



SECTOR REPORT

PRODUCING PHARMACEUTICAL LEAFLETS

Exploring market trends and challenges and the subsequent opportunities with digital print

Canon

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INTRODUCTION

Pharmaceutical leaflet or printing is a specialism for good reason. While pharmaceutical products bring enormous health – even life-saving – benefits to millions, the same products, used incorrectly, can be deadly. Including clear, accurate and understandable information in pharmaceutical leaflets is vital to ensure that products are used as the manufacturers intended, so it is no surprise that the regulations surrounding their production, like the regulations surrounding the pharmaceutical industry more broadly, are rigorously precise, complex and ever evolving. From the size and clarity of the typeface, to the colour of the ink, the layout, and the precise written content that needs to be included.

Then there are the extra complexities of multiple language requirements for different markets, faster and more frequent changes to regulations, and regulations that vary by territory as well. In addition, pharmaceutical printers have to print to very thin paper, which can be as light as 40gsm or even lighter, as the amount – and sometimes even lighter – as the amount of information that has to fit into a very small package typically means that the leaflet needs to be folded multiple times.

The pharmaceutical market is expanding, with more and more drugs entering the market and a growing number of product variants produced in much smaller quantities for much faster distribution. All in all, it's clear that remaining compliant with regulations and fulfilling responsibilities to drug manufacturers and, most importantly, to patients is a complex task that is growing more challenging by the year. And it's not just drug manufacturers; it's personal care and cosmetics brands too.

While traditional offset printing processes will continue to have a significant role to play in the production of pharmaceutical leaflets and packaging, the increasing demand for much shorter runs and

much faster turnaround times is proving impossible to meet with offset solutions alone, and digital alternatives are increasingly being adopted. But for such a specialist sector, with so much at stake, digital printing solutions and a digital print partner need to be chosen with extreme care.

At Canon, we understand the unique challenges this sector faces and we have the technology and a proven track record in partnering with pharmaceutical print specialists to provide robust, adaptable and reliable digital print solutions to meet the challenges of today and to prepare for the future.

Pharmaceutical print specialists have a vital role to play in the evolving industry. In this white paper we outline the state of the pharmaceutical industry landscape – from the specific challenges posed by the COVID-19 pandemic, to the broader state of the industry. We look at the main challenges and pain points faced by pharmaceutical printers and how the right digital print solution, supported by the right digital print solutions partner, is vital to help navigate the requirements of this rapidly changing sector.



COVID-19 AND THE PHARMACEUTICAL LANDSCAPE

The COVID-19 pandemic has caused enormous supply chain and production challenges as well as commandeering a huge amount of industry R&D resource and capacity in recent months. But as important as it is, the COVID-19 pandemic is just part of a complex modern pharmaceutical landscape in which the essential business of developing, manufacturing, packaging and supplying life-saving and life-enhancing medicines of all kinds carries on.

The global pharmaceutical market is worth an estimated \$1 trillion worldwide¹ in 2020 and it's growing rapidly. While the US has both the biggest market share and forecast growth, the European market is the second largest globally and is also growing fast.

A recent Deloitte survey also found that 'establishing a presence in global markets' ranked the highest of today's priorities, but slipped to second place when pharmaceutical companies thought ahead to the next five years. With a heady mix of EU and national-level regulations to navigate - and multiple languages in which to provide information - pharmaceutical leaflet production in Europe is complex, and extra challenges are presenting themselves all the time.

For example, as of 1 January 2021, EU pharmaceutical law applies to and in the UK in respect of Northern Ireland only.



Speed to market:

COVID-19 has been a generation-defining event that has had a significant global impact on all industries, and the development of vaccines and effective medical treatments has inevitably meant that the impact of the pharmaceutical industry has been bigger than ever. But one particularly noteworthy trend in recent years, not just brought on by the pandemic, has been the adoption of just-in-time manufacturing. As in many other industries, suppliers and retailers are increasingly reluctant to hold large amounts of stock, not to mention the fact that many pharmaceutical products have a strictly limited shelf life before their use becomes unsafe.



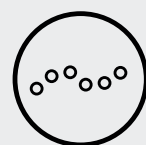
Supply chain shortages:

The pandemic and associated lockdowns around the world have also played havoc with manufacturing supply chains, leading to shortages of raw product ingredients and potentially to higher prices for consumers and for healthcare providers in the long run.



Distribution & delivery:

On a practical level, the logistics involved in manufacturing and distributing COVID-19 vaccines pose enormous challenges.



Flexibility & customisation:

Short-run drug variants are also becoming more and more common and there's one other significant trend that's pushing pharmaceutical print and packaging towards a just-in-time model: late-stage customisation. A tool to safeguard against counterfeiting, late-stage customisation involves product serialisation, which forms part of a full audit trail and has been mandatory in the EU since February 2019 under the Falsified Medicines Directive, 2011/62/EU.²



Recouping R&D costs:

A recent Deloitte survey found that 63% of pharmaceutical companies surveyed saw R&D as their highest priority over the next five years. That's up from 43% this year.³ Enormous costs have been sunk into vaccines and treatment R&D for COVID-19, and these costs will be difficult to recoup.

Add these challenges all together and the need for pharmaceutical printers to be adaptable and flexible has never been more apparent especially as, for a variety of reasons that we will examine in more detail later, traditional offset print production methods are finding it more challenging when it comes to delivering on these modern industry requirements.

¹<https://www.statista.com/topics/1764/global-pharmaceutical-industry/>

²<https://packagingeurope.com/late-stage-customisation-challenge-pharmaceutical-logistics/>

³<https://www2.deloitte.com/xe/en/insights/industry/life-sciences/pharmaceutical-industry-trends.html>

STAKEHOLDER TRENDS IN THE PHARMACEUTICAL SUPPLY CHAIN

Why the industry centres around the patient

In this section, we examine some of the trends surrounding key stakeholders in the pharmaceutical supply chain, beginning with the patient, the stakeholder the whole industry centres around – and with very good reason.

⁴<https://www.hcpc-europe.org/wp-content/uploads/2017/12/HCPC-Europe-White-Paper-Patient-Friendly-Pharmaceutical-Pack-Design.pdf>
⁵<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5998458/>

The Retailer/ Pharmacy



Digital trends, which are allowing pharmaceutical manufacturers direct contact with consumers through social media and customised healthcare portals, pose a challenge to traditional established distribution channels, such as pharmacies and other pharmaceutical retailers. There are also a growing number of online specialist providers, and brand owners are also developing direct-to-consumer sales and advertising channels.⁵

Healthcare professionals remain important gatekeepers to an extent, but when more and more drugs are supplied without any personal interaction with a doctor or pharmacist, the clarity and accuracy of both the packaging and the inserts take on an even higher level of importance.

The Pharmaceutical Manufacturer



Many of the trends and challenges facing pharmaceutical manufacturers have been mentioned already in the previous sections. These include compliance with a growing and ever-changing regulatory framework, flexibility and a move towards just-in-time manufacturing, and having direct lines of communication to patients, something which is both a tremendous opportunity and a significant challenge.

The patient



In the previous section, we referred to a survey recently conducted for a Deloitte Insight report, published in August 2020. That same survey asked the question: What top five issues will have the greatest impact on your company in the coming year? Of the pharmaceutical company respondents, 80% included “changes in consumer attitudes and behaviour” in their “top five” – comfortably more than the 70% who opted for the second-placed “cyber security threats” or the 68% who selected “advances in technology”. For all the stakeholders involved in the industry, it is the patient who the product is created for, and it has to work for them.

According to the Healthcare Compliance Packaging Council (HCPC), patient compliance is one of the most pressing issues facing the industry today.⁴ Studies have shown that, while almost all patients begin taking their medicines as prescribed,

compliance rates fall off very quickly indeed – most steeply between months one and four. After 18 months, compliance rates can fall to as low as 30% even for those who are taking medication for very serious, even life-threatening conditions. For milder ailments, the compliance rates typically fall further still.

After all the millions spent developing drugs, getting the necessary regulatory approvals and bringing them to market, they are only effective if taken correctly, consumed when they should be and in the correct doses.

User-friendly packaging and inserts, in terms of clear instructions for use, have a crucial role to play in this adherence. Ingredients, possible side effects, dosage, how to store – all must be clearly displayed for ease of reading before any medication is taken.

Printing & Converting

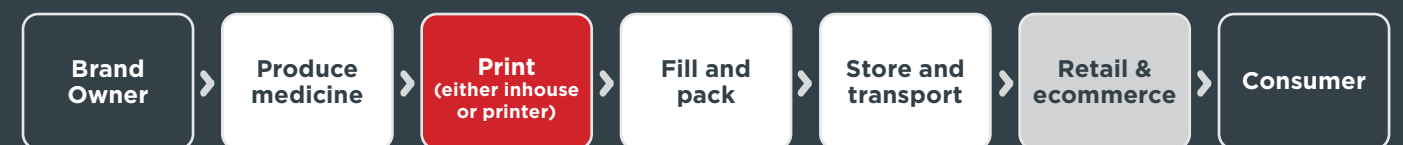


Pharmaceutical packaging and insert production are being affected by all the trends and challenges we’ve examined so far. Print and converting companies involved in this specialism therefore need to weigh up their obligations to the brand owners and manufacturers whose products they are dealing with, to the pharmacists and other retailers who sell to the patient and, as we come back full circle to where we began, to the patients themselves.

Developing more flexibility is key to being able to deliver shorter runs and greater job variability with faster lead times. On the following pages, read about some pharmaceutical printers who have done just that.



Supply Chain Dynamics



THE VIEWS OF PHARMACEUTICAL LEAFLET MANUFACTURERS

Eureco-Pharma BV reaps rewards after bringing its digital leaflet printing in-house

Objective

To slash lead times, add flexibility and reduce waste by gaining control of the printing process of Dutch language leaflets for imported medicines.

Approach

After consulting with a number of equipment manufacturers, including Canon, Eureco-Pharma installed a varioPRINT 6160 Ultra line along with a Horizon cutting and folding machine.

Benefits

- Lead times cut from 4 weeks to just 24 hours.
- Significantly reduced wastage, helping to save thousands of euros per year.
- Automated the folding and counting process, saving manpower.

“Our previous printing model restricted our overall flexibility, which was a significant disadvantage as medicine import and sales is a highly volatile market. Patient information leaflets are increasingly subject to modification due to newly discovered side-effects and various other information changes. This would mean existing patient information leaflets would have to be destroyed.”

“From my initial conversation with Canon, I had more of an idea of the benefits of investing in a digital printing solution. I looked at the associated costs of the new equipment and the potential savings. It became clear – once the capital cost of the new equipment had been taken into account – that the cost of printing the leaflets in-house would be approximately the same as outsourcing. However, we could see that the improvement in flexibility and autonomy was potentially enormous. I would estimate we save somewhere between five and ten thousand euros just from the reduction in waste. We also make additional profit from having shorter lead times, although it is harder to quantify these figures.”

Jan de Kreijl,
Managing Director and Owner, Eureco-Pharma BV

Challenges

- Outsourced leaflet production meant delays of up to a month and large amounts of waste.
- Overreliance on external supplier meant very limited flexibility.
- Manual process of folding and counting leaflets was labour-intensive and time-consuming.

Pharmaceutical inserts manufacturer improves supply chain efficiencies

Objective

A long-standing manufacturer of pharmaceutical packaging developed an innovative supply chain solution to achieve just-in-time delivery, while including quality control within the production process. Clients benefit from shorter lead times, complete data integrity, reduced stock and freed up capital.

Challenges

- Comply with good manufacturing practice (GMP) and regulations within the pharmaceutical sector
- Ensure efficient and lean, end-to-end print production to meet quality requirements on lightweight paper and streamline cutting and folding ready for immediate insertion
- Integrate quality inspection to achieve just-in-time delivery capability

Digital production strategy helps Rattpack rise to pharmaceutical industry demands

Objective

To have the flexibility to produce shorter runs of sensitive, black & white, patient instruction leaflets, as well as enabling high-quality printing on media as light as 45gsm for pharmaceutical pharmaceutical packaging inserts.

Approach

Rattpack Print and Packaging has been evolving its black & white digital print line-up over the last ten years, with the aim of increasing flexibility to manage shorter runs and print on lighter substrates in line with market demand.

Challenges

- To meet growing demand for shorter run lengths and quicker turnaround times.
- To print reliably on delicate lightweight paper at high volumes, with perfect front-to-back registration.
- To meet the security standards of the highly regulated pharmaceutical industry.

Benefits

- Increased productivity and reliability of black & white production.
- Flexibility to accommodate urgent jobs and offer shorter turnaround times.
- High-quality printing on challenging substrates as light as 45gsm, meeting stringent industry regulations.

“Legislation on the readability of packaging inserts, for example font sizes, is constantly changing; the text needs to be as clear and decipherable as possible for the pharmaceutical user, without any mistakes. This frequently changing legislation, and the increase in pharma products targeting specific audiences, for example, medication produced only for women, has substantially impacted production run lengths.”

“With digital print technology from Canon, we have been able to reduce print run lengths from 50,000 to under 10,000 on average, which has significant financial benefits to our business. We can produce pharmaceutical leaflets economically thanks to digital print and don’t have wasted stock if, for example, regulations change. Now we only print exactly what’s required by our customers.”

Martin Schmutterer,
Business Development Manager, Rattpack

COMMON PAIN POINTS IN PHARMACEUTICAL LEAFLET PRODUCTION

In this section we elaborate in more detail on some of the major pain points facing pharmaceutical leaflet producers.

Out-of-date content

Whether because of a change in regulations or a change to the product itself or how it is to be administered, printed content can fall out of date rapidly and need to be quickly replaced. The key here is investing in the flexibility to turn such jobs around swiftly.

Increasing variants

Drug variants for specific purposes are increasingly common in the industry. And variants, no matter how subtle the differences, require corresponding changes to be made to the packaging and inserts that accompany them.

Just-in-time delivery

It is far from unique to the pharmaceutical industry, but it is an increasingly recognisable feature of it. Complex supply chains, frequent regulatory changes and a reluctance on the part of suppliers to hold large quantities of stock all contribute to a growing need for on-demand production.

Lighter papers

The thin papers required for pharmaceutical insert printing pose a range of extra challenges – from the need to ensure consistently high quality, with pinpoint registration of small fonts, to the specialist paper-handling systems a lighter substrate requires.

Legacy equipment

As the level of quality and accuracy demanded on pharmaceutical leaflets, and the speed at which they are required, continues to increase, trying to ensure these standards are met on ageing, analogue equipment can be a huge challenge.

Shorter time to market

Where a delivery in a matter of weeks was once the norm, it's now expected in days. And this is a trend that is only going to continue.

Compliance and quality control

The flexibility to regularly update content to meet new regulations, the maintenance of good manufacturing practice (GMP) and meeting the constant need for real-time, quality-control inspection and late-stage product serialisation are ongoing challenges for all pharmaceutical printers

THE BENEFITS OF DIGITAL PRINT TO PHARMACEUTICAL LEAFLET PRODUCTION

Meeting the challenges of shortening medical product lifecycles, medical trials, medicines for rare diseases and small order batches, while still maintaining quality and zero-defect requirements, can be difficult. However, advances in workflow management and the ability of digital printing to produce the documents on demand with quick turnaround times can make even the shortest run lengths cost-effective.

With timely production scheduling, integrated quality and data integrity inspection, digital print can reduce product delivery time from weeks to days. An on-demand workflow capability, meanwhile, can ensure constant availability, while also substantially reducing capital tied up in stock.

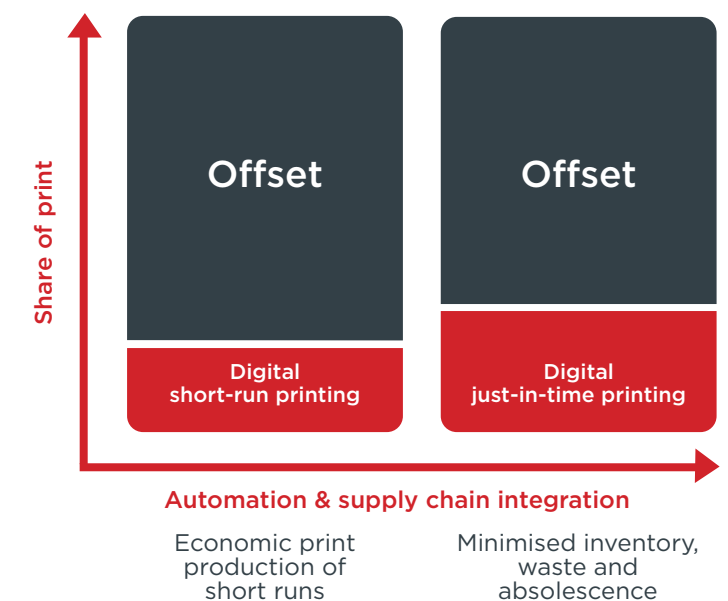
For a fully automated workflow solution for zero-defect production, combine a high-speed digital inkjet printer with camera integrity check systems and inline or nearline finishing equipment. The diversion of incorrect prints is then very straightforward, and a high degree of automation is possible, with no manual steps between printing, cutting, checking and diverting.

There are two established business models for digital print in the pharmaceutical industry. One of which we can refer to as **short-run printing**. This brings production efficiencies and faster time to market, but many processes in the wider workflow remain manual.

The second is a more highly automated proven business model for **just-in-time manufacturing**. This offers higher automation with a focus on quality control, finishing and dispatching. This can reduce delivery time from weeks to days, with the added confidence of guaranteeing zero defects due to removing manual production processes and thus, risk of error.

The benefits of digital

-  Just-in-time production for reduced inventory
-  Shorter turnaround times for faster delivery
-  Compliance with GMP
-  Flexibility of shorter runs and ability to change/update information easily
-  Quality control – every single sheet is validated against the Golden Master for zero defects and serialisation



USING DIGITAL TO STREAMLINE PRODUCTION

Offset vs digital

Offset production

For long runs of pharmaceutical leaflets, offset is obviously the best. However, as the nature of the offset process mainly involves manual steps, it's not always the most suitable when you need to provide quick turnarounds, minimum orders or update some of the content due to changing regulations, for example. The large volumes printed offset also have to be stored in warehouses and may have to be thrown away if the printed content becomes outdated, adding additional cost.

With offset production, the process starts by receiving the Golden Master and then making the plates and print ready for production.

Once produced, the print-outs are stacked and moved to the next stage of the production process, which involves checking the printed Golden Master manually for any errors. Once it has been checked, the print-outs are stacked again and moved to the next station. If any errors are detected, the incorrect sheets are diverted elsewhere and the operator has to restart the process from the beginning again. If no errors are found, then the leaflets go to the final stages of production, which include cutting the print leaflets into the final format, folding them to the appropriate size for the packaging and then packing them for delivery or shipment.

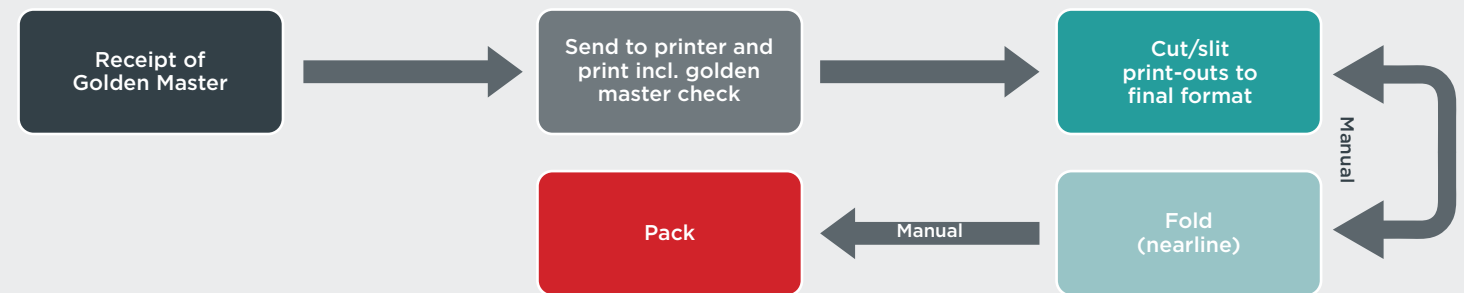
Digital production

The most advanced digital systems already print consistent and reliable quality at high speeds, whether for a print run of one or of thousands. Thanks to digital end-to-end workflow solutions, there are only five steps required in the production set-up in order to optimise process efficiencies.

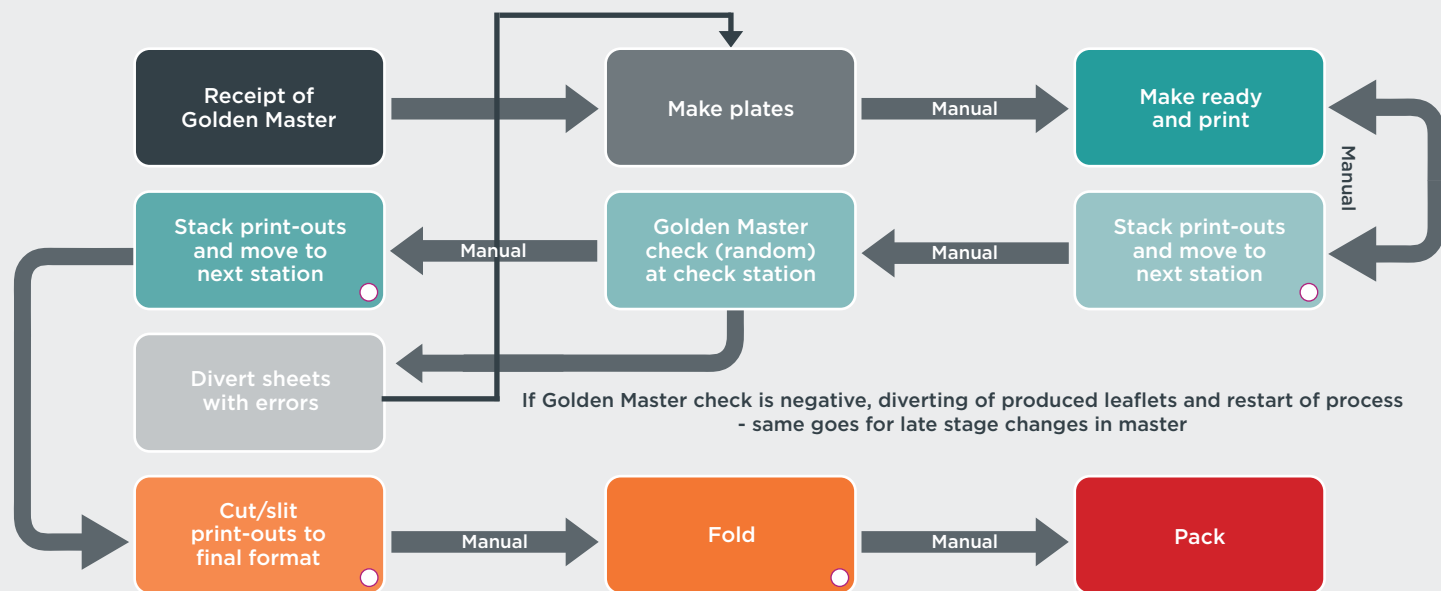
As with offset production, the digital equivalent begins with receiving the Golden Master file. The file is then sent directly to the printer and printed with automatic data inspection to ensure there are

no defects and that the quality is optimised and consistent. If any errors are found, the relevant sheets are automatically diverted. The sheets that are correctly printed are sent straight to the inline cutting machine, so that the only manual processes in the workflow involve moving the sheets to a nearline folder and then packing them for delivery. Thanks to the seamless integration with cutting and folding solutions, pharmaceutical leaflet manufacturers can maximise capacity and create production efficiencies and, as a result, increase profit.

Digital Workflow Pharma Insert Production

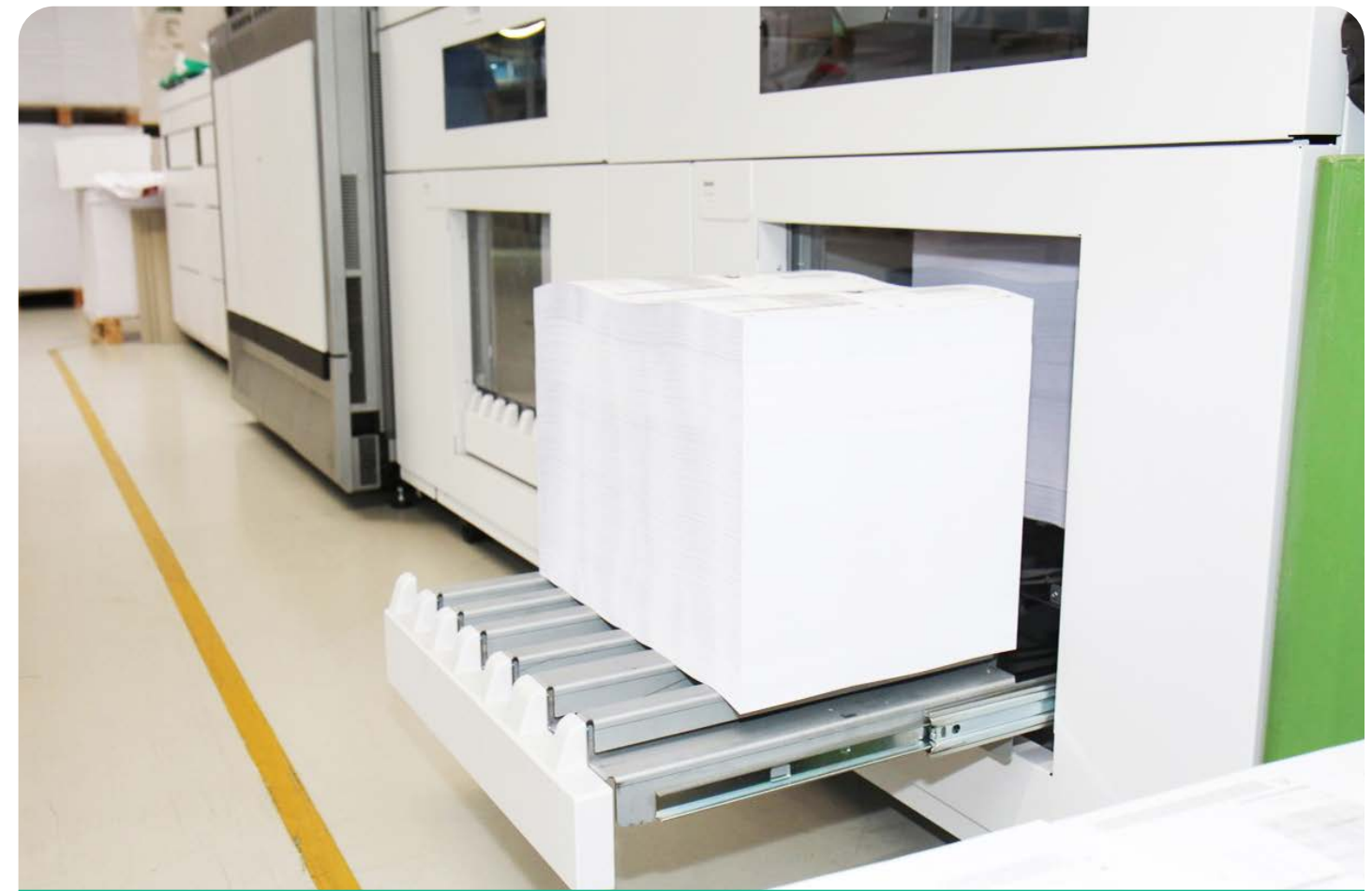


Offset Workflow Pharma Insert Production



- In total, nine process steps that are mainly manual tasks -

○ Indicates line clearance is necessary - removal of printing plates and print-outs plates from the whole production area



CONSIDERATIONS FOR PHARMACEUTICAL LEAFLET MANUFACTURERS

Adhering to standards like PS 9000:2016 – the standard developed by the Pharmaceutical Quality Group (PQG) to ensure pharma materials are safe and appropriate for the use they are intended – is critical, as is keeping pace with changing regulations. As regulations change within the industry, the requirements for all aspects of the supply chain may be affected.

Furthermore, aside from regulatory compliance, there is also the important matter of changes in customer expectations to consider.

As a pharmaceutical print provider today, the above trends give you opportunities to talk to your customers, the pharmaceutical brand owners, around their packaging requirements.

The following questions could be used as a guideline to support these discussions:

- Is there an increasing requirement for regional and multiple language versions?
- Are you challenged with frequent content changes, requiring documents to be updated more often?
- Have you found that font and font size legislation has been changed to ensure better legibility for the reader and had an impact on spacing and white space?
- Can you provide short runs and just-in-time printing linked to your customers' ERP systems?
- Are your customers considering customising promotional inserts?
- Have you seen growing demand for colour in packaging inserts?

How Canon can help you



At Canon, we work hard to understand the pharmaceutical sector and support customers to successfully service pharmaceutical brand owners. We can work with you to devise the best digital print solution for your needs – including the necessary finishing equipment and end-to-end workflow solutions. And we have a proven track record of doing this.

From understanding the needs of the lightest paper weights, inline folding equipment, workflow integration and real-time quality control, these complex solutions require a partner that plans, implements and provides ongoing support.

In addition to pharmaceutical leaflets, our solutions can help you to produce patient information leaflets (PILs) and flyers, miniature folded instruction leaflets offering guidance on how to use a medical device for example, or onserts such as a sticker label on a medication bottle, and much more. And thanks to our latest digital print technology, you can even add value to the patient's experience by being able to fully customise this information to their exact needs.

Canon ColorStream Series

A highly versatile inkjet web press that offers both outstanding quality and flexibility, the ColorStream Series is designed for the fast, reliable printing of pharmaceutical leaflets.



With its production speed of up to 160 metres per minute, the ColorStream inkjet press meets the required capacity to fulfil demand for tight production timelines. Powered by Canon's DigiDot and multilevel print technology, the ColorStream delivers high-precision print quality for font sizes as small as 1.5 point and fonts as detailed as Asian language characters, as well as ensuring offset-like quality and minimised shine-through on lightweight paper.

For added precision, the ColorStream can be integrated with a Hunkeler automatic camera control system to check each print, sheet by sheet, in real time to ensure it matches the PDF of the original job file. The quality control workflow between the printer's production management system, PRISMAproduction, and the web inspection solution meets zero-defect production standards, verifying that products are consistently produced according to rigorous quality standards.

Canon varioPRINT 6330 TITAN

Delivering monochrome excellence with truly impressive print quality, this pioneering high-volume unit blends innovation and robust engineering to deliver a solution that is second to none.



Not only is it the fastest printer in its segment, with speeds up to 328ipm, but it's also the hardest working, delivering up to 10 million images per month. The PRISMAsync server boosts efficiency, allowing up to eight hours of job scheduling. Vast paper capacity offers greater convenience, with four hours of unattended printing. Gemini simultaneous duplexing meanwhile ensures immaculate registration, while CopyPress and ScreenPoint technologies deliver a sharp, elegant, matte output.

Capable of printing on 45gsm stock and media up to 350x500mm, the Canon varioPRINT 6330 TITAN is an ideal production machine for black & white pharmaceutical leaflet production. And it's also the

greenest black & white production press on the market, emitting low ozone as well as producing minimal toner wastage and heat output.

The trends discussed in this sector report offer really exciting opportunities for pharmaceutical printers with digital end-to-end printing solutions. Our aim is to help you to maximise these possibilities with digital print and to grow your business.

Boost efficiency, gain faster time to market, cut waste and give yourself the flexibility to take advantage of every opportunity.

For more information on pharmaceutical insert solutions or on how we can help your business explore these growth opportunities, please feel free to get in touch with our team by visiting <https://www.canon-europe.com/business/solutions/pharmaceutical-insert-printing/>



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