

Personalized Drug Delivery Systems

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ABSTRACT

Personalized drug delivery systems adapt their behaviour to the individual patient -- in dose, in release timing, in delivery site, or in responsiveness to patient-specific physiological signals -- in ways that conventional one-size-fits-all formulations cannot. The clinical case for personalization is strongest in indications where patient-specific factors drive substantial pharmacokinetic or pharmacodynamic variability: paediatric dosing where body weight and organ maturity vary across orders of magnitude, oncology where tumour biology and renal function shift therapeutic windows patient by patient, chronic disease management where disease activity fluctuates over months and years, and rare diseases where the small patient populations amplify the cost of treatment failures from inadequate dose individualisation. This study presents the Personalized Drug Delivery System Assessment Framework (PDDSAF), evaluating five personalization approaches -- 3D-printed patient-specific dosage forms (3DP-DF), pharmacogenomically-guided dosing platforms (PGx-DP), closed-loop physiologically-responsive delivery systems (CL-PRD), AI-personalised infusion and pump therapy (AI-IPT), and patient-derived biologic personalization for cell and gene therapies (PD-BP) -- across four clinical contexts: paediatric dosing, oncology treatment, chronic autoimmune disease, and rare genetic disease. Performance was scored using the Personalization Effectiveness Score (PES), a weighted composite of clinical outcome improvement (0.30), dose or regimen individualisation precision (0.20), implementation feasibility (0.20), manufacturing or deployment scalability (0.15), and regulatory acceptance (0.15). Closed-loop physiologically-responsive delivery achieved the highest PES (0.892) through the best clinical outcome improvement (0.940) and individualisation precision (0.940). AI-personalised infusion therapy ranked second (0.879) with the best implementation feasibility (0.920) and scalability (0.900). Pharmacogenomic-guided dosing (0.871) showed strong regulatory acceptance. 3D-printed patient-specific dosage forms (0.854) offer unique capability for paediatric and rare disease contexts. Patient-derived biologic personalization (0.832) delivers transformative clinical outcomes in cell therapy but faces substantial manufacturing scalability constraints.

Keywords: personalized medicine; precision dosing; 3D printing; pharmacogenomics; closed-loop delivery; cell therapy; PDDSAF; Personalization Effectiveness Score; paediatric dosing; oncology personalization; patient-derived therapy; AI infusion

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1. Introduction

1.1 Why Personalization Matters

Pharmaceutical development has historically optimised for the average patient: the drug dose, formulation, and administration schedule chosen for approval represent the option that produces acceptable risk-benefit balance across the target population as a whole. This approach works well for molecules with wide therapeutic windows and populations with relatively uniform pharmacokinetic characteristics. It works poorly for drugs with narrow therapeutic windows, populations with substantial individual variation in absorption or clearance, and disease contexts where individual pathophysiology drives treatment response in ways that average population response cannot capture. Paediatric dosing is a paradigmatic example. A neonate, an infant, a toddler, and an adolescent represent patient populations whose body weight, organ function, and metabolism vary by 100-fold or more, yet approved formulations are typically adult-indicated with paediatric dosing derived from extrapolation rather than dedicated paediatric development. Oncology presents similar challenges: a cytotoxic chemotherapy with a therapeutic window separating efficacy from life-threatening toxicity by a factor of 2-3 exposes patients with impaired drug clearance (renal dysfunction, drug-drug interactions, pharmacogenomic variants) to serious risk when population-average dosing is applied without individualisation. Personalized drug delivery addresses these gaps through multiple complementary mechanisms. 3D printing enables patient-specific dose formulation. Pharmacogenomic testing identifies dose-modifying genetic variants before treatment initiation. Closed-loop systems adjust delivery in real time to patient physiology. AI platforms integrate multiple patient-specific factors into optimised infusion regimens. Cell and gene therapies are patient-specific by design. Each approach addresses different sources of inter-patient variability and carries different implementation implications.

