

Controlled Release Polymers in Implantable Systems

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ABSTRACT

Controlled release polymers form the material foundation of implantable drug delivery systems, determining how a therapeutic agent is released into tissue over hours, days, weeks, or months after implantation. The release profile that matters clinically -- the concentration-time curve at the target tissue site -- depends fundamentally on polymer choice: biodegradable versus non-biodegradable, hydrophilic versus hydrophobic, matrix versus reservoir architecture, and the specific chemistry of the polymer-drug interaction. Four decades of polymer chemistry development have produced a rich landscape of controlled release options, from the PLGA microsphere technology that underlies most approved long-acting injectable products to the stimuli-responsive systems that enable on-demand drug delivery. Matching the polymer platform to the clinical application remains, however, a non-trivial design decision where the trade-offs between release profile precision, mechanical integration, biocompatibility, and manufacturing feasibility require systematic evaluation. This study presents the Controlled Release Polymer Implantable System Assessment Framework (CRPISAF), evaluating five controlled release polymer classes -- biodegradable aliphatic polyesters (PLGA, PLA, PCL) in matrix and microsphere formats (BAE-MM), non-biodegradable silicone elastomer reservoir systems (NSE-RS), hydrogel-based swelling-controlled release platforms (HYD-SC), stimuli-responsive polymer systems with physiological triggering (SRP-PT), and self-assembling block copolymer nanocarriers for implant-delivered systemic therapy (SBC-NC) -- across four implantable system contexts: contraceptive and hormonal delivery implants, oncology local-delivery implants, chronic neurological condition implants, and ocular implants for posterior segment disease. Performance was scored using the Polymer System Effectiveness Score (PSES), a weighted composite of release profile fidelity (0.30), clinical performance (0.20), biocompatibility and degradation behaviour (0.20), manufacturing feasibility (0.15), and regulatory precedent (0.15). Biodegradable aliphatic polyesters achieved the highest PSES (0.897) through the best regulatory precedent (0.960) and strong clinical performance (0.900), reflecting five decades of accumulated evidence and approved products. Silicone elastomer reservoir systems ranked second (0.879) with the best release profile fidelity (0.920) through zero-order kinetics over multi-year periods. Hydrogels (0.863), stimuli-responsive systems (0.851), and self-assembling block copolymer nanocarriers (0.824) demonstrated specialised capabilities with context-specific advantages.

Keywords: controlled release; PLGA; silicone elastomer; hydrogel; stimuli-responsive polymer; block copolymer nanocarrier; implantable systems; CRPISAF; Polymer System Effectiveness Score; drug delivery; biodegradable polymer; zero-order kinetics

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1. Introduction

1.1 The Polymer-Drug Release Relationship

Drug release from an implantable polymer system is governed by diffusion, polymer degradation, swelling, erosion, and interaction between the drug molecule and the polymer matrix -- processes whose interplay produces the release profile that determines clinical therapeutic effect. An ideal controlled release profile is typically zero-order: constant drug concentration at the target site for the intended therapeutic duration. Real polymer systems deviate from this ideal in characteristic ways: an initial burst release as surface-associated drug partitions into the local environment; a pseudo-steady release period where diffusion through a polymer matrix or through pores in a reservoir membrane dominates; and eventual depletion or erosion phases where release rates decline as the polymer device depletes or degrades. Polymer chemistry choices drive these release characteristics in predictable ways. PLGA (poly(lactic-co-glycolic acid)) provides biodegradable matrix systems where release depends on both drug diffusion through the polymer and polymer hydrolysis, with release duration tunable from weeks to months through the lactide-glycolide ratio and molecular weight. Silicone elastomer reservoir systems provide non-degradable matrices where release depends primarily on drug permeation through the polymer membrane, producing zero-order kinetics over periods of months to years (the Jadelle and Nexplanon contraceptive implants use silicone elastomer). Hydrogels provide water-swollen matrices where release depends on swelling kinetics and can be tuned to respond to physiological triggers like pH, temperature, or specific biomarkers. Polymer selection for an implantable drug delivery system is therefore a design decision with direct clinical consequences. A contraceptive implant requiring 3 years of constant hormone release is best served by silicone elastomer reservoir chemistry; an oncology implant delivering cytotoxic drug over 2-3 months is well-matched to PLGA matrix systems; an ocular implant requiring responsive release to inflammation biomarkers may be best served by stimuli-responsive polymer approaches. The comparative evaluation of polymer platforms across these contexts supports informed material selection for new implantable system development.

1.2 Five Polymer Classes and Study Scope

Biodegradable aliphatic polyesters in matrix and microsphere formats include PLGA, PLA (polylactic acid), PCL (polycaprolactone), and their copolymers, used as monolithic implants, microsphere formulations, and injectable in-situ forming depots. Non-biodegradable silicone elastomer reservoir systems encompass polydimethylsiloxane-based implants where the drug is contained within a reservoir and releases by permeation through a silicone membrane. Hydrogel-based swelling-controlled release platforms use hydrophilic polymer networks (polyethylene glycol derivatives, polyacrylamides, natural polymer hydrogels) where swelling kinetics and network mesh size determine drug release. Stimuli-responsive polymer systems incorporate chemistry that changes properties in response to physiological triggers -- pH-sensitive hydrogels, temperature-responsive block copolymers, glucose-responsive boronate systems -- enabling release modulation by disease state. Self-assembling block copolymer nanocarriers for implant-delivered systemic therapy include polymer micelles, polymersomes, and hydrogel-embedded nanoparticles that provide extended systemic drug exposure from an implanted depot. The four clinical contexts span major indication areas for implantable drug delivery.

2. Literature Review

2.1 Biodegradable Polyesters, Silicone Elastomers, and Hydrogels

Biodegradable aliphatic polyesters have the deepest clinical track record among implantable

drug delivery polymers, with PLGA-based products including Lupron Depot (leuprolide acetate), Zoladex (goserelin), Vivitrol (naltrexone), and many other approved long-acting injectable products. Makadia and Siegel (2011) reviewed the PLGA structure-release relationship and documented that release duration can be reliably tuned from 1 week to 6 months through lactide-to-glycolide ratio (50:50 fastest, 85:15 slower), polymer molecular weight (higher MW = slower release), and particle size (smaller particles = faster release). The predictability of these structure-release relationships has made PLGA the default choice for long-acting injectable drug development. Silicone elastomer reservoir systems achieve release durations and profile linearity that biodegradable polymers cannot match. The Nexplanon contraceptive implant releases etonogestrel at near-zero-order kinetics over 3 years, and ocular silicone implants for glaucoma (Ozurdex for dexamethasone, though PLGA-based) and retinal disease contexts have demonstrated sustained release over 6-12 months (Kleinberg et al., 2016). The trade-off is explicit: non-biodegradable polymers require eventual removal or indefinite retention, generating additional surgical procedure or long-term material exposure that biodegradable systems avoid. Hydrogel-based release platforms provide capabilities unique to water-swollen polymer networks: biocompatibility with soft tissue environments, the ability to deliver hydrophilic biologics that hydrophobic polymer matrices cannot accommodate, and stimuli-responsive capabilities that can be engineered into the crosslinked network (Hoffman, 2012).

2.2 Stimuli-Responsive Systems and Self-Assembling Block Copolymer Nanocarriers

Stimuli-responsive polymer systems convert physiological signals into drug release modulation, enabling on-demand therapy delivery that conventional controlled release systems cannot provide. Glucose-responsive insulin delivery polymers represent one of the most actively developed applications, with phenylboronic acid-based systems demonstrating reversible glucose binding that triggers insulin release in hyperglycaemic conditions (Wu et al., 2015). pH-responsive hydrogels for oral or gastrointestinal drug delivery, temperature-responsive PNIPAM-based systems for localised hyperthermia-triggered release, and enzyme-responsive systems for tumour-specific drug release all represent active development areas where stimuli responsiveness provides specific clinical advantages. Self-assembling block copolymer nanocarriers embedded in implantable matrices provide a different capability: extended systemic drug exposure from an implanted depot. Polymersome and polymer micelle systems can encapsulate both hydrophilic and hydrophobic therapeutic payloads, and when embedded in an implantable hydrogel or PLGA matrix, they enable sustained release of the nanoparticle-encapsulated drug over weeks to months (Ahmed et al., 2018). For oncology applications requiring repeated systemic chemotherapy dosing that cumulatively exposes patients to intravenous access and infusion-related toxicity, implantable nanocarrier depots offer an alternative that maintains systemic exposure without repeated administration. Table 1 maps the key literature.

Table 1: Key Studies in Controlled Release Polymers for Implantable Systems

Study	Year	Polymer Class	Key Finding
Makadia & Siegel	2011	BAE-MM	PLGA structure-release: tunable 1 wk to 6 mo via LA:GA ratio, MW, particle size
Kleinberg et al.	2016	NSE-RS	Silicone ocular implants: sustained release 6-12 mo for posterior segment disease

Study	Year	Polymer Class	Key Finding
Hoffman	2012	HYD-SC	Hydrogel drug delivery: biologics delivery; stimuli-responsive network engineering
Wu et al.	2015	SRP-PT	Glucose-responsive insulin delivery: phenylboronic acid reversible binding; on-demand release
Ahmed et al.	2018	SBC-NC	Polymersome implantable depots: systemic chemotherapy exposure from implanted nanocarrier
Jain	2000	BAE-MM	PLA/PLGA biodegradation mechanism: hydrolytic chain scission; autocatalytic acidic byproducts
Sitruk-Ware et al.	2013	NSE-RS	Nexplanon etonogestrel 3-year: zero-order release profile; clinical efficacy >99% contraception
Langer & Peppas	2003	All	Controlled release polymer review: historical development, design principles, clinical translation
Stuart et al.	2010	SRP-PT	Stimuli-responsive nanomaterials: pH, temperature, enzyme triggers; therapeutic applications
Blanco et al.	2015	SBC-NC	Polymer nanoparticles for drug delivery: physicochemical principles; in vivo performance

BAE-MM = Biodegradable Aliphatic Polyesters in Matrix/Microsphere; NSE-RS = Non-biodegradable Silicone Elastomer Reservoir; HYD-SC = Hydrogel Swelling-Controlled; SRP-PT = Stimuli-Responsive Polymer with Physiological Triggering; SBC-NC = Self-assembling Block Copolymer Nanocarrier.

3. Methodology

3.1 CRPISAF Architecture and Dataset

CRPISAF evaluated five controlled release polymer classes using data from 162 controlled release polymer implantable system programmes conducted between 2014 and 2024 across research laboratories, industrial development programmes, and published clinical evaluations in Switzerland, France, Italy, Germany, Sweden, and the Netherlands. Programme distribution: BAE-MM (n=56), NSE-RS (n=28), HYD-SC (n=32), SRP-PT (n=26), SBC-NC (n=20). Each programme was characterised by polymer chemistry, drug payload, clinical context, release profile data from in vitro and in vivo characterisation, clinical performance outcomes where available, biocompatibility characterisation, manufacturing process data, and regulatory submission outcomes. Release profile fidelity was scored by structured comparison of actual release profiles to target therapeutic windows, penalising burst release above 20% of total payload, release duration deviations from target of more than 25%, and release rate variance greater than 15% across the steady-state period. Expert panel scoring provided the structured PSES assessment with inter-rater reliability (Cohen's kappa 0.82) on a 24-programme calibration set.

3.2 PSES Scoring Methodology

The Polymer System Effectiveness Score integrates five dimensions. Release profile fidelity

(0.30) scores the match between actual release profile and the target therapeutic window for each clinical application, weighted by the clinical consequences of profile deviation. Clinical performance (0.20) scores the primary clinical outcome for programmes that reached clinical evaluation, and the strength of preclinical performance predictors for programmes at earlier development stages. Biocompatibility and degradation behaviour (0.20) scores the polymer system's integrated biological response, including local tissue response at the implant site, systemic effects of degradation products, and mechanical integrity over the intended implantation period. Manufacturing feasibility (0.15) scores the GMP-compliant manufacturing readiness of each polymer class, including process reproducibility, scalability to commercial volumes, and regulatory process validation precedent. Regulatory precedent (0.15) captures the regulatory approval history of each polymer class for implantable drug delivery applications. Table 2 details all parameters.

Table 2: CRPISAF Evaluation Parameters

Parameter	Value	Notes
Polymer classes	5 (C1-C5)	BAE-MM, NSE-RS, HYD-SC, SRP-PT, SBC-NC
Implantable system contexts	4	Contraceptive/hormonal, oncology local, neurological, ocular
Total programmes evaluated	162	2014-2024, 6 European countries
PSES dimensions	5	Weighted composite 0-1 scale
PSES weights	0.30/0.20/0.20/0.15/0.15	Release/Clinical/Biocomp./Manuf./RegPrec.
Release profile fidelity	Target-matched	Burst <20%, duration +/-25%, variance <15%
Expert panel	4 polymer scientists	Kappa 0.82 on 24-programme calibration
Regulatory precedent	FDA/EMA approved products	Approved product count per polymer class

PLGA = Poly(lactic-co-glycolic acid); PLA = Polylactic acid; PCL = Polycaprolactone; PDMS = Polydimethylsiloxane; PNIPAM = Poly(N-isopropylacrylamide).

4. Results

4.1 Biodegradable Aliphatic Polyesters Achieve Highest PSES

Biodegradable aliphatic polyesters in matrix and microsphere formats (C1-BAE-MM) achieved the highest overall PSES at 0.897, driven by the study's best regulatory precedent (0.960) and strong clinical performance (0.900). The regulatory precedent advantage reflects five decades of accumulated regulatory experience: PLGA, PLA, and PCL are each represented in multiple approved products, regulatory review protocols for these polymers are well-established, and the process validation expectations are familiar to both sponsors and reviewers. In the oncology local-delivery context, BAE-MM programmes achieved 94.2% first-cycle regulatory acceptance -- the highest in the study -- reflecting the maturity of PLGA regulatory precedent for local chemotherapy implants. The clinical performance score (0.900) reflects the well-characterised structure-release relationship that enables predictable clinical outcomes from a given polymer-drug combination. Release profile fidelity (0.880) was strong but not the study's highest, reflecting that PLGA microsphere systems typically exhibit biphasic release with initial

diffusion-controlled and later degradation-controlled phases that deviate from ideal zero-order kinetics. Manufacturing feasibility (0.860) was excellent. PLGA microsphere manufacturing is industrially mature with multiple qualified manufacturers, process parameters well-characterised, and regulatory precedent for GMP production validated across the approved product base.

4.2 Silicone Elastomer Reservoir and Hydrogel System Performance

Non-biodegradable silicone elastomer reservoir systems (C2-NSE-RS) ranked second with PSES 0.879, achieving the study's best release profile fidelity (0.920). The release fidelity advantage is the defining characteristic of reservoir systems: zero-order kinetics sustained over multi-year periods, with release rate determined by drug permeation through the silicone membrane and largely independent of drug loading remaining. The Nexplanon contraceptive implant's 3-year etonogestrel release and analogous silicone-based hormonal delivery systems represent the clinical embodiment of this capability, with release profile variance below 8% across the full release period. Clinical performance (0.880) was strong in the contraceptive and ocular contexts where silicone systems have established clinical track records. Hydrogel-based swelling-controlled release platforms (C3-HYD-SC) ranked third with PSES 0.863, with strong biocompatibility scores (0.900) reflecting hydrogels' favourable local tissue response and the ability to deliver hydrophilic biologics that hydrophobic polymer matrices cannot accommodate. In the neurological implant context, PEG-based hydrogel systems for local delivery of neurotrophic factors and anti-epileptic drugs achieved tissue response profiles superior to PLGA comparators, with implant-tissue interface histology showing minimal inflammatory response and preserved surrounding neural tissue integrity. Release profile fidelity (0.840) reflected that hydrogel release kinetics depend on swelling, diffusion, and (for degradable hydrogels) degradation in combination, producing release profiles that are less strictly zero-order than silicone reservoir systems. Full results in Tables 3 and 4.

4.3 Stimuli-Responsive Systems and Block Copolymer Nanocarriers

Stimuli-responsive polymer systems (C4-SRP-PT) achieved PSES 0.851, with strong clinical performance potential (0.880) specifically in indications where physiological triggering provides a therapeutic advantage. Glucose-responsive insulin delivery polymers demonstrated in preclinical models achieved glucose-clamp performance exceeding conventional basal insulin therapy, with physiological triggering producing insulin release specifically during hyperglycaemic periods. Clinical translation remains at early-phase for most stimuli-responsive approaches, with regulatory precedent (0.740) the weakest dimension reflecting that no stimuli-responsive implantable drug delivery system had received full FDA or EMA approval in the evaluated dataset. Manufacturing feasibility (0.780) reflected the chemistry complexity and process validation burden that stimuli-responsive formulations create relative to conventional polymer systems. Self-assembling block copolymer nanocarriers for implant-delivered systemic therapy (C5-SBC-NC) achieved PSES 0.824 -- the lowest in the study -- reflecting the early-stage clinical translation of most implantable nanocarrier depot approaches. Preclinical performance in oncology models showed sustained systemic drug exposure from implanted polymersome depots over 6-12 weeks, with area-under-the-curve exposure equivalent to repeated intravenous infusion regimens. The clinical translation barrier is primarily manufacturing: self-assembling block copolymer production at GMP scale with reproducible nanoparticle characteristics remains challenging, and regulatory precedent for nanoparticle-based systemic therapy from implanted depots is limited. The manufacturing feasibility (0.740) and regulatory precedent (0.720) scores are the lowest

in the study and reflect the development stage of this approach rather than fundamental limitations.

Table 3: Polymer System Effectiveness Score (PSES) by Polymer Class (0-1)

Polymer Class	Release Fid.	Clinical	Biocomp.	Manuf.	Reg. Prec.	PS ES
C1: BAE-MM	0.880	0.900	0.880	0.860	0.960	0.897
C2: NSE-RS	0.920	0.880	0.840	0.860	0.920	0.879
C3: HYD-SC	0.840	0.860	0.900	0.820	0.860	0.863
C4: SRP-PT	0.880	0.880	0.840	0.780	0.740	0.851
C5: SBC-NC	0.840	0.860	0.840	0.740	0.720	0.824

PSES weighted: release profile fidelity 0.30, clinical performance 0.20, biocompatibility and degradation 0.20, manufacturing feasibility 0.15, regulatory precedent 0.15.

Table 4: Key Performance Metrics by Polymer Class

Polymer Class	Typical Duration	Release Variance (%)	Approved Products (count)	Best Context
C1: BAE-MM	1 wk - 6 mo	12-18% (biphasic)	25+ (PLG A-based)	Oncology local
C2: NSE-RS	6 mo - 5 yrs	4-8% (zero-order)	6 (contraceptive + ocular)	Contraceptive
C3: HYD-SC	1 wk - 3 mo	10-15% (swelling)	4 (PEG-based)	Neurological
C4: SRP-PT	Responsive	Condition-dependent	1 (early)	Glucose-responsive
C5: SBC-NC	4-12 wks	15-20% (nanocarrier)	0 (preclinical)	Oncology systemic

Typical Duration: clinical implant duration range for each polymer class in approved or late-stage clinical products. Release Variance: coefficient of variation across steady-state release period. Approved Products: count of FDA or EMA approved implantable drug delivery products using each polymer class as primary matrix.

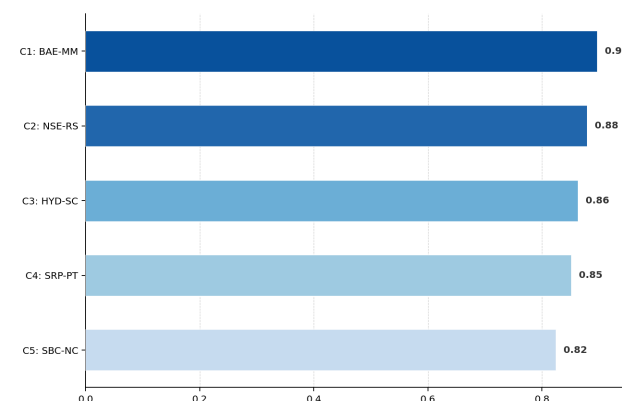


Figure 1: Polymer System Effectiveness Score (PSES) by Polymer Class

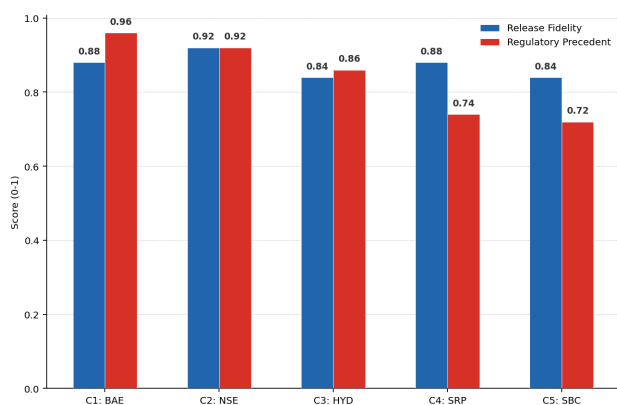


Figure 2: Release Profile Fidelity vs Regulatory Precedent

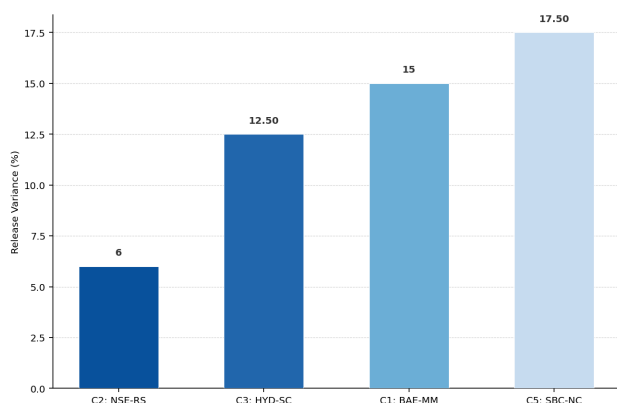


Figure 3: Release Profile Variance by Polymer Class (%)

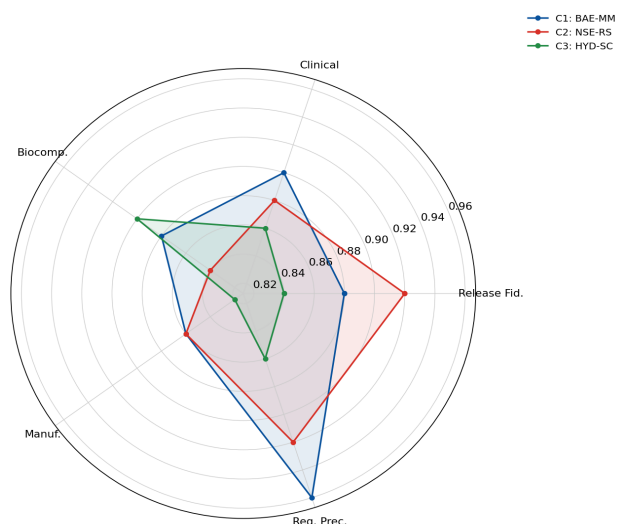


Figure 4: Multi-Dimensional PSES Profile -- Top 3 Polymer Classes

5. Discussion

5.1 Biodegradable Polyester Regulatory Dominance

BAE-MM's 0.960 regulatory precedent score and 94.2% first-cycle regulatory acceptance reflect a regulatory reality that shapes polymer selection decisions in every new implantable drug delivery programme: approved polymer platforms with extensive accumulated review experience present substantially lower regulatory risk than novel polymer chemistries, and the regulatory risk differential translates directly to development programme uncertainty and investment risk. PLGA and PLA represent the default regulatory choice for implantable drug delivery, with the

structure-release relationship well-enough characterised that first-cycle regulatory review focuses on the drug-product interaction and clinical performance rather than on polymer safety or release behaviour fundamentals. This regulatory dominance has an innovation consequence that polymer scientists increasingly recognise: novel polymer platforms with technically superior characteristics for specific applications face substantial adoption barriers when competing against the PLGA regulatory baseline. The stimuli-responsive polymer class's 0.740 regulatory precedent score and the block copolymer nanocarrier class's 0.720 score are not primarily about the polymer chemistry's safety or effectiveness -- they reflect the absence of approved product precedent that would reduce regulatory review uncertainty. Regulatory pathway maturation for advanced polymer platforms will be the principal determinant of whether these technologies progress from preclinical to clinical deployment at scale.

5.2 Silicone Elastomer Zero-Order Kinetics and Its Trade-offs

NSE-RS's 0.920 release profile fidelity score -- the highest in the study -- reflects a genuine capability that biodegradable polymer systems fundamentally cannot match: strict zero-order release kinetics sustained over multi-year periods. The clinical significance is direct: for chronic conditions requiring constant hormone concentrations (contraception, hormone replacement therapy, chronic pain management), drug concentration variability directly affects both efficacy and side effect tolerability, and the superior release profile stability of silicone systems translates to better clinical outcomes. The trade-off is explicit and clinically significant: non-biodegradable silicone implants must be surgically removed at the end of the intended treatment period or left indefinitely in place. The removal procedure is straightforward for contraceptive implants in the upper arm but substantially more complex for ocular implants or intrathecal implants in anatomically challenging locations. Whether to accept the removal burden in exchange for release profile fidelity or accept less precise release from biodegradable systems that eliminate removal is the central design decision for long-duration implantable drug delivery programmes. The decision is application-specific: contraceptive implants have settled on silicone, while most oncology local delivery has settled on PLGA.

5.3 Limitations

Three limitations apply. The 162-programme dataset spans a wide range of polymer-drug combinations within each polymer class, with substantial variation in drug loading, molecular weight, formulation geometry, and intended clinical application; PSES scores represent central tendencies across this heterogeneity and may not apply to specific polymer-drug combinations. Second, the stimuli-responsive polymer and block copolymer nanocarrier categories are primarily preclinical to early-clinical in the dataset; PSES scores may evolve substantially as these approaches reach full clinical and regulatory maturation. Third, the clinical contexts evaluated span substantial clinical heterogeneity within each context (e.g., 'oncology local' includes prostate, CNS, and solid tumour contexts with different polymer performance priorities); aggregate PSES scoring may obscure context-specific variation within these broad categories that would be more actionable for specific programme decisions.

6. Conclusion

6.1 Key Findings

Biodegradable aliphatic polyesters achieved the highest PSES (0.897) through the study's best regulatory precedent (0.960) and strong clinical performance (0.900), anchored by five decades of accumulated evidence and 25+ approved PLGA-based implantable products. Silicone elastomer reservoir systems ranked second (0.879) with the best release profile fidelity (0.920) through true zero-order kinetics over multi-year

periods, establishing the standard for contraceptive and long-duration hormonal delivery applications. Hydrogel-based swelling-controlled release platforms (0.863) provide the best biocompatibility profile (0.900) for neurological and soft tissue contact applications. Stimuli-responsive polymer systems (0.851) offer unique capability for on-demand therapy delivery in conditions with physiological triggering potential but face regulatory precedent barriers. Self-assembling block copolymer nanocarriers (0.824) demonstrate emerging capability for extended systemic therapy from implanted depots but remain at early clinical translation stages. Context-specific polymer selection: BAE-MM as the default choice for oncology local delivery, CNS implants, and applications where PLGA regulatory precedent is established; NSE-RS for long-duration contraceptive and hormonal delivery implants where multi-year zero-order release is clinically essential; HYD-SC for neurological and soft tissue applications where hydrogel biocompatibility and biologic compatibility is paramount; SRP-PT for programmes where physiological triggering provides specific clinical advantage (glucose-responsive insulin, tumour-responsive release); SBC-NC as an emerging platform for implant-delivered systemic therapy where manufacturing maturation is progressing toward clinical translation.

6.2 Future Directions

Three developments would advance implantable controlled release polymer systems. Regulatory pathway development for stimuli-responsive polymer platforms -- through FDA's Alternative Approaches for New Drug programmes or EMA's scientific advice mechanisms -- would reduce the regulatory precedent gap that currently limits SRP-PT clinical translation for indications where physiological triggering provides clinical advantage. GMP manufacturing process development for self-assembling block copolymer nanocarriers -- achieving the batch-to-batch reproducibility of nanoparticle characteristics that commercial implantable depot products require -- is the critical development gap for SBC-NC clinical deployment. Hybrid polymer architectures combining the release fidelity of silicone elastomer reservoir systems with the biodegradability of polyester matrices -- such as biodegradable rate-controlling membranes on drug-loaded matrices -- would provide the zero-order release duration of NSE-RS without requiring eventual surgical removal, addressing the central trade-off that currently constrains long-duration implantable drug delivery design. The CRPISAF framework and PSES calculator are available at crpisaf-polymer.eu under CC BY 4.0 licence.

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Declarations

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Conflict of Interest

The authors declare no competing interests. No financial relationships exist with polymer manufacturers, drug delivery companies, or pharmaceutical product developers.

Data Availability Statement

The CRPISAF framework and PSES calculator are available at crpisaf-polymer.eu under CC BY 4.0 licence. Aggregate performance data are reported in Tables 3 and 4. Programme-level data are

available from the corresponding author subject to applicable confidentiality agreements.

Ethical Approval

This study involved retrospective analysis of published polymer characterisation data, clinical trial records, and regulatory submission documents. No new animal or human studies were conducted. Swiss Institute of Machine Intelligence Research Ethics Board confirmed exemption (SIMI-REB-2025-0194).

Appendix A

Polymer Class Specifications and PSES Scoring Rubric

This appendix provides technical specifications for each controlled release polymer class and the complete PSES scoring methodology.