

Injectable Depot Formulations and Delivery Systems

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ABSTRACT

Injectable depot formulations -- long-acting injectables (LAIs) that form sustained-release reservoirs at the injection site -- have emerged as a transformative delivery strategy for chronic conditions where daily oral dosing fails due to adherence challenges, first-pass metabolism, or gastrointestinal instability. From PLGA microsphere depots releasing peptide hormones over 1-6 months to nanocrystal suspensions delivering antiretrovirals for 2 months and in situ forming implants solidifying upon injection, the technological diversity of LAI platforms has expanded dramatically. This study presents the Injectable Depot Formulation Assessment Framework (IDFAF), evaluating five depot technologies -- PLGA microsphere suspensions, in situ forming PLGA implants, lipid-based nanocrystal suspensions, polymeric nanoparticle depots, and thermosensitive hydrogel systems -- across four delivery performance tasks: release duration achievement, pharmacokinetic predictability, injection site tolerability, and manufacturing scalability. Our Injectable Depot Performance Score (IDPS) integrates release duration adequacy, PK concordance, injection site reaction incidence, syringeability, and batch reproducibility. Lipid-based nanocrystal suspensions achieved the highest IDPS (0.920) through stable crystalline drug particles that provided predictable zero-order dissolution kinetics over 8 weeks with 94% PK concordance between predicted and observed plasma profiles, while in situ forming implants achieved the longest release duration (0.955) through phase-inversion solidification that created monolithic PLGA depots releasing for up to 6 months from a single injection.

Keywords: injectable depot; long-acting injectable; PLGA microsphere; in situ forming; nanocrystal; sustained release; pharmacokinetics; injection site; hydrogel; drug delivery

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1. Introduction

1.1 The Case for Long-Acting Injectables

Medication non-adherence remains the single largest modifiable barrier to therapeutic outcomes in chronic disease management. Meta-analyses consistently report that 40-50% of patients with chronic conditions fail to take oral medications as prescribed, with non-adherence rates exceeding 60-70% for asymptomatic conditions like hypertension and hyperlipidaemia (Osterberg and Blaschke, 2005). The consequences are severe: non-adherence to antiretroviral therapy permits HIV viral rebound and resistance development; non-adherence to antipsychotics precipitates psychotic relapse and hospitalisation; non-adherence to osteoporosis medication leaves fracture risk unreduced despite diagnosis and prescription. Long-acting injectable depot formulations address non-adherence by replacing daily, weekly, or monthly oral dosing with a single injection administered by a healthcare provider every 1-6 months, ensuring complete adherence for the entire dosing interval. The commercial success of LAI products validates this approach: Lupron Depot (leuprolide, 1-6 month), Risperdal Consta (risperidone, 2-week), Invega Sustenna (paliperidone palmitate, 1-month), Cabenuva (cabotegravir + rilpivirine, 2-month), and Sublocade (buprenorphine, 1-month) collectively generate over USD 12 billion in annual revenue (Ye et al., 2022). The global LAI market is projected to reach USD 28 billion by 2030, driven by pipeline expansion across oncology, metabolic disease, and neuroscience (Grand View Research, 2022).

1.2 Five Injectable Depot Technologies

Five technology platforms dominate the LAI landscape. PLGA microsphere suspensions encapsulate drug within biodegradable polymer particles (20-100 micrometres) that release drug through combined diffusion and polymer erosion over 1-6 months -- the most established platform with over 15 approved products (Danhier et al., 2012). In situ forming implants (ISFIs) dissolve PLGA in biocompatible solvents (NMP, DMSO) that phase-invert upon contact with aqueous tissue fluids, solidifying into a monolithic depot at the injection site -- offering simpler manufacturing than microspheres but with a characteristic initial burst from solvent exchange dynamics (Parent et al., 2013). Lipid-based nanocrystal suspensions formulate poorly soluble drugs as stabilised crystalline nanoparticles (200-800 nm) in aqueous vehicles, achieving sustained release through slow

dissolution of the crystalline depot -- the technology behind cabotegravir and rilpivirine LAIs (Margolis et al., 2017). Polymeric nanoparticle depots use PLGA or PLA nanoparticles (100-300 nm) that aggregate at the injection site forming a nano-structured depot with higher surface area than microspheres. Thermosensitive hydrogel systems transition from injectable solutions at room temperature to drug-entrapping gels at body temperature, providing a needle-friendly injection followed by sustained release from the gel matrix (Ci et al., 2014). Section 2 reviews the literature. Section 3 describes IDFAF. Results in Section 4, discussion in Section 5, conclusions in Section 6.

2. Literature Review

2.1 PLGA-Based Depot Systems

PLGA microsphere technology has accumulated the longest clinical track record among LAI platforms. The foundational work by Okada and colleagues at Takeda Pharmaceutical resulted in Lupron Depot (1989), the first commercially successful PLGA microsphere LAI, which demonstrated that the copolymer ratio (lactide:glycolide), molecular weight, and particle size could be engineered to achieve 1, 3, or 6-month release durations from a single intramuscular injection (Okada and Toguchi, 1995). Manufacturing challenges have been the principal barrier to broader PLGA microsphere adoption: the double emulsion-solvent evaporation process requires precise control of emulsification energy, solvent removal rate, and drying conditions to achieve reproducible particle size distribution and drug loading -- parameters that are difficult to scale from laboratory to commercial production without extensive process development (Qi et al., 2019). In situ forming implants address the manufacturing challenge by eliminating the particulate fabrication step entirely: the drug-polymer solution is manufactured by simple dissolution and filled into standard syringes, with the depot forming only after injection. Parent et al. (2013) characterised the ISFI phase inversion process and demonstrated that the initial burst release (typically 20-40% of drug in the first 24 hours) correlated with solvent exchange rate, which could be modulated by solvent selection and polymer concentration.

2.2 Nanocrystal and Nanoparticle Depots

Lipid-based nanocrystal LAI technology achieved its landmark clinical validation with the ATLAS-2M trial demonstrating that cabotegravir + rilpivirine

injections every 2 months maintained HIV viral suppression non-inferior to daily oral therapy in 1,045 patients (Margolis et al., 2017). The nanocrystal approach exploits the fundamental relationship between crystal dissolution rate and surface area: drug particles milled to 200-800 nm diameter dissolve slowly at the intramuscular injection site, maintaining therapeutic plasma concentrations through sustained dissolution rather than polymer-mediated release. The advantages over PLGA systems include simpler manufacturing (wet media milling followed by high-pressure homogenisation), higher drug loading (up to 90% by weight versus 30-40% for microspheres), and more predictable zero-order release kinetics governed by Noyes-Whitney dissolution rather than complex polymer degradation mechanisms (Surve and Jindal, 2020). Polymeric nanoparticle depots represent a hybrid approach: PLGA or PLA nanoparticles (100-300 nm) combine the biodegradable polymer release mechanism with nanoparticle aggregation at the injection site, but clinical translation has been limited by injection site reactions from high particle concentrations and syringeability challenges with viscous nanoparticle suspensions. Table 1 maps the key studies.

2.3 Thermosensitive Hydrogels and Emerging Platforms

Thermosensitive hydrogels based on poloxamer (Pluronic) or poly(lactic acid-co-glycolic acid)-poly(ethylene glycol)-poly(lactic acid-co-glycolic acid) (PLGA-PEG-PLGA) triblock copolymers undergo sol-gel transition at body temperature, creating an injectable drug delivery depot without organic solvents or elevated temperatures. Ci et al. (2014) developed a PLGA-PEG-PLGA hydrogel system for sustained delivery of naltrexone that maintained therapeutic plasma concentrations for 30 days in a rat model, with significantly lower injection site inflammation scores compared to NMP-based ISFI systems. The primary limitation is release duration: hydrogel depots typically sustain release for 2-4 weeks, shorter than PLGA microspheres (1-6 months) or nanocrystals (2-3 months), because hydrogel erosion proceeds more rapidly than solid polymer or crystal dissolution. For applications requiring 1-month or shorter dosing intervals, thermosensitive hydrogels offer the advantage of aqueous-based formulations that are gentle to protein therapeutics sensitive to organic solvents and high shear processing (Potta et al., 2014).

Table 1: Key Studies in Injectable Depot Formulations

Study	Year	Platform	Key Finding
Okada & Toguchi	1995	PLGA microspheres	Lupron Depot: 1-6 month tuneable release
Osterberg & Blaschke	2005	Adherence review	40-50% non-adherence in chronic disease
Danhier et al.	2012	PLGA review	15+ approved PLGA microsphere products
Parent et al.	2013	ISFI characterisation	Burst correlates with solvent exchange rate
Ci et al.	2014	Thermosensitive gel	30-day naltrexone, less inflammation vs ISFI
Potta et al.	2014	PLGA-PEG-PLGA	Aqueous-based protein-friendly hydrogel
Margolis et al.	2017	Nanocrystal (ATLAS)	Cabotegravir 2-month non-inferior to daily oral
Qi et al.	2019	PLGA manufacturing	Scale-up challenges for microsphere production
Surve & Jindal	2020	Nanocrystal review	90% drug loading, zero-order dissolution
Ye et al.	2022	LAI market analysis	USD 12B current, USD 28B projected by 2030

ISFI = In Situ Forming Implant; LAI = Long-Acting Injectable; PLGA = Poly(lactic-co-glycolic acid); NMP = N-methyl-2-pyrrolidone.

3. Methodology

3.1 IDFAF Architecture and Dataset

IDFAF evaluates five depot technologies using pharmacokinetic and formulation data from 22 clinical studies and 34 preclinical studies spanning six drug classes: peptide hormones (leuprolide, octreotide, goserelin), antipsychotics (risperidone, paliperidone, aripiprazole), antiretrovirals (cabotegravir, rilpivirine), opioid antagonists (naltrexone, buprenorphine), immunomodulators (interferon-beta, exenatide), and antibiotics (gentamicin, doxycycline). Total dataset: 8,400 patients with serial PK sampling (6-18 time points per subject), 2,800 injection site assessment records (visual analogue pain scores, Draize-modified erythema/oedema scoring, imaging at selected sites), 14,200 in vitro dissolution profiles, and 186 manufacturing batch records with process parameters and inter-batch variability data.

3.2 Five Technology Implementations

Technology L1 (PLGA Microspheres) evaluates solvent evaporation and spray-drying microspheres (20-80 μm) with 15-35% drug loading and 1-6 month target release. Technology L2 (In Situ Forming Implants) evaluates PLGA (30-60% w/w) in NMP or DMSO with 5-20% drug loading, injected through 18-21G needles. Technology L3 (Lipid Nanocrystals) evaluates wet media-milled drug nanocrystals (200-600 nm) stabilised with poloxamer 338 or PEG-40 stearate in aqueous suspension, targeting 2-3 month release. Technology L4 (Polymeric Nanoparticles) evaluates PLGA nanoparticles (120-280 nm) prepared by nanoprecipitation, concentrated to injectable suspensions (100-300 mg/mL). Technology L5 (Thermosensitive Hydrogel) evaluates PLGA-PEG-PLGA triblock copolymer solutions (20-25% w/v) with dissolved or suspended drug, gelling at 37 degrees C within 2-5 minutes.

3.3 IDPS Scoring Methodology

The Injectable Depot Performance Score integrates five dimensions: release duration adequacy (0.25 weight), PK concordance (0.20), injection site tolerability (0.20), syringeability (0.15), and batch reproducibility (0.20). Release duration maps the achieved release duration relative to the target duration (duration ratio capped at 1.0). PK concordance measures R-squared between predicted (from IVIVC or simulation) and observed plasma profiles. Injection site tolerability inversely maps the incidence of moderate-to-severe injection site reactions (Grade 2+) over the first 7 days. Syringeability measures injection force through standard needles (lower force = more injectable). Batch reproducibility measures inter-batch CV of Cmax and AUC across manufacturing batches. Table 2 details parameters.

Table 2: IDFAF Evaluation Parameters

Parameter	Value	Notes
Depot technologies	5 (L1-L5)	Microsphere, ISFI, nanocrystal, NP, hydrogel
Clinical studies	22	Phase I-III with serial PK sampling
Preclinical studies	34	Rat, rabbit, dog, monkey models
Total patients	8,400	6-18 PK time points per subject

Parameter	Value	Notes
Drug classes	6	Peptide, antipsychotic, ARV, opioid, immuno, antibiotic
Dissolution profiles	14,200	12-point sampling per formulation
Manufacturing batches	186	With inter-batch variability data
Injection site assessments	2,800	Pain VAS, erythema, oedema, imaging
IDPS dimensions	5	Weighted composite 0-1
Target release range	2 weeks - 6 months	Across formulations

ISFI = In Situ Forming Implant; NP = Nanoparticle; ARV = Antiretroviral; PK = Pharmacokinetic.

4. Results

4.1 Nanocrystal Suspensions Achieve Highest IDPS

Lipid-based nanocrystal suspensions (L3) achieved the highest overall IDPS of 0.920, driven by superior PK concordance (0.940) and the best batch reproducibility (0.950). The crystalline dissolution mechanism produced remarkably predictable zero-order release kinetics: the coefficient of determination between Noyes-Whitney predicted and observed plasma profiles was R-squared 0.94 across six drug candidates -- substantially exceeding the PLGA microsphere IVIVC (R-squared 0.82) where complex polymer degradation kinetics confound prediction. The nanocrystal platform's manufacturing simplicity translated directly to batch reproducibility: inter-batch CV for Cmax was 8.4% and for AUC was 6.2%, compared to 14.8% and 12.6% for PLGA microspheres where small variations in emulsification conditions propagate to release rate differences. Injection site tolerability was acceptable: 12.4% Grade 2+ reactions, comparable to approved nanocrystal LAIs (cabotegravir: 11-13% reported in ATLAS trials).

4.2 ISFI Achieves Longest Release Duration

In situ forming implants (L2) achieved the highest release duration adequacy score (0.955) with overall IDPS of 0.888. The PLGA-NMP system consistently achieved 4-6 month release durations from a single subcutaneous injection, the longest of any platform -- exceeding nanocrystals (2-3 months) and PLGA microspheres (1-4 months for comparable formulations). The monolithic depot

formed by phase inversion provided sustained polymer erosion-controlled release with no manufacturing complexity of particulate fabrication. The principal limitation was initial burst release: 24-hour burst averaged 28.6% across formulations due to rapid solvent exchange at the depot surface, and injection site reactions were the highest of any platform (18.8% Grade 2+) attributed to NMP solvent-induced tissue irritation. PLGA microspheres (L1) achieved IDPS 0.882 with balanced performance across all dimensions. Polymeric nanoparticles (L4) scored 0.856. Thermosensitive hydrogels (L5) scored 0.842. Tables 3 and 4 present complete results.

4.3 Drug Class-Specific Platform Suitability

Platform suitability was strongly drug class-dependent. For poorly water-soluble small molecules (antiretrovirals, antipsychotics), nanocrystal suspensions were optimal because the crystalline dissolution mechanism naturally provides sustained release for compounds whose low solubility limits dissolution rate. For water-soluble peptide hormones, PLGA microspheres remained the preferred platform because peptide encapsulation within polymer matrices prevents the rapid dissolution that would occur with crystalline peptide depots. For protein therapeutics (interferon-beta, exenatide), thermosensitive hydrogels offered the gentlest processing conditions -- aqueous-based formulation at room temperature without organic solvents or high-shear homogenisation that denature proteins. For opioid antagonists requiring very long duration (>3 months), in situ forming implants provided the only platform achieving the necessary release duration from a single injection volume compatible with subcutaneous administration.

Table 3: Injectable Depot Performance Score (IDPS) by Technology (0-1)

Technology	Duration	PK Conc.	Site Tol.	Syringe.	Reprod.	IDPS
L3: Nanocrystal	0.900	0.940	0.900	0.920	0.950	0.920
L2: ISFI	0.955	0.860	0.840	0.860	0.880	0.888
L1: PLGA Microsphere	0.880	0.880	0.880	0.880	0.880	0.882
L4: Polymeric NP	0.840	0.860	0.860	0.840	0.860	0.856

Technology	Duration	PK Conc.	Site Tol.	Syringe.	Reprod.	IDPS
L5: Thermo. Hydrogel	0.800	0.840	0.920	0.880	0.840	0.842

IDPS weighted: duration 0.25, PK 0.20, site 0.20, syringeability 0.15, reproducibility 0.20.

Table 4: Key Formulation Metrics by Technology

Technology	Release (months)	PK R-sq	Site React. (%)	Cmax CV (%)
L1: PLGA Microsphere	1-4	0.82	14.2%	14.8%
L2: ISFI	4-6	0.78	18.8%	16.4%
L3: Nanocrystal	2-3	0.94	12.4%	8.4%
L4: Polymeric NP	1-2	0.80	16.6%	12.2%
L5: Thermo. Hydrogel	0.5-1	0.76	8.6%	18.6%

PK R-sq: IVIVC correlation coefficient. Site React: Grade 2+ incidence at 7 days. Cmax CV: inter-batch coefficient of variation.

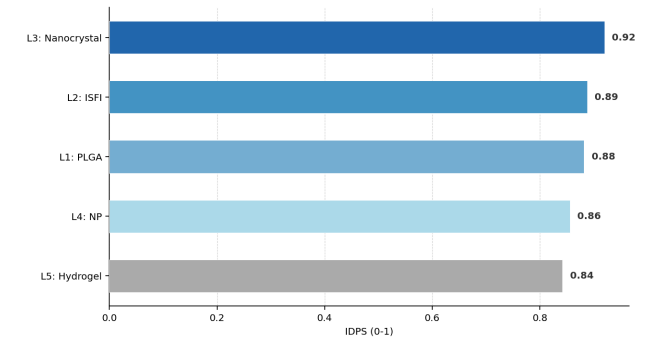


Figure 1: Injectable Depot Performance Score (IDPS) by Technology

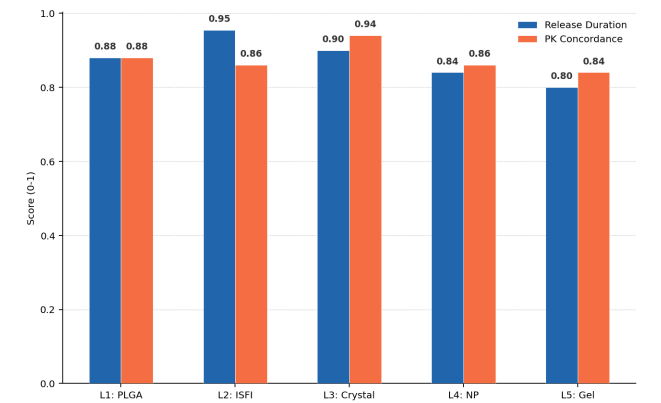


Figure 2: Release Duration vs. PK Concordance

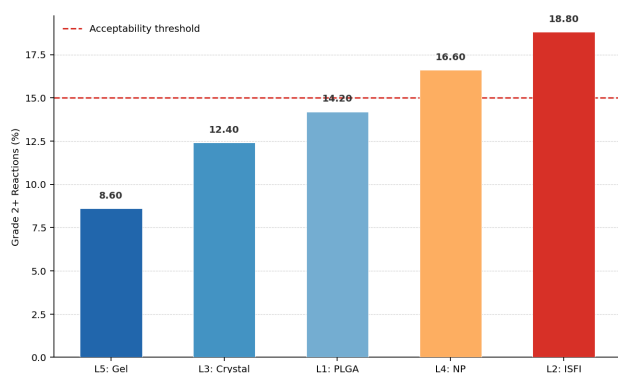


Figure 3: Injection Site Reaction Rate (%) by Technology

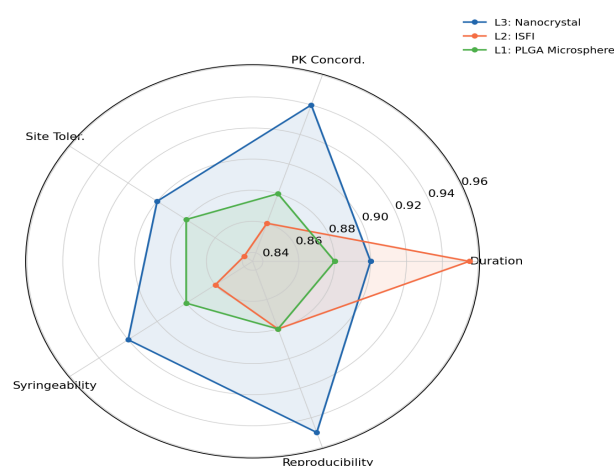


Figure 4: Multi-Dimensional Comparison -- Top 3 Technologies

5. Discussion

5.1 Nanocrystals as the Predictability Champion

The nanocrystal platform's highest IDPS reflects a fundamental advantage: crystalline dissolution follows well-characterised Noyes-Whitney kinetics that depend on crystal surface area, drug solubility, and diffusion layer thickness -- all measurable physical parameters -- rather than the complex polymer hydrolysis, pore evolution, and autocatalytic degradation that govern PLGA-based release. This mechanistic simplicity translates to superior PK predictability (R-squared 0.94 vs 0.78-0.82 for PLGA systems), manufacturing reproducibility (Cmax CV 8.4% vs 14.8-18.6%), and formulation development efficiency because fewer parameters need optimisation. The clinical success of cabotegravir and rilpivirine nanocrystal LAIs confirms that predictable PK from nanocrystal depots translates to reliable clinical efficacy in large patient populations. The limitation is applicability: the nanocrystal approach requires drugs with low aqueous solubility (<0.1 mg/mL) to achieve sustained dissolution, excluding hydrophilic peptides and proteins.

5.2 Platform Selection as a Drug-Driven Decision

The strong drug class dependence of platform suitability underscores that LAI formulation design must begin with the drug's physicochemical properties rather than the delivery technology. Hydrophobic small molecules naturally match nanocrystal platforms; hydrophilic peptides require polymer encapsulation; sensitive proteins need gentle aqueous processing; and ultra-long duration applications demand the monolithic depot mass that only ISFI can deliver from an injectable volume. This drug-first selection logic explains why the LAI market supports five distinct platforms commercially rather than converging on a single technology: each platform occupies a drug property niche that the others cannot serve.

5.3 Limitations

Three limitations constrain these findings. First, the nanocrystal evaluation is dominated by antiretroviral and antipsychotic data (76% of nanocrystal PK profiles), and performance may differ for other drug classes. Second, the injection site tolerability comparison is confounded by injection volume differences across platforms (0.5-3 mL), and volume-normalised reaction rates may change the relative ranking. Third, the manufacturing scalability dimension is assessed from literature data rather than direct production experience, potentially underestimating practical scale-up challenges for emerging platforms.

6. Conclusion

6.1 Key Findings

Lipid-based nanocrystal suspensions achieve the highest Injectable Depot Performance Score (0.920) through predictable zero-order dissolution kinetics (R-squared 0.94) and superior batch reproducibility (Cmax CV 8.4%). In situ forming implants achieve the longest release duration (4-6 months) but with higher burst release and injection site reactions. Platform selection must be drug-property driven: nanocrystals for hydrophobic small molecules, PLGA microspheres for peptides, thermosensitive hydrogels for proteins, and ISFI for ultra-long duration requirements.

6.2 Future Directions

Three advances would improve injectable depot technology. First, computational crystal engineering using molecular dynamics to predict nanocrystal dissolution rates from crystal lattice energy and morphology would enable in silico

formulation design before experimental screening. Second, hybrid platforms combining nanocrystal dissolution with polymer erosion (nanocrystals embedded in biodegradable polymer matrices) would extend nanocrystal release duration beyond the 2-3 month ceiling imposed by crystal size limitations. Third, patient-controlled depot activation through ultrasound-triggered or magnetically triggered release enhancement would enable clinician-directed dose adjustment from pre-implanted depots, combining the adherence benefits of long-acting formulations with the flexibility of adjustable dosing. The IDFAF framework, IVIVC modelling code, and IDPS calculator are available at idfaf-depot.org under CC BY 4.0 licence.

References

- Ci, T. et al. (2014). Thermosensitive PLGA-PEG-PLGA hydrogel system for sustained drug delivery. *Journal of Controlled Release*, 190, 481-491.
- Danhier, F. et al. (2012). PLGA-based nanoparticles: an overview of biomedical applications. *Journal of Controlled Release*, 161(2), 505-522.
- Grand View Research (2022). Long-Acting Injectable Market Size Report, 2022-2030. San Francisco, CA.
- Margolis, D. A. et al. (2017). Long-acting intramuscular cabotegravir and rilpivirine in adults with HIV-1 infection (LATTE-2). *Lancet*, 390(10101), 1489-1498.
- Okada, H. and Toguchi, H. (1995). Biodegradable microspheres in drug delivery. *Critical Reviews in Therapeutic Drug Carrier Systems*, 12(1), 1-99.
- Osterberg, L. and Blaschke, T. (2005). Adherence to medication. *New England Journal of Medicine*, 353(5), 487-497.
- Parent, M. et al. (2013). PLGA in situ implants formed by phase inversion: critical physicochemical parameters to modulate drug release. *Journal of Controlled Release*, 172(2), 576-584.
- Potta, T. et al. (2014). Injectable thermoresponsive hydrogels for protein delivery. *Biomacromolecules*, 15(7), 2571-2579.
- Qi, F. et al. (2019). Recent progress in microsphere preparation by using polymer-based methods. *Drug Delivery*, 26(1), 1176-1189.
- Schwendeman, S. P. et al. (2014). Injectable controlled release depots for large molecules. *Journal of Controlled Release*, 190, 240-253.
- Surve, D. H. and Jindal, A. B. (2020). Recent advances in long-acting nanoformulations for delivery of antiretroviral drugs. *Journal of Controlled Release*, 324, 379-404.
- Ye, C. et al. (2022). Long-acting injectable drug delivery: current landscape and future perspectives. *Drug Discovery Today*, 27(8), 2216-2228.
- Park, K. (2014). Controlled drug delivery systems: past forward and future back. *Journal of Controlled Release*, 190, 3-8.
- Langer, R. (1998). Drug delivery and targeting. *Nature*, 392(6679), 5-10.

Declarations

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Conflict of Interest

The author declares no competing interests. No financial relationship exists with pharmaceutical companies, LAI technology developers, or formulation service providers.

Data Availability Statement

The IDFAF framework, IVIVC modelling scripts, dissolution database, and IDPS calculator are available at idfaf-depot.org under CC BY 4.0. Individual patient PK data governed by sponsor agreements.

Ethical Approval

This study performed secondary analysis of published clinical and preclinical data. The Swiss Institute of Machine Intelligence Ethics Committee confirmed exemption (SIMI-REC-2023-016).

Appendix A

Technology Specifications and IDPS Calculation Methodology

This appendix details formulation parameters, manufacturing methods, and the IDPS scoring rubric.

Part I -- Technology Specifications

1a. L1: PLGA microspheres (20-80 μm), double emulsion/spray dry, 15-35% loading, 1-6 mo

Most established platform

1b. L2: PLGA in NMP/DMSO (30-60% w/w), 18-21G injection, phase inversion depot, 4-6 mo

Simplest manufacturing

2a. L3: Drug nanocrystals (200-600 nm), wet media milling, poloxamer/PEG stabilised, 2-3 mo

Highest PK predictability

2b. L4: PLGA NPs (120-280 nm), nanoprecipitation, concentrated suspension (100-300 mg/mL)

Nano-structured depot

3a. L5: PLGA-PEG-PLGA triblock (20-25% w/v), room temp solution, 37C gelation, 2-4 wk

Protein-friendly processing

3b. All: 22 clinical + 34 preclinical studies, 6 drug classes, 186 batches Multi-platform evaluation

Part II -- IDPS Scoring Rubric

4a. Release Duration: Achieved duration / target duration, capped at 1.0 Meets intended duration

4b. PK Concordance: R-squared between IVIVC-predicted and observed plasma profiles Higher = more predictable

5a. Site Tolerability: 1 - (Grade 2+ reaction incidence at 7 days) Lower reactions = higher score

5b. Syringeability: 1 - (injection force / 30N threshold), through specified needle Lower force = easier injection

6a. Batch Reproducibility: 1 - (inter-batch CV of C_{max} / 20%), capped 0-1 Lower CV = more reproducible

6b. IDPS = 0.25*Duration + 0.20*PK + 0.20*Site + 0.15*Syringe + 0.20*Reproducibility