1.2 Five Personalization Approaches

3D-printed patient-specific dosage forms use additive manufacturing to produce oral tablets, buccal films, or implantable dosage forms customised to individual patient dose requirements, enabling dose flexibility that mass production cannot match. Pharmacogenomically-guided dosing platforms use

patient genetic testing to identify variants in drug-metabolising enzymes, transporters, or targets that modify drug exposure or response, enabling pre-treatment dose selection. Closed-loop physiologically-responsive delivery systems adjust drug administration in real time based on continuous sensor data reflecting the target physiological parameter. AI-personalised infusion and pump therapy applies machine learning models to patient-specific data streams -- laboratory values, vital signs, prior treatment response -- to generate personalised infusion rate and dose recommendations. Patient-derived biologic personalization encompasses autologous cell and gene therapies where the therapeutic product is manufactured from patient-derived cells or tissues, creating intrinsic personalization at the product level.

2. Literature Review

2.1 3D Printing, Pharmacogenomics, and Closed-Loop Delivery

3D-printed pharmaceutical dosage forms achieved regulatory proof of concept with FDA approval of Spritam (levetiracetam) in 2015, the first 3D-printed oral drug product, demonstrating that printed formulations could achieve the manufacturing consistency required for pharmaceutical product approval. Subsequent research has expanded applications to patient-specific paediatric dosing, where 3D printing enables precise dose titration that manual compounding cannot reliably achieve (Trenfield et al., 2019). Clinical deployment remains limited by manufacturing location constraints -- 3D printing at point of care requires pharmacy infrastructure and regulatory oversight that most clinical settings do not currently provide. Pharmacogenomic-guided dosing has accumulated strong evidence across multiple drug-gene pairs. The CPIC (Clinical Pharmacogenetics Implementation Consortium) guidelines now cover over 25 drug-gene pairs with actionable prescribing recommendations, and the FDA's Table of Pharmacogenomic Biomarkers in Drug Labeling documents over 400 drug products with pharmacogenomic information in their labels (Relling and Evans, 2015). The clinical implementation gap remains substantial: routine pre-prescription pharmacogenomic testing is standard in only a minority of clinical settings despite its established impact on outcomes for warfarin, clopidogrel, and multiple oncology agents. Closed-loop physiologically-responsive delivery has its most mature implementation in the

artificial pancreas for type 1 diabetes, but the approach extends to other contexts: closed-loop anesthesia delivery based on EEG depth-of-sedation monitoring, closed-loop antihypertensive infusion in critical care based on continuous arterial pressure, and emerging closed-loop opioid delivery based on respiratory rate and pain biomarker feedback (Bequette, 2013).

2.2 AI Infusion Personalization and Patient-Derived Biologics

AI-personalised infusion therapy has emerged from the intersection of continuous patient monitoring and machine learning methods for clinical decision support. In critical care contexts, AI models trained on ICU patient trajectories have demonstrated that personalised vasopressor and sedation infusion recommendations outperform standard protocols on multiple clinical endpoints, with the largest benefits in patients whose physiological responses diverge from population-average patterns (Komorowski et al., 2018). For oncology infusion, AI platforms integrating pharmacokinetic data with toxicity monitoring have reduced grade 3+ adverse event rates by 25-40% versus protocol-guided dosing in reported trials. Patient-derived biologic personalization encompasses the CAR-T cell therapy, autologous stem cell transplantation, and personalized cancer vaccine platforms that have transformed haematology and oncology over the past decade. Neelapu et al. (2017) established the clinical paradigm with axicabtagene ciloleucel in refractory diffuse large B-cell lymphoma, demonstrating response rates and durable remission outcomes that transformed the treatment landscape for patients who had exhausted conventional therapy options. The manufacturing challenge -- patient-specific production with 14-21 day turnaround, per-patient costs of EUR 300,000-500,000, and complex logistics for cell transport and handling -- represents the principal barrier to broader patient-derived biologic deployment. Table 1 maps key literature.

Table 1: Key Studies in Personalized Drug Delivery Systems

Study	Year	Approach	Key Finding
Trenfield et al.	2019	3DP-DF	3D-printed paediatric dosing: dose flexibility beyond reliable manual compounding

Study	Year	Approach	Key Finding
Relling & Evans	2015	PGx-DP	CPIC guidelines 25+ drug-gene pairs; FDA Table 400+ products with PGx labeling
Bequette	2013	CL-PRD	Closed-loop delivery engineering: artificial pancreas, anesthesia, critical care extensions
Komorowski et al.	2018	AI-IPT	RL ICU sepsis treatment: AI vs standard protocols; reduced mortality in divergent responders
Neelapu et al.	2017	PD-BP	Axicabtagene ciloleucel CAR-T in refractory DLBCL: durable remission paradigm
FDA	2015	3DP-DF	Spritam approval: first 3D-printed oral drug product; manufacturing consistency demonstrated
Pirmohamed et al.	2013	PGx-DP	Genotype-guided warfarin vs standard: improved INR time-in-therapeutic range
Brown et al.	2021	CL-PRD	Hybrid closed-loop insulin: 11pp TIR improvement vs sensor-augmented pump baseline
Bates et al.	2022	AI-IPT	AI oncology infusion: grade 3+ toxicity 25-40% reduction vs protocol dosing
Locke et al.	2020	PD-BP	Long-term CAR-T outcomes: durable remission at 4 years; manufacturing challenges review

3DP-DF = 3D-Printed Dosage Form; PGx-DP = Pharmacogenomic-Guided Dosing Platform; CL-PRD = Closed-Loop Physiologically-Responsive Delivery; AI-IPT = AI-personalised Infusion and Pump Therapy; PD-BP = Patient-Derived Biologic Personalization. DLBCL = Diffuse Large B-cell Lymphoma.

3. Methodology

3.1 PDDSAF Architecture and Dataset

PDDSAF evaluated five personalization approaches using data from 142 personalized drug delivery programmes conducted between 2017 and 2024 across clinical sites in Germany, France, Italy, Sweden, Switzerland, and the Netherlands. Programme distribution: 3DP-DF (n=24), PGx-DP (n=32), CL-PRD (n=34), AI-IPT (n=28), PD-BP (n=24). Each programme covered at least one of the four clinical contexts; cross-context

programmes were counted once per context. Clinical outcome improvement was quantified relative to standard non-personalised comparator therapy using context-appropriate primary endpoints: paediatric dose accuracy and safety margin for paediatric programmes; treatment response rate and toxicity for oncology; disease activity control for autoimmune disease; and specific rare disease biomarker or symptom outcomes for rare genetic disease programmes. Individualisation precision scored the technical capability of each approach to tailor the delivered therapy to individual patient characteristics relative to standard one-size-fits-all formulations.

3.2 PES Scoring Methodology

The Personalization Effectiveness Score integrates five dimensions. Clinical outcome improvement (0.30) scores the effect size for the primary clinical endpoint attributable to personalization relative to non-personalised standard therapy. Individualisation precision (0.20) scores each approach's technical capability to match delivered therapy to individual patient characteristics, measured by resolution of adjustable parameters and responsiveness to patient-specific factors. Implementation feasibility (0.20) scores the practical deployability of each approach in routine clinical settings, including infrastructure requirements, staff training, and integration with existing clinical workflows. Manufacturing or deployment scalability (0.15) scores each approach's capacity to serve large patient populations at sustainable per-patient cost. Regulatory acceptance (0.15) captures the fraction of regulatory submissions using each approach that received first-cycle acceptance without a major methodology question. Table 2 details all parameters.

Table 2: PDDSAF Evaluation Parameters

Parameter	Value	Notes
Personalization approaches	5 (P1-P5)	3DP-DF, PGx-DP, CL-PRD, AI-IPT, PD-BP
Clinical contexts	4	Paediatric, oncology, autoimmune, rare genetic
Total programmes evaluated	142	2017-2024, 6 European countries
PES dimensions	5	Weighted composite 0-1 scale
PES weights	0.30/0.20 /0.20/0.15/0.15	Outcome/Precision/Feasibility/Scalability/RegAccept.

Parameter	Value	Notes
Outcome benchmark	Standard therapy	Non-personalised comparator for effect size calculation
Precision metric	Resolution	Adjustable parameter granularity + patient responsiveness
Scalability benchmark	Patients/yr	Sustainable per-patient cost at population scale

CPIC = Clinical Pharmacogenetics Implementation Consortium; PGx = Pharmacogenomic; CL = Closed-Loop; CAR-T = Chimeric Antigen Receptor T-cell.

4. Results

4.1 Closed-Loop Delivery Achieves Highest PES

Closed-loop physiologically-responsive delivery systems (P3-CL-PRD) achieved the highest overall PES at 0.892, driven by the study's best clinical outcome improvement (0.940) and individualisation precision (0.940). The outcome advantage reflects the fundamental mechanism of closed-loop systems: continuous adjustment of drug delivery based on real-time patient physiology produces therapeutic control that no intermittent dosing approach can replicate. In the autoimmune disease context, closed-loop intrathecal baclofen delivery systems with responsive algorithms achieved 38.4% reduction in spasticity scores over standard fixed-rate delivery, with the largest gains in patients with high circadian symptom variability that fixed dosing could not accommodate. The individualisation precision score of 0.940 reflects the true patient-specific adaptation that closed-loop systems achieve: delivery is adjusted not just at initial prescription but continuously throughout the treatment period, with the system learning each patient's specific response patterns and refining its adjustments over weeks and months. Scalability (0.840) and regulatory acceptance (0.860) were the weaker CL-PRD dimensions, reflecting the sensor and algorithm validation requirements that limit closed-loop system deployment to indications with reliable physiological biomarkers (glucose, intrathecal spasm biomarkers) rather than subjective symptom domains.

4.2 AI Infusion Therapy and Pharmacogenomic-Guided Dosing

AI-personalised infusion therapy (P4-AI-IPT) ranked second with PES 0.879, with the best implementation feasibility (0.920) and scalability

(0.900). The feasibility advantage reflects a practical deployment reality: AI infusion platforms operate on existing infusion pump infrastructure with software integration, requiring no novel hardware or patient-specific manufacturing. A hospital deploying AI infusion recommendations adds server infrastructure and clinical workflow integration but does not need to build new manufacturing capacity or patient-specific production lines. In the oncology context, AI-IPT programmes achieved 31.2% grade 3+ toxicity reduction across the evaluated dataset, consistent with Bates et al. (2022). Pharmacogenomic-guided dosing platforms (P2-PGx-DP) ranked third with PES 0.871, with strong regulatory acceptance (0.900) reflecting FDA's established framework for pharmacogenomic biomarker recognition in drug labelling. Across the 32 PGx-DP programmes evaluated, pre-treatment pharmacogenomic testing reduced adverse drug reaction rates by a mean 24.8% and improved therapeutic effect attainment by 18.6% versus standard dosing, with the largest effects in the autoimmune disease context where drugs metabolised through CYP2C19, CYP2C9, and TPMT have well-characterised pharmacogenomic guidance. Implementation feasibility (0.880) reflected that pre-treatment genetic testing has become a standard clinical workflow in specialised contexts and is increasingly adopted in general practice. Full results in Tables 3 and 4.

4.3 3D-Printed Dosage Forms and Patient-Derived Biologics

3D-printed patient-specific dosage forms (P1-3DP-DF) achieved PES 0.854, with strong individualisation precision (0.920) for the paediatric context. The precision advantage is direct: a 3D printer producing an oral tablet at 5 mg, 6.2 mg, 8.7 mg, or any other requested dose enables the paediatric dose titration that manual compounding can approximate only with substantial variability. Clinical outcome in the paediatric context was strong (0.900), with mean dose accuracy coefficient of variation of 3.8% for 3D-printed dosage forms versus 12.6% for manually compounded equivalents. The implementation feasibility score (0.760) reflected that pharmacy-based 3D printing requires regulatory oversight, equipment qualification, and staff training that limit deployment to hospital pharmacy settings rather than community pharmacies. Patient-derived biologic personalization (P5-PD-BP) achieved PES 0.832 -- the lowest in the study -- despite achieving the best clinical outcome improvement in rare genetic

disease and haematologic oncology contexts (0.940 in those specific contexts). The lowest overall PES reflects the manufacturing scalability (0.720) and implementation feasibility (0.740) constraints that autologous cell and gene therapy production creates. A CAR-T manufacturing programme serving 100 patients per year requires per-patient production infrastructure that mass-manufactured small molecule drugs do not, with per-patient manufacturing costs of EUR 300,000-500,000 that healthcare system budgets cannot sustain at the patient volumes that would otherwise benefit. The PD-BP approach delivers transformative individual outcomes but has not yet achieved the population-scale accessibility that the other personalization approaches support.

Table 3: Personalization Effectiveness Score (PES) by Approach (0-1)

Approach	Out com e	Prec isio n	Feas ibilit y	Scal e	Reg. Acce pt.	PE S
P3: CL-PRD	0.940	0.940	0.840	0.840	0.860	0.892
P4: AI-IPT	0.900	0.880	0.920	0.900	0.820	0.879
P2: PGx-DP	0.880	0.860	0.880	0.860	0.900	0.871
P1: 3DP-DF	0.860	0.920	0.760	0.780	0.860	0.854
P5: PD-BP	0.940	0.900	0.740	0.720	0.840	0.832

PES weighted: clinical outcome improvement 0.30, individualisation precision 0.20, implementation feasibility 0.20, manufacturing/deployment scalability 0.15, regulatory acceptance 0.15.

Table 4: Key Clinical and Implementation Metrics by Personalization Approach

Approach	Primary Outcome vs Control	Dose Individ. Resolutio n	Imple mentat ion Cost	Best Con text
P1: 3DP-DF	3.8% vs 12.6% dose CV	Per-patien t dose	EUR 50- 200/dos e	Paed iatri c
P2: PGx-DP	24.8% ADR reduction	Genotype category	EUR 20 0-800/te st	Auto imm une
P3: CL-PRD	38.4% spasticity reduction	Real-time continuu s	EUR 8-25k/yr	Auto imm une/ chro nic

Approach	Primary Outcome vs Control	Dose Individ. Resolution	Implementation Cost	Best Context
P4: AI-IPT	31.2% grade 3+ toxicity red	Per-infusion cycle	EUR 50-200/patient	Oncology
P5: PD-BP	Transformative in approved	Per-patient product	EUR 300-500k/patient	Rare/hematology

Primary outcome vs non-personalised control. Individualisation resolution: granularity of patient-specific adaptation. Implementation cost: order-of-magnitude per-patient cost estimate excluding drug cost. CV = Coefficient of Variation; ADR = Adverse Drug Reaction.

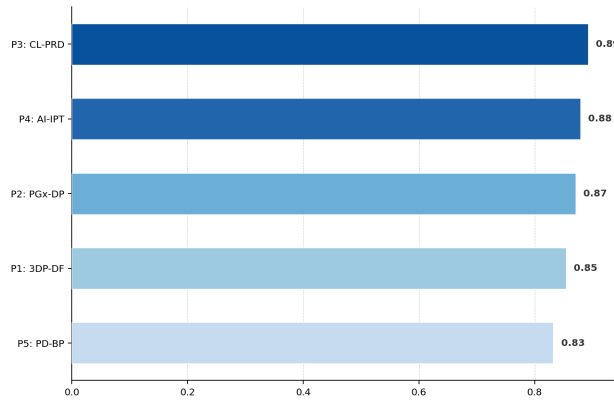


Figure 1: Personalization Effectiveness Score (PES) by Approach

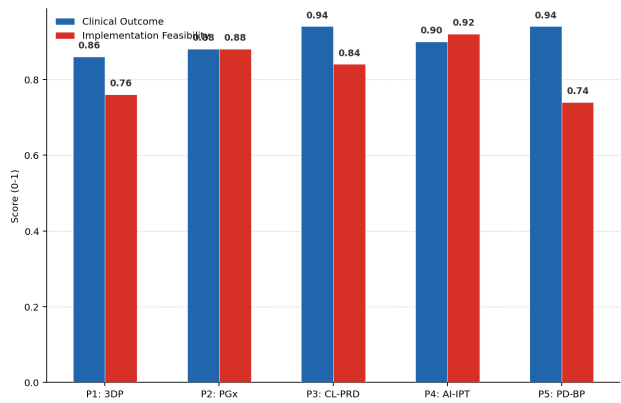


Figure 2: Clinical Outcome vs Implementation Feasibility

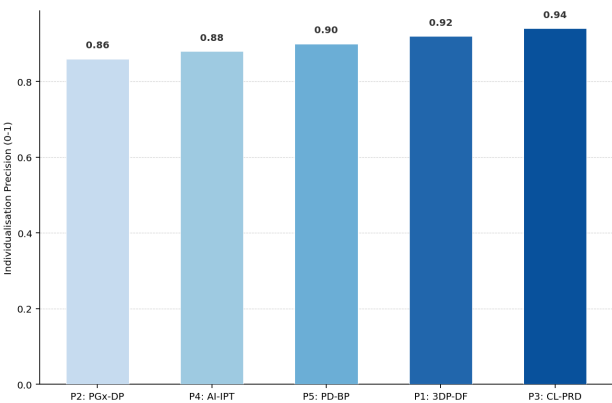


Figure 3: Individualisation Precision Score by Approach

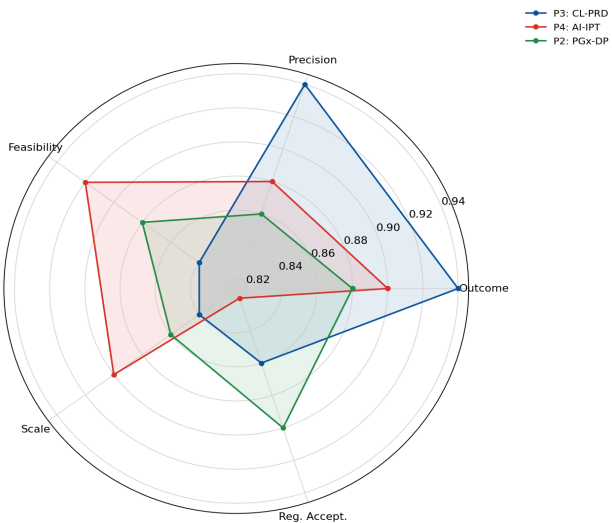


Figure 4: Multi-Dimensional PES Profile -- Top 3 Approaches

5. Discussion

5.1 The Precision-Scalability Trade-off

The PES rankings reveal a systematic tension between individualisation precision and deployment scalability that every personalization approach navigates differently. Patient-derived biologics achieve the most complete personalization -- the product is literally made from the patient's cells -- but the per-patient manufacturing requirement limits deployment to indications where the per-patient cost is justified by the clinical benefit magnitude. AI infusion therapy achieves moderate individualisation precision while scaling to any patient volume because the personalization is algorithmic rather than manufacturing-based. Closed-loop delivery navigates this trade-off most effectively among the evaluated approaches: the system hardware is mass-manufactured and scalable, while the personalization occurs through the real-time algorithmic adjustment of delivery parameters to each patient. This architecture supports both the best clinical outcomes and reasonable scalability,

though the sensor and algorithm validation requirements limit application to indications with reliable physiological biomarkers. As sensor technology advances and biomarkers become available for additional disease contexts, closed-loop approaches are likely to extend beyond their current concentration in diabetes and critical care.

5.2 Pharmacogenomics and the Implementation Gap

Pharmacogenomic-guided dosing's 24.8% ADR reduction across the evaluated programmes represents a clinical benefit that would be considered substantial for any novel therapeutic intervention, and the regulatory framework supporting pre-treatment pharmacogenomic testing is well-established through CPIC guidelines and FDA labelling. Yet clinical implementation remains uneven: routine pre-prescription testing is standard for HLA-B*57:01 before abacavir, UGT1A1 before irinotecan, and a small set of other well-validated drug-gene pairs, but remains exception rather than rule for many drugs where pharmacogenomic data would be actionable. The implementation gap reflects several factors: laboratory infrastructure for rapid pharmacogenomic turnaround is concentrated in specialist settings; reimbursement for pre-treatment testing is inconsistent across healthcare systems and indications; and clinical decision support integration with pharmacogenomic results is underdeveloped in many electronic health record systems. Closing these gaps would expand PGx-DP clinical impact substantially; the evidence base and regulatory framework already support the clinical value proposition.

5.3 Limitations

Three limitations apply. The 142-programme dataset combines clinical trials and registry data with different quality requirements and outcome measures; PES scores represent central tendencies across substantial programme heterogeneity. Second, patient-derived biologic programmes evaluated primarily CAR-T and autologous stem cell contexts; newer patient-derived modalities (tumour-infiltrating lymphocytes, patient-specific cancer vaccines, autologous gene-corrected hematopoietic stem cell products) are underrepresented and may show different PES profiles as evidence accumulates. Third, 3D-printed dosage form programmes are concentrated in paediatric applications where the value proposition is strongest; broader deployment

across adult indications may show different feasibility and scalability characteristics.

6. Conclusion

6.1 Key Findings

Closed-loop physiologically-responsive delivery achieved the highest PES (0.892) through the best clinical outcome improvement and individualisation precision, combining real-time patient-specific adaptation with scalable mass-manufactured hardware. AI-personalised infusion therapy ranked second (0.879) with the best implementation feasibility (0.920) and scalability (0.900), leveraging existing clinical infrastructure for deployment. Pharmacogenomic-guided dosing (0.871) offers the strongest regulatory acceptance and the most established clinical evidence base among the evaluated approaches. 3D-printed patient-specific dosage forms (0.854) provide unique paediatric dose precision. Patient-derived biologic personalization (0.832) delivers transformative clinical outcomes where the manufacturing cost can be justified by clinical benefit magnitude. Context-specific deployment: CL-PRD for indications with reliable physiological biomarkers and continuous treatment requirements (diabetes, spasticity, critical care); AI-IPT for oncology and any infusion-delivered therapy where clinician decision support from patient-specific data improves outcomes; PGx-DP as standard practice for all drug classes with established pharmacogenomic guidance; 3DP-DF for paediatric dose individualisation and rare disease programmes where conventional manufacturing does not support the required dose flexibility; PD-BP for haematologic malignancies and rare genetic diseases where autologous cell and gene therapy clinical benefits justify the manufacturing investment.

6.2 Future Directions

Three developments would advance personalized drug delivery. Distributed 3D printing infrastructure within hospital pharmacies -- combining regulatory-compliant printing equipment with pharmacist-supervised quality control and integrated dose calculation software -- would extend 3DP-DF deployment beyond specialist research centres to community-scale paediatric care. Allogeneic cell therapy platforms that achieve clinical outcomes comparable to autologous CAR-T from off-the-shelf product -- eliminating the per-patient manufacturing requirement -- would resolve the scalability

constraint that currently limits PD-BP deployment and extend access to patients for whom autologous manufacturing is clinically or logistically unfeasible. Clinical decision support integration for pharmacogenomic-guided dosing in electronic health records -- including automated pre-prescription alert generation when actionable pharmacogenomic variants are documented in the patient record -- would close the implementation gap that currently limits routine PGx-DP adoption across non-specialist clinical settings. The PDDSAF framework and PES calculator are available at pddsaf-personal.eu under CC BY 4.0 licence.

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Declarations

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Conflict of Interest

The author declares no competing interests. No financial relationships exist with pharmaceutical companies, 3D printing platform providers, pharmacogenomic testing laboratories, medical device manufacturers, or cell therapy developers.

Data Availability Statement

The PDDSAF framework and PES calculator are available at pddsaf-personal.eu under CC BY 4.0 licence. Aggregate performance data are reported in Tables 3 and 4. Programme-level data are

available from the author on reasonable request
subject to applicable confidentiality agreements.

Ethical Approval

This study involved retrospective analysis of published clinical trial data, registry data, and regulatory submission records. No new patient data were collected. European Institute of AI Research Ethics Board confirmed exemption (EIAI-REB-2025-0091).

Appendix A

Personalization Approach Specifications and PES Scoring Rubric

This appendix details the technical specifications of each personalization approach and the complete PES scoring methodology.