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Designing Dosage Forms across Competing Objectives: A Decision-Theoretic Framework for Artificial Intelligence–Guided Formulation Development Linking Excipient Compatibility, Drug Release, Manufacturability, and Patient Use

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ABSTRACT

Artificial intelligence is increasingly used to predict formulation performance, screen excipient combinations, estimate drug-release behavior, characterize manufacturing processes, and prioritize candidate dosage forms. Yet formulation development rarely presents a single objective for which the highest predicted value identifies the most defensible product. A formulation with favorable release behavior may create incompatibility risk, processing difficulty, scale-up vulnerability, unacceptable quality variation, or burdensome administration for the intended patient population. This article develops a non-empirical decision-theoretic account of AI-guided formulation development in which compatibility, release, manufacturability, quality, and patient use are represented as interacting but analytically distinct decision dimensions. The framework distinguishes predictive evidence from decision consequences, compensable trade-offs from feasibility violations, and model confidence from the evidentiary sufficiency required to advance a candidate. It also treats patient-use requirements as upstream formulation objectives rather than downstream implementation considerations. The central proposition is that AI becomes most useful when it helps identify trade-offs, update uncertain evidence states, and prioritize informative experiments rather than when it collapses heterogeneous formulation objectives into a single optimization score. A candidate should therefore advance only when its advantages remain defensible after objective-specific uncertainty, manufacturing feasibility, compatibility evidence, release relevance, and patient-use consequences are considered together. Under conditions of domain shift, incomplete validation, non-compensable constraints, or decision-relevant uncertainty, the appropriate response may instead be to revise the formulation, request additional evidence, or stop development. This formulation-centered decision logic provides a basis for using AI without allowing predictive performance to substitute for pharmaceutical judgment.

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Introduction

Artificial intelligence has moved beyond isolated applications in molecular discovery and is now used across formulation development, pharmaceutical manufacturing, quality control, and other stages of the product lifecycle [1]. That expansion changes the practical problem faced by formulation scientists. The relevant question is no longer simply whether a model can predict a useful formulation property. It is whether predictions generated for different properties can be combined into a defensible choice among candidate dosage forms. Methodological work on machine learning in drug formulation already emphasizes reliability, interpretability, data quality, and appropriate validation as requirements for useful implementation [2].

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Broader assessments of artificial intelligence in drug delivery similarly describe considerable technical opportunity while retaining concerns about heterogeneous data, model transparency, transferability, and implementation [3]. These limitations become especially important when the object of prediction is not itself the final object of decision.

Solid-dosage development illustrates why this distinction matters. Formulation performance emerges from interactions among active pharmaceutical ingredient characteristics, excipient selection, composition, processing conditions, critical quality attributes, and release behavior [4]. Machine learning can help search these high-dimensional relationships, particularly where conventional intuition or sequential experimentation struggles with nonlinear structure–function associations [5]. Yet increasing predictive power does not make the development problem one-dimensional. A model may predict dissolution, physical stability, compressibility, particle size, or another output accurately while leaving unresolved whether that predicted improvement is worth the consequences imposed on other objectives. The computational task of identifying a promising region of formulation space is therefore related to, but not equivalent to, the pharmaceutical task of selecting a product for continued development.

Recent formulation studies make this separation increasingly visible. Bayesian optimization has been applied to biologic formulations in which several developability properties were optimized simultaneously and responses to formulation conditions could move in different directions [6]. Automated active-learning approaches likewise show how experiments can be selected iteratively so that new observations update a multi-property formulation search [7]. These approaches are important because they replace exhaustive exploration with informed sequential learning. They do not, however, resolve the downstream normative question of how a development team should act when objectives remain in conflict, when a nominal optimum is poorly supported by evidence, or when an apparently superior candidate violates a practical feasibility condition. A Pareto-efficient candidate can still be unsuitable for advancement if its location on the trade-off surface depends on evidence that is too uncertain or if an important objective has been omitted.

One frequently omitted objective is the way the intended patient must actually use the product. Patient-centric product-development roadmaps argue that patient needs should influence target product characteristics during development rather than being considered only after a dosage form is substantially fixed [8]. This principle extends beyond convenience. Characteristics such as route of administration, handling complexity, dosing burden, and the match between product demands and patient capabilities can become pharmaceutical design considerations [9]. Reviews linking product design to adherence further indicate that dosage-form characteristics may influence whether medicines can be accepted and used as intended, although adherence is also shaped by behavioral, clinical, economic, and social factors outside formulation itself [10]. Patient use should therefore enter the decision as a design objective without being treated as a deterministic outcome of formulation.

The need for contextual interpretation is equally important. Interviews with older people, carers, and healthcare professionals have identified tablet identification, handling, and swallowability as concrete characteristics affecting acceptance and use [11]. Industrial analyses of patient-centric development nevertheless describe practical tensions between incorporating patient input and established development timelines, technical constraints, and organizational processes [12]. Formulation innovation can reduce dosing burden, enable alternative routes, improve convenience, or support more targeted administration, but the relevance of those benefits depends on the therapy and the intended population [13]. Moreover, methods for comparing acceptability across patient populations remain incomplete, making it inappropriate to represent patient centricity as a universal scalar attribute that can simply be maximized [14].

The formulation problem addressed here is consequently more specific than the general proposition that AI can improve pharmaceutical development. Candidate dosage forms must be evaluated across objectives that differ in measurement, evidentiary maturity, consequences of failure, and potential for compensation. Compatibility may operate as a feasibility condition; release behavior may be a performance objective whose interpretation depends on the intended mechanism and test conditions; manufacturing feasibility may constrain what can be scaled reproducibly; and patient-use requirements may be either minimum acceptability conditions or preference-sensitive objectives. The analytical task is to explain how these objectives should coexist within one decision architecture without assuming that a single predictive score can legitimately substitute for their differences.

Formulation Development as a Multiobjective Decision Problem

Manufacturability makes the multiobjective character of formulation development particularly clear because the dosage form ultimately has to exist as a reproducible product, not merely as a favorable laboratory composition. Artificial neural networks and related methods have increasingly been used within process analytical technology to connect process measurements with pharmaceutical manufacturing states and quality attributes [15]. Artificial intelligence and machine learning are also being investigated for prediction, monitoring, optimization, and control across biopharmaceutical manufacturing [16]. These developments show that process behavior can be modeled, but they also expose an important distinction: a model that predicts manufacturing behavior contributes evidence about feasibility; it does not make manufacturing feasibility interchangeable with therapeutic or biopharmaceutical performance.

Excipient compatibility provides a different type of decision pressure. Machine-learning methods can classify drug–excipient combinations and prioritize likely incompatibilities from molecular representations and associated descriptors [17]. Such predictions can reduce the number of combinations requiring undirected experimental screening, but compatibility differs from a preference-like objective. If an excipient creates a sufficiently serious chemical or physical incompatibility under relevant conditions, favorable performance elsewhere may not compensate for that defect. Compatibility therefore often behaves as a

constraint that can remove a candidate from consideration rather than as a dimension on which poor performance can always be traded for greater benefit on another attribute. Predictive uncertainty matters correspondingly more when the consequence of a false reassurance is costly.

Drug release creates a second type of conflict because it is desirable only relative to the intended product concept. Comparative modeling of extended-release matrix tablets has shown that different data-driven approaches can reproduce release behavior from formulation information, while relative model performance depends on the formulation and analytical context [18]. Machine learning applied to Raman spectra has likewise predicted release from polysaccharide coatings under simulated colonic conditions, demonstrating how an orthogonal measurement can become informative about a performance property [19]. These studies support the use of predictive models for release-related decisions, yet neither predicted nor experimentally measured in vitro release is automatically equivalent to clinical benefit. A formulation may achieve an attractive release profile while demanding excipients, coating structures, process conditions, or dosage-form dimensions that worsen manufacturing robustness or patient use.

The same interdependence appears when composition and processing are considered together. In pharmaceutical suspensions, machine-learning analysis has been combined with structured formulation experiments to identify interactions among stabilizer choice, concentration, processing conditions, particle size, and physical stability [20]. In liposomal development, machine-learning models have been used to relate lipid composition and microfluidic process variables to formation behavior, particle characteristics, and production parameters [21]. Such studies undermine a simple separation in which formulation is optimized first and manufacturing is checked later. Material choices can alter the process window, while process constraints can alter which material combinations are practically attractive. The candidate formulation and the method by which it can be made are therefore partly co-determined.

Scale-up makes this coupling consequential. Formulation-development decisions that disregard scale can produce candidates whose laboratory advantages are difficult to preserve when translated into larger, faster, or differently configured production systems [22]. Independent process measurements can consequently provide evidence capable of changing an earlier formulation judgment. For example, ultrasonic measurements coupled with machine learning have been investigated for nondestructive assessment of tablet quality attributes relevant to continuous manufacturing and real-time release concepts [23]. The point is not that a specific monitoring technology should determine formulation selection. Rather, manufacturing evidence can reveal that a composition which appears favorable on compatibility or release grounds carries a quality or process penalty that materially changes its overall development value.

The principal conflicts are therefore not all of the same kind. Some objectives admit graded trade-offs; others can become feasibility conditions. Some are measured directly, while others are model-derived. Some concern the product, others the process through which the product is made, and others the interaction between dosage form and patient. Treating them as independent columns in an optimization dataset would conceal precisely the relationships that make formulation development difficult. The relevant unit of analysis is instead the decision conflict created when improvement on one formulation dimension changes the value, feasibility, or evidentiary interpretation of another.

The characteristic conflicts established in this section are summarized in **Table 1**.

Table 1. Decision conflicts that make AI-guided dosage-form development genuinely multiobjective

Decision-conflict archetype	Formulation advantage initially sought	Competing or limiting consideration	Why the conflict is not reducible to one prediction target	Potential reversal condition	Appropriate decision interpretation
Compatibility–performance conflict	Higher loading, preferred excipient function, improved stability or release	Chemical or physical incompatibility	Compatibility may operate as a feasibility condition rather than a compensable preference	Confirmatory evidence indicates clinically or pharmaceutically consequential incompatibility	Reject or reformulate even when predicted performance is favorable
Release–manufacturing conflict	Desired release kinetics or dissolution behavior	Processability, coating reproducibility, compression behavior, scale sensitivity	A release optimum may depend on a composition or process window that is difficult to reproduce	Scale-up or process evidence shows unacceptable variability or narrow operating tolerance	Revise composition or manufacturing route rather than preserve release target at any cost
Stability–process conflict	Reduced aggregation, sedimentation, degradation, or physical instability	More complex processing, restricted material choices, longer cycle time or increased process sensitivity	Stability and process robustness arise from interacting material/process choices	Stability gain is achieved only within impractical processing conditions	Rebalance material and process variables
Quality–throughput conflict	Tight control of a critical quality attribute	Production rate, process flexibility, monitoring burden	Local quality improvement can reduce overall	Required control strategy becomes impractical or	Reassess the candidate or manufacturing strategy

		or control complexity	manufacturing viability	unreliable at intended scale	
Performance–patient-use conflict	Optimized release, protection, targeting, or dose delivery	Swallowability, administration complexity, handling, dosing burden or acceptability	Product performance is meaningful only if the intended population can use the dosage form appropriately	Product architecture undermines intended use for a material patient subgroup	Modify dosage form, strength, geometry, route, packaging or administration strategy
Prediction–evidence conflict	High model-predicted desirability	Limited validation, domain shift or inadequate uncertainty characterization	A precise model output is not equivalent to sufficient evidence for a consequential decision	New experiments could plausibly reverse candidate ordering	Acquire discriminating evidence before advancement
Local-optimum–development conflict	Strong performance within a laboratory design space	Scale, regulatory, quality, supply or platform constraints	Optimization inside a bounded experimental domain may exclude decisive downstream conditions	Candidate cannot be manufactured or controlled consistently within realistic conditions	Redirect search toward a developable region of formulation space

Table 1 distinguishes conflicts that are superficially similar but carry different decision consequences. A poor value on one performance objective may be accepted if compensated elsewhere; a serious compatibility or feasibility violation may instead remove a candidate from the admissible set. This distinction becomes central when heterogeneous evidence is integrated.

Integrating Compatibility, Release, Manufacturing and Patient-Use Requirements

The first requirement for integration is to resist assigning one global confidence value to an AI-generated formulation. Reviews of machine learning in oral-solid process modeling describe continuing challenges in model transfer, scalability, interpretability, and uncertainty characterization [24]. These problems do not affect every objective equally. A model may be highly credible for one formulation property and weakly transportable for another. Manufacturing-route specificity illustrates the point: machine-learning approaches can help predict whether candidate formulations are viable for continuous direct compression from formulation and material characteristics, but the inference concerns that manufacturing route rather than manufacturability in the abstract [25]. The relevant evidence state must therefore be objective-specific and context-specific.

A second requirement is staged evidentiary challenge. Computer-assisted formulation development can combine molecular or computational screening with laboratory formulation, characterization, dissolution testing, and pharmacokinetic or biopharmaceutical evaluation. In a dipyridamole dry-nanosuspension development study, computational approaches were incorporated into excipient and formulation selection and then connected to experimental and translational assessment [26]. The value of the workflow lies not in treating the initial computational proposal as the answer, but in allowing later evidence to confirm, revise, or invalidate earlier assumptions. This logic is particularly important when an AI recommendation rests on indirect features whose connection to the final product attribute is conditional.

Quality-by-design approaches provide a compatible structure for such staged reasoning. Machine learning has been integrated with design-of-experiments approaches to model relationships among material attributes, process parameters, and critical quality attributes in formulation optimization [27]. The two approaches need not be treated as competing paradigms. Experimental design can define and interrogate a bounded region of formulation space; machine learning can represent nonlinear associations within that region; and pharmaceutical judgment can determine whether the resulting evidence is sufficient for the decision being made. Higher predictive fit does not by itself establish that the design space has captured every objective capable of changing candidate selection.

Optimization outputs require similar restraint. Process-parameter modeling can link quality prediction with algorithmic recommendations for parameter adjustment, as illustrated by work combining random-forest prediction with reinforcement-learning-based optimization in tablet compression [28]. Such results are relevant to formulation decision making because they show how model outputs may be coupled to an action. They also clarify why an action recommendation and an advancement decision should remain distinct. A process recommendation generated from historical or simulated evidence remains conditional on the applicability of the model, the completeness of the represented quality attributes, and subsequent validation under the intended operating environment.

Data provenance adds another layer of uncertainty. A structured oral-formulation database containing hundreds of marketed products has been used to identify formulation patterns and train models for release-category prediction [29]. Such databases can provide informative priors about excipient use, product composition, and release strategies. They cannot establish that frequently observed combinations are optimal for a new drug substance or that relationships learned from marketed products are transferable without qualification. An AI system trained on formulation precedents may therefore generate plausible candidates while remaining systematically blind to unrepresented chemistries, patient requirements, processing routes, or unsuccessful historical formulations.

These differences imply that evidence requirements should be tied to the claim being used to justify advancement. Compatibility claims require evidence appropriate to the proposed drug–excipient system and relevant storage or processing conditions. Release claims require test conditions and models that reflect the intended dosage-form mechanism. Manufacturing claims require evidence that connects laboratory composition to a feasible process and quality-control strategy. Patient-use claims require information drawn from the population, route, administration context, and dosage-form characteristics that actually matter to intended users. **Table 2** organizes these claims by the type of evidentiary failure that could reverse a formulation decision.

Table 2. Evidence escalation conditions for compatibility and release claims before formulation advancement

Claim being used in candidate selection	Minimum evidentiary question	Evidence that can strengthen the claim	Decision-relevant uncertainty that remains	Signal that additional evidence is required	Claim that remains unjustified
Drug and excipient are compatible	Has incompatibility been evaluated within the relevant chemical and formulation domain?	Targeted physicochemical testing, orthogonal analytical characterization, stress or stability evidence appropriate to the system	Unseen interactions, time dependence, processing-induced change, domain shift	The compatibility prediction materially determines whether the candidate remains viable	"Model-predicted compatible" means long-term compatibility is established
Release profile is acceptable	Does the test represent the mechanism and conditions relevant to the proposed dosage form?	Repeated dissolution/release experiments, mechanistically informative measurements, orthogonal spectroscopic or structural evidence	In vitro–in vivo transfer, variability, model dependence, manufacturing sensitivity	Candidate preference depends strongly on predicted rather than observed release	Predicted release establishes therapeutic performance
Formulation variables explain release	Has the model been evaluated on formulations sufficiently similar to the candidate?	External/held-out formulation testing, alternative modeling approaches, sensitivity analysis	Extrapolation outside composition/process domain	Candidate sits near or beyond the validated design-space boundary	Statistical fit establishes mechanistic causation
Process can reproduce desired performance	Are the relevant process variables and critical quality attributes represented?	Pilot-scale runs, PAT measurements, independent quality testing, route-specific feasibility assessment	Scale effects, equipment differences, narrow process windows	Scale-up could change candidate ranking	Laboratory manufacturability proves commercial robustness
Database precedent supports an excipient or architecture	Is the candidate represented by the chemistry, dosage form, route and product classes in the underlying database?	Mechanistic rationale, drug-specific studies, formulation experiments	Selection bias, absent failed products, underrepresented chemistries	Recommendation derives mainly from frequency or similarity rather than direct evidence	Commonly marketed means optimal for the new product
Patient-use advantage is asserted	Has the relevant use requirement been identified for the intended population and administration context?	User research, acceptability evidence, handling/swallowability assessment, patient-informed target product criteria	Population heterogeneity, disease state, environment, preference variation	User-facing attribute could plausibly alter correct administration or acceptance	A technical formulation advantage automatically improves adherence

Manufacturability provides a particularly strong test of this evidence-escalation logic because industrial constraints can overturn rankings derived from laboratory performance. Reviews of complex injectable products, for example, identify formulation, stability, sterility, manufacturing, scale-up, and regulatory considerations that have to coexist within the same development strategy [30]. The exact constraints differ between lipid-based injectables and solid oral dosage forms, but the general lesson is transferable: an attractive formulation property has decision value only within a product architecture that can be manufactured and controlled under its intended conditions.

Patient use creates a similarly integrative constraint, although the relevant failure mode is different. Multiparticulate and multi-unit systems illustrate how one dosage-form architecture can simultaneously alter release behavior, manufacturability, dosing flexibility, administration, and patient-facing characteristics [31]. This means that technical and patient objectives should not be represented as independent stages in which engineering optimization occurs first and usability is assessed afterward. A

formulation decision can instead change several domains at once. The same architecture may improve dose flexibility while complicating processing, improve release control while affecting administration burden, or facilitate use for one population while creating difficulty for another.

The evidence assembled across these domains therefore supports an asymmetric multiobjective formulation field rather than a linear development pipeline. Compatibility, release, manufacturing, quality, and patient use occupy different evidentiary positions and do not contribute to candidate selection in identical ways. Compatibility and manufacturing feasibility can create boundaries beyond which compensation is inappropriate; release behavior is a performance objective whose value depends on mechanism and context; patient-use requirements can function as either minimum conditions or preference-sensitive attributes; and AI predictions operate throughout the field as uncertain evidence rather than as a separate superior layer. A candidate formulation can consequently move from apparently attractive to unacceptable when information from another domain becomes available.

This relationship is represented in **Figure 1**.

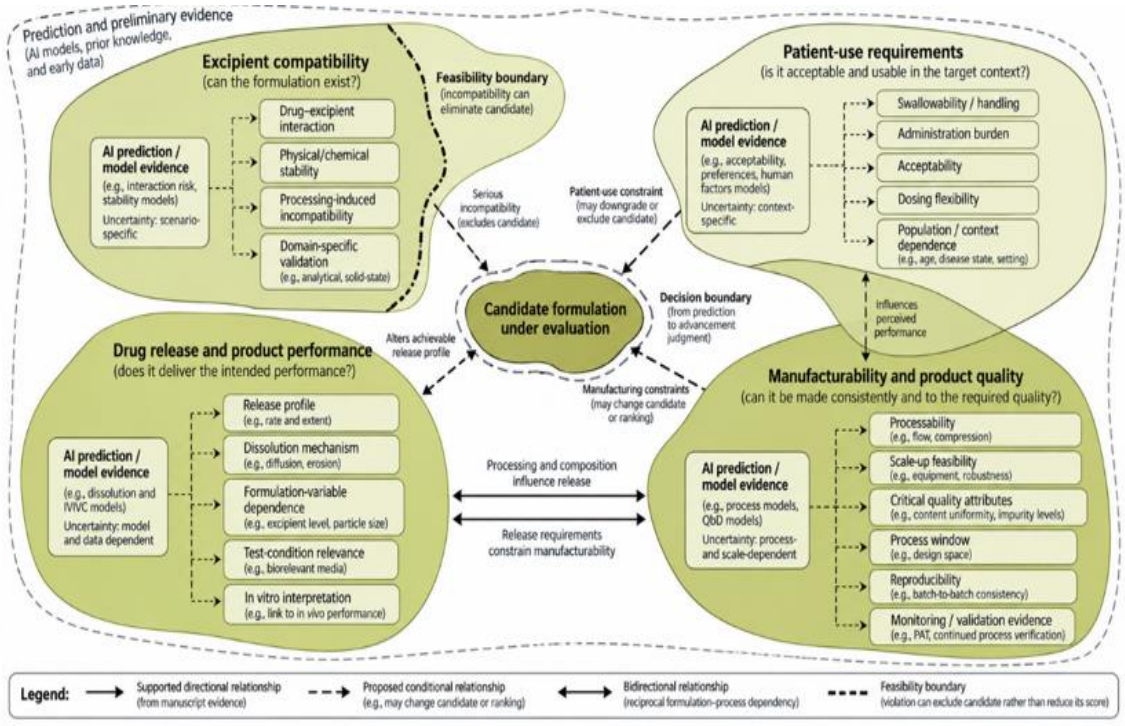


Figure 1. Where competing formulation objectives overturn an apparently attractive dosage-form candidate

Proposed Decision-Theoretic Framework

The preceding evidence suggests that the decision object should not be represented as a single predicted formulation score. A candidate is better represented as a set of objective-specific evidence states describing compatibility, release behavior, manufacturability and quality, and patient use. Multiobjective formulation studies demonstrate that desirable properties can respond differently to the same formulation choices [6]. Iterative active-learning approaches further show that those evidence states can change when new experiments are performed [7]. The proposed framework therefore treats an AI recommendation as a provisional description of a candidate's position across several objectives, each accompanied by its own uncertainty and applicability conditions.

Compatibility illustrates why these states should remain separate. Predictive models can identify drug–excipient combinations that warrant greater or lesser concern, but their output does not itself establish long-term compatibility in every relevant environment [17]. A candidate that performs strongly on other dimensions should therefore not receive compensatory credit when unresolved incompatibility crosses a development-relevant feasibility boundary. This constitutes a non-compensable condition: once the compatibility evidence indicates a sufficiently consequential violation, gains in release or convenience cannot automatically restore admissibility. The exact experimental criterion for such a violation remains product specific and should not be replaced by an invented universal threshold.

Release evidence requires a different decision rule. Data-driven models can estimate dissolution or release behavior within defined formulation spaces [18], and orthogonal analytical information can strengthen prediction for particular delivery systems [19]. Release is therefore treated as a graded performance objective whose value depends on whether the model, test conditions, and formulation domain correspond to the intended product. A candidate should not be ranked as superior merely because a model predicts a preferred release curve if the candidate lies outside the validated composition space or if uncertainty in that prediction could plausibly change its relative position.

Manufacturability occupies both a graded and a boundary role. Scale-up considerations can materially alter the development value of a formulation that appeared favorable under laboratory conditions [22]. Reviews of pharmaceutical process modeling likewise identify transferability and uncertainty characterization as continuing limitations when machine-learning models move across equipment, scales, and operating contexts [24]. Manufacturing evidence is therefore treated first as an objective—for example, when candidates differ in process robustness—and second as a feasibility condition when the intended production route cannot reproducibly generate a product that satisfies required quality characteristics. Route-specific feasibility models can inform that assessment, but their interpretation must remain limited to the manufacturing context in which they were developed [25].

These distinctions produce the decision structure summarized in **Table 3**.

Table 3. Manufacturability and quality conditions that can reverse an apparently optimal AI-generated formulation

Formulation situation	Apparent AI-supported advantage	Manufacturing or quality challenge	Decision status before additional evidence	What could reverse the original preference
High-performing composition with narrow process tolerance	Strong predicted release or stability	Small process deviations materially alter product quality	Conditionally attractive	Evidence of poor robustness at realistic operating variability
Candidate dependent on a route-specific process assumption	Favorable predicted product attributes	Manufacturing route may be unsuitable for material properties	Unresolved feasibility	Route-specific viability evidence showing incompatibility with intended process
Formulation optimized in a small laboratory design space	Local optimum across modeled attributes	Scale-dependent mixing, compression, drying, coating, or handling effects	Provisional	Pilot- or scale-relevant evidence changing product quality or reproducibility
Candidate requiring intensive control to maintain quality	Tight predicted critical-quality performance	Control burden may be impractical or fragile	Trade-off required	Independent measurements showing unacceptable sensitivity or monitoring burden
Model-supported process recommendation outside validated operating region	Higher predicted efficiency or quality	Domain shift and uncertain model transfer	Evidence request required	Validation demonstrating that the recommendation is not reproducible in the intended environment
Candidate with technically strong performance but problematic product architecture	Strong laboratory properties	Manufacturing, packaging, administration, or population-use constraints	Context dependent	Evidence showing that another architecture better satisfies the full product requirement set

Patient-use requirements enter the same architecture without assuming that every preference can be translated into a fixed utility weight. Patient-centric development frameworks support early consideration of user needs [8], while acceptability evidence remains population and dosage-form dependent [14]. In some contexts, a requirement such as the ability to swallow, manipulate, identify, or administer the dosage form may function as a minimum condition. In others, convenience, dosing flexibility, or handling may be preference-sensitive attributes that can legitimately trade against other benefits. The decision model therefore allows the status of an objective to change with the intended population instead of imposing one universal patient-use score.

A further component is decision-relevant uncertainty. The methodological literature on formulation machine learning emphasizes that apparent predictive performance must be interpreted alongside data quality, applicability, and model transparency [2]. The framework consequently asks not only whether uncertainty exists, but whether reducing that uncertainty could change the preferred action. If two candidates remain ordered under plausible variation in the uncertain evidence, further testing may have little decision value. Conversely, when new compatibility, release, manufacturing, or patient-use evidence could reverse candidate ranking, additional evidence becomes strategically important. This is a qualitative value-of-information principle rather than a claim that a validated numerical value-of-information algorithm already exists for pharmaceutical formulation development.

The resulting decision states are advance, revise, and stop. Advancement is justified when the candidate remains admissible across feasibility conditions and its advantages persist despite material uncertainty. Revision is appropriate when a promising candidate fails on a potentially correctable formulation or process dimension, or when additional evidence could alter the trade-off. Stopping is appropriate when a non-compensable constraint is violated or when the cost of correcting a limitation would undermine the original development rationale. A high AