



HASELMEIER™

A medmix Brand

Excellence through SIMPLICITY



PICCOJECT™ AUTOINJECTOR WHITEPAPER

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DRUG DELIVERY



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Introduction

Effective self-management of chronic diseases requires healthcare solutions that are easy and convenient for patients. This is one of the key drivers for our patient-focused development of innovative drug delivery solutions.

The simplicity of PiccoJect™, combined with our sustainability philosophy, is reflected in the entire supply chain to reduce waste and minimize environmental impacts. In addition to investing in green electricity and the use of sustainable feedstocks, we focus on the development of regional supply chains for the US and European markets. 'Excellence through simplicity' sums up our patient-centered and sustainable philosophy.

Chronic diseases are on the rise

The number of chronic diseases and conditions is increasing worldwide. Changing social behaviours and aging populations are the main causes of the steady spread of these common and costly diseases. Emerging economies, with their rapid population growth, are the most affected.

The World Health Organization (WHO) estimates that non-communicable chronic diseases will cause some 41 million deaths per year^[1] – equivalent to 71% of all deaths globally.^[2] The WHO also predicts that the prevalence of chronic diseases will reach 49% by the year 2030.^[3]

Rapid progress in the development of medicines, combined with more effective therapies, can help improve and prolong the lives of patients suffering from such diseases.

In 2021, a total of 50 new drugs were approved by the U.S. Food and Drug Administration (FDA): 36 as new molecular entities (NMEs) under new drug applications (NDAs), and 14 as new therapeutic biological products under biologics license applications (BLAs) – excluding FDA approvals for generics and biosimilars.^[4]

The terms 'biologics' and 'biosimilars' refer to various substances – including antibodies, therapeutic proteins, and peptides – that have a 'biological' origin.^{[4][5][6][7]}

Biologics are changing medical practice due to their distinct advantages in efficacy and selectivity, and their application will continue to expand. To date, the majority of growth has occurred in the therapeutic areas of cancer and cancer-related diseases, rare diseases, neurological disorders, and autoimmune diseases.^[7]

Haselmeier™
develops and delivers
best-in-class drug
delivery systems and
related services that
are simple in design
but highly reliable and
safe in function.





The increasing number of patients with chronic diseases is leading to a growing demand for convenient and safe drug delivery devices for self-treatment.

However, the specific physiochemical properties of biologics mean that delivering them as active agents into the body can be challenging. As a result, innovations in drug development today are not only limited to substances and therapies, but also to the patient-centered development of delivery devices. These systems play an increasingly important role in making administration easier, faster, and more efficient.

Self-administration – a key element in the effective treatment of chronic diseases

Self-administration has become increasingly important in this context. Set to surpass oral and other routes of administration, parenteral drugs are expected to see their market share grow from 52% (or \$604 billion) in 2019 to 55% (or \$1,206 billion) by 2026.^{[8][9][10]} This global growth is mainly driven by the growing importance of preventive medicine, the aging population, and the general shift towards home care.^{[11][12][13]}

The vast majority of biologics are currently administered intravenously (IV) and subcutaneously. This applies both to biologics that are already approved and marketed, and to biologics in development. However, subcutaneous self-administration is increasing in prevalence, and represents a valuable alternative to intravenous administration. With a 41% share, subcutaneous bolus injection is already the preferred route of administration for biologics in the development pipeline.^{[6][7][14][15]}

This growth is mainly due to the safety and effectiveness of subcutaneous dosing, which both patients and healthcare professionals greatly appreciate. After a short training session, patients and/or healthcare professionals can administer the drug very quickly at home. This leads to an improved quality of life, a reduction in the time spent traveling to the healthcare facility, and consequently a reduction in costs and environmental impact. Again, this aligns strongly with our approach of 'excellence through simplicity'.

Injection systems for self-administration have evolved into a pivotal tool for the effective treatment of chronic diseases. The growing demand for such systems is driven by factors such as the convenience patients enjoy when safe and easy self-administration at home saves them the time and effort involved in trips to healthcare facilities. At the same time, autoinjectors are straightforward and safe to use by patients or their caregivers, reducing the burden on more highly skilled healthcare professionals.^{[5][16]} Flexible care at home is not only convenient for patients but also has a positive impact on sustainability. Far fewer ambulance transports or trips to the hospital or clinic are required. In addition, the number of hospitalizations is significantly reduced.^{[17][18][19]}

Addressing the entire value chain

In view of the long-term nature of chronic diseases, a favorable patient experience is paramount. However, continuous improvements in ease of administration, pain reduction, compliance and adherence are just part of the picture. Other key aspects that call for attention include the quality of the entire value chain in the drug delivery process.

With the healthcare and pharmaceutical experts on the Haselmeier team, we conducted multiple interviews with customers and subject matter experts in drug delivery devices and combination products. These interviews addressed the drug delivery value chain from end to end – from the conceptual idea of the drug delivery solution, through its design and manufacture, to the packaged combination product including its supply and use. We also reviewed feedback and inquiries from clinicians, plus discussions with current users of existing autoinjectors. Our findings identified several unmet needs that inspired us to develop a new generation of autoinjectors which seamlessly combine functionality, convenience, user-friendliness and sustainability.

The outcome of this development is the PiccoJect™ Autoinjector Platform. Its ease of use, inherent safety



and sustainability characteristics set this platform apart from existing offerings in the marketplace. It includes two variants of the highly compact PiccoJect™ autoinjector, supported by a rich set of services (including customization, pre- and final assembly and packaging) along the entire value chain.



Simplicity is key to efficiency

'Excellence through simplicity' sums up the key features of the PiccoJect™ autoinjector design. It all starts with an extremely low part count: the PiccoJect™ autoinjector is made up of only eight parts. Apart from the syringe, the highly integrated delivery mechanism consists of five injection-molded plastic parts, two springs and one metal component.



