroom secondary packaging in two inner layers of permeable and one or two outer layers of non-permeable vacuum-sealed bags. Like their RTU vial counterparts, RTU stoppers and seals can enter the fill environment directly. Stoppers additionally meet the Elastomeric closures for injection standards (USP <381>/EP 3.2.9) and ship with a Certificate of Analysis detailing lot control, processing standards, and shelf life.

RTU pre-assembled snap caps

An alternative to aluminum seals and stoppers is a pre-assembled RTU snap cap. The RayDyLyo® snap cap is composed of a pre-assembled RTU stopper inside a plastic RTU Snap-On cap for a single-step closure process. RayDyLyo® snap caps are produced by pre-assembling customer-preferred ISO standard serum or lyophilization stoppers into the flip cap, then double-bagged or nested and bagged in a cleanroom, gamma sterilized and shipped with a third-party certificate of conformity (COC). RTU snap caps further improve workflows by streamlining the traditional two-step capping process to an efficient single-capping step that reduces the risk of particulate contamination possible with aluminum seals.

RayDyLyo® RTU Snap Caps

RTU kits

Quantity-matched RTU vials, stoppers, and seals are available in convenient WHEATON® COMPLETEPAK kits. WHEATON® COMPLETEPAK is an off-the-shelf packaging solution that simplifies your supply chain through the single sourcing of a validated container closure system.

RTU Aluminum Seals & Stoppers and WHEATON® COMPLETEPAK RTU Kits

DWK RTU consultation

The injectable drug industry is preparing for continued migration from risk-based, time-consuming, capital and operational-intensive, in-house/inline processing to the streamlined and flexible benefits offered through RTU primary packaging. Developers, clinical packagers, and commercial packagers are overcoming challenges by using industry standard RTU vials, stoppers, seals, snap caps and associated TCO and regulatory compliance benefits.

The manufacture of highly complex biologics, specialty, and small-batch drugs, having strict sterility and regulatory requirements, along with advances in flex-filling equipment, and adoption of Isolators/RABs is driving interest in injectable RTU container closure systems. The range of RTU configurations offered by DWK meets specific development and operational requirements, benefiting both hand and automated fill processes, and compatibility with RABs/Isolation systems.

DWK employs a consultative approach to properly support drug developers and packagers to simplify RTU selection most suitable for their drug product, workflow, and operation. Customized quantities, formats, and packing configurations are available to simplify your workflow and meet specific operational and run rate needs.

Source: https://www.dwk.com/na/primary-packaging/ready-to-use-and-custom-solutions

Excellence in your hands

Contact us at **DWK.com**

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