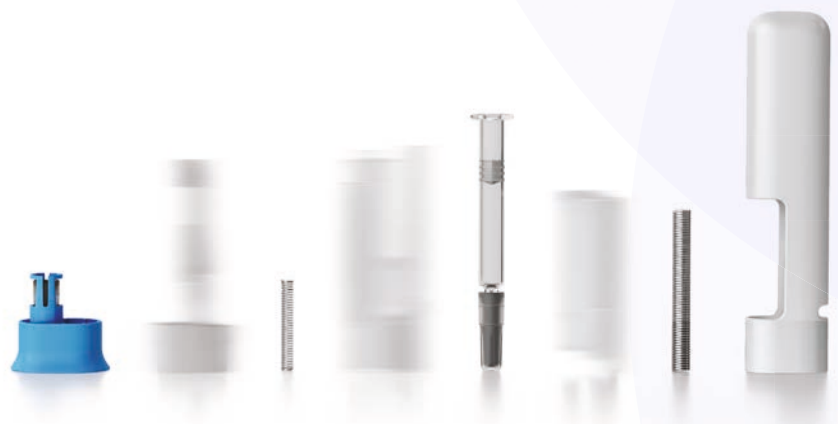
only eight parts



full-service platform



standard 1 ml or 2.25 ml pre-filled syringe



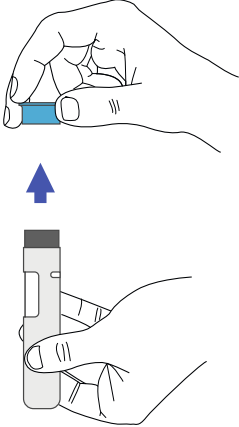
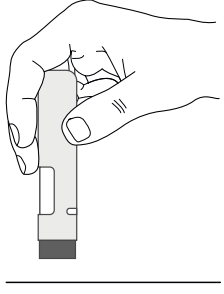
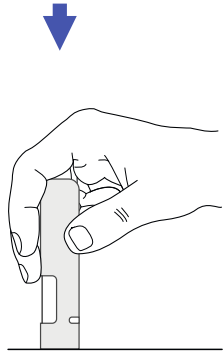
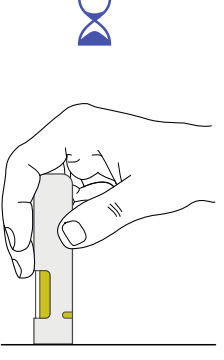
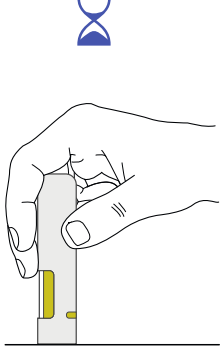
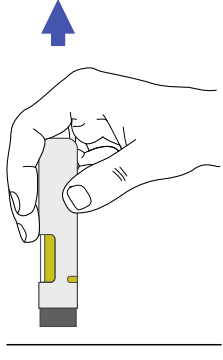
The delivery mechanism of the PiccoJect™ autoinjector accommodates any standard 1 ml long and 2.25 ml pre-filled glass or plastic syringe with a small round or cut flange. The same mechanism is available with two different cross-sections, tailored to the applicable syringe size to provide two discrete and user-friendly device form factors.



Delivering a better user experience

To help ensure adherence, the PiccoJect™ autoinjector is designed from the ground up for ease of use. It features a large wrap-around drug window for visual inspection of the drug prior to use, visual and audible feedback on the device status, and integrated needle safety. These features plus its small size, slightly flattened (rather than circular) cross-section and intuitive feedback make this device particularly straightforward to handle.

The PiccoJect™ autoinjector features an ergonomic design and provides clear feedback.

<p>1</p> <p>Remove cap by pulling it away from the autoinjector body</p> 	<p>2</p> <p>Align with body (either abdomen or thigh)</p> 	<p>3</p> <p>Gently press down so that the needle guard depresses (you may hear or feel a click)</p> 
<p>4</p> <p>Hold still and wait for the injection to finish (drug window and status indicator change to yellow)</p> 	<p>5</p> <p>Wait a further 3 seconds after the indicator changes to allow the injection to complete</p> 	<p>6</p> <p>Remove the autoinjector from the skin and place in the sharps bin</p> 



safe & convenient
self-administration



ergonomic shape for a
more convenient grip



audible clicks at the start &
end of injection



colored status indicator
provides visual feedback

PiccoJect™ is a compact, customizable, and intuitive two-step autoinjector for safe and convenient self-administration, designed for subcutaneous delivery of drug products. To keep patient discomfort to a minimum, the needle guard provides a relatively large contact area that reduces pressure on the skin. Audible clicks at the start and end of each injection as well as visual feedback help ensure that the user holds the device in place until the full dose has been injected. A dedicated status indicator provides easy-to-understand binary information about the usage status of the autoinjector. For instance, upon completion of the injection procedure, the colored status indicator notifies the user that the syringe is depleted, and the device has been used.

IP positioning

Part of Haselmeier's IP strategy is to constantly maximize and expand patent protection for PiccoJect™ technology through continuous innovation and new applications. Haselmeier has already filed several patents for the PiccoJect™ autoinjector, covering various innovative technologies, safety features, and digitization.





PiccoJect™ - 100

PiccoJect™ - 225

Technical specifications

SPECIFICATIONS	PICCOJECT™ – 100	PICCOJECT™ – 225
Part count	5 plastic components, 2 springs, 1 metal component	
Primary container	1 ml long glass or plastic syringe	2.25 ml glass or plastic syringe
Syringe flange	Small round or cut flange	
Fill volume (how to adapt the fill volumes)	0.2 – 1 ml	0.6 – 2 ml
Injection time*	< 10 s	< 15 s
Viscosity**	Up to 20 cP	
Needle insertion depth	6 mm (nominal); customization possible	
User feedback	Audible click at start and end of dose; visual feedback in drug window and dedicated status indicator	
Needle safety	Automatic needle shielding with needle hidden before, during and after use	
Needle type and gauge	27G and 29G, normal wall through special thin wall	
Weight	26 g (without syringe)	34 g (without syringe)
Dimensions	H = 130 (cap on), W = 26, D = 15 mm	H = 134 (cap on), W = 30, D = 19 mm

*, ** Injection time and viscosity capability are dependent on needle diameter and fill volume.

Customization options

Thanks to its versatile design, the PiccoJect™ autoinjector can easily adapt to a range of customer requirements. Standard customization options include cap color, the size of the drug window, and spring force. Agility is key: these customization options are available without any detrimental impact on development timelines.



different colors options
for cap and label



customizable size
of the drug window



optimized
spring force





Connectivity for data-driven insight

Haselmeier is currently developing connectivity options that will enable the PiccoJect™ platform to integrate seamlessly with existing digital ecosystems, allowing injection-related data to be collected automatically at the point of care. We draw on experience gained through our D-Flex™ Ecosystem and D-Flex™ Logbook technologies. The idea is to equip the PiccoJect™ autoinjector with a smart add-on that collects data and transmits it to a private cloud for clinical evaluation. Again, the guiding principle is excellence through simplicity. Our approach to connectivity aims to minimize any impact on the injection process, reduce patient training and eliminate the need for a patient app.

Smart medical devices that drive a steady increase in self-care, personalization of treatments, predictability of outcomes or proactive intervention will help elevate the quality of care to a new level. Connected drug delivery systems in digital healthcare workflows are starting to prove their worth. For instance, a clinical trial^[20] conducted by a major player in healthcare monitored the adherence patterns of 75 diabetes patients with the help of a connected drug delivery device. The trial results underscored the need to gain a better understanding of patient behavior and adherence to the prescribed therapy.

Automatic collection and storage of treatment data helps patients save time because there is no need to document each injection event on paper.

Furthermore, it may reduce the risk of missed or incorrect data entry. In this way, connected devices complement digital solutions, contributing to reducing the need for patient visits during clinical testing.

Committed to sustainability

At Haselmeier, sustainability is embedded in our daily business and in the foundations of our corporate strategy.^[21] Our sustainability objectives address the rights and needs of people, profitability, and the necessities of protecting our planet against severe short- and long-term impacts.

In line with the global sustainability strategy pursued by medmix, Haselmeier is proactively implementing steps aimed at reducing our global carbon footprint, reducing waste landfills, improving our water usage management systems, and implementing low-carbon electricity throughout our sites. Haselmeier development and design initiatives embrace sustainability during the entire lifecycle of our products.

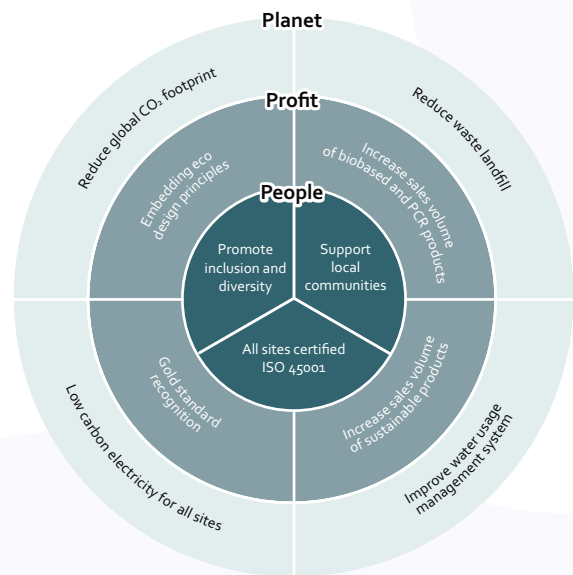
The sustainability goals of our customers and partners in the biopharmaceutical industry are equally important to us. Our Haselmeier sustainability objectives are in line with the emission reduction goals of the pharmaceutical industry. Currently, this global industry is driving major initiatives for reducing its carbon emissions.^[22] It is our corporate strategy to support the industry in achieving its ambitious goals of greater eco-friendliness.^[23] Haselmeier proactively addresses such issues and is willing to collaborate with customers to jointly develop and implement appropriate solutions for reducing emissions and driving sustainability. We are committed to implementing specific measures along the entire value chain from conceptual design, manufacturing and packaging solutions, through to supply chain topics.

Sustainability is fundamental

We focus on evidence-based local and global efforts that:

-  **Ensure a safe and healthy place to work and develop professionally**
-  **Reduce our environmental footprint through efficient energy consumption, water use, and waste management**
-  **Minimize the environmental impact for our partners and patients**

The sustainability goals of our customers and partners in the biopharmaceutical industry are fundamental to us and are embedded in our strategy.



Our sustainability efforts have not gone unnoticed. The Haselmeier s.r.o manufacturing site in the Czech Republic has received the prestigious Silver rating from EcoVadis, one of the world’s most trusted business sustainability rating entities. We achieved a score of 63/100 and performed particularly strongly within our

environment, labor, and human rights sectors. With the same sustainability practices incorporated throughout our sites in Europe, we are on the right track.

The underlying design concept of the PiccoJect™ autoinjector was driven by sustainability requirements.

Its parts were optimized to allow for the use of materials with minimal environmental impact – such as plastics based on attributed bio-circular key raw materials via a mass balance approach. In line with the medmix approach to keeping shipping routes short, our manufacturing and distribution facilities are located in the geographies where our customers and partners are based. The PiccoJect™ autoinjector will be manufactured at Haselmeier sites that rely on low-carbon electricity.

Haselmeier™ eco-design principles

Disposable drug delivery devices still offer advantages in terms of ease of use and reimbursement over reusable products, especially for less frequent injections. In addition, contamination and hygiene issues impose limitations on the circularity of healthcare products. Consequently, we believe that the pharmaceutical industry and its customers will continue to request disposable products for some time to come. To offset this impact, Haselmeier's eco-design principles aim to reduce the environmental footprint of these products by:

- Optimizing component wall thicknesses to minimize excess materials
- Avoiding the use of materials with high carbon intensities, such as polyamide (PA) 6
- Selecting eco-friendly materials where the supplier provides sustainable feedstock options
- Minimizing the use of tray handling for individual components during assembly
- Manufacturing trays and cartons from post-consumer materials

We are always open to new ideas and are happy to support our clients from clinical studies to commercial launch of their combination products.



The development and production of an inherently sustainable autoinjector underscores our commitment to environmental and social responsibility.

We reach out to our customers, understand their challenges and collaborate with them to create solutions tailored to their specific needs.



About Haselmeier™

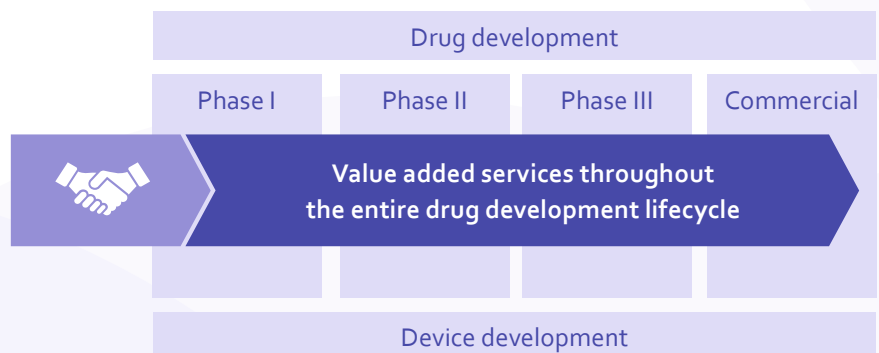
Haselmeier, the drug delivery device business division of medmix, designs, develops and manufactures advanced drug delivery systems such as pen injection systems and autoinjectors. Patient comfort and customers' needs are always at the heart of the company's practices.

With its broad portfolio of technologies and services, Haselmeier delivers user-friendly injection systems that enable patients to self-administer their medication reliably and accurately.

Haselmeier is known for its excellent and long-standing track record in providing these innovative drug delivery devices based on its proprietary IP business model. The company collaborates closely with its customers in the pharmaceutical and biopharmaceutical industries. medmix, with its precision injection molding capabilities and expertise in liquid micro-dosing plus financial strength and global footprint, helps Haselmeier accelerate innovation in healthcare.

With more than 100 years of expertise in the development and manufacture of drug delivery devices, our global footprint, nearly 250 distinguished and motivated experts, more than 200 patents granted, and numerous patents pending, Haselmeier remains committed to developing innovative solutions that support our customers and help improve the health of millions of people worldwide.

From clinical testing to commercialization Our service offering



Partner for drug delivery devices & combination products

- Platform strategy
- Customized development
- Updating packaging solutions
- Final assembly & packaging
- Regulatory support
- Post-sales support



Sources and references

- World Health Organization, Newsroom, "Noncommunicable diseases", April 13, 2021
- World Health Organization, Health Topics, "Noncommunicable diseases", February 3, 2022
- The Silver Book, "Percentage of the Population With Chronic Diseases, 1995-2030", May 2009
- U.S. Food and Drug Administration (FDA), "Advancing Health through Innovation: New Drug Therapy Approvals 2020", January 2021
- G de la Torre, B., & Albericio, F. (2019). The pharmaceutical industry in 2018. An analysis of FDA drug approvals from the perspective of molecules. *Molecules*, 24(4), 809
- Ahil N. Ganesh, Carolyn Heusser, Sudhakar Garad, Manuel Vicente Sánchez-Félix Patient-centric design for peptide delivery: Trends in routes of administration and advancement in drug delivery technologies, *Medicine in Drug Discovery*. Article 100079, March 2021
- Jonaitis, L., Marković, S., Farkas, K. et al. Intravenous versus subcutaneous delivery of biotherapeutics in IBD: an expert's and patient's perspective. *BMC Proc* 15, 25 (2021)
- DCAT Value Chain Insights, "The Pharma Pulse: Small Molecules and Biologics", May 26, 2021
- Evaluate Pharma World Preview 2020, "Outlook to 2026", July 2020
- IQVIA, "The Prospects for Biosimilars of Orphan Drugs in Europe – Current Landscape and Challenges Ahead", Institute Report, July 21, 2020
- IMS Institute for Healthcare Informatics, "Global Medicines Use in 2020 – Outlook and Implications", November 2016
- DCAT Value Chain Insights, "Industry Roundtable: Parenteral Drug Manufacturing", February 10, 2021
- American Pharmaceutical Review, Featured Articles, "The Congruence Between Small Molecule Generic Medicine and Biosimilar Medicine Business Models", October 15, 2017
- De Cock E et al, "A time and motion study of subcutaneous versus intravenous Trastuzumab in patients with HER2-positive early breast cancer". *Cancer Medicine*, 2016, Vol 5(3), pp 389-387.
- Bittner B, Richter W, Schmidt J. Subcutaneous Administration of Biotherapeutics: an overview of current challenges and opportunities. *BioDrugs*. 2018;32(5):425–440.
- Contract Pharma, "Injectables: The New Oral?", May 04, 2016
- The Lancet Planetary Health, Volume 5, Issue 2, Pages e84-e92, "Health care's response to climate change: a carbon footprint assessment of the NHS in England", 2021
- British Journal of Cancer, Waller, C. et al., "Intravenous and subcutaneous formulations of trastuzumab Biosimilars implication for clinical practice", February 2021
- De Cock, E. et al., "Time savings with Rituximab subcutaneous injection versus Rituximab intravenous infusion: A time and motion study in eight countries", *PLoS One*. 2016; 11(6): e0157957.
- U.S. National Library of Medicine, ClinicalTrials.gov, "Insulin Dosing Practices in Persons With Diabetes on Multiple Daily Injections", August 14, 2018
- medmix Annual Report 2021, "Sustainability Review"
- Brighter World, "Big Pharma emits more greenhouse gases than the automotive industry", May 28, 2019
- Pharma Technology Focus, "Turning Pharma Green: an Eco-Wish List for the Industry", 2020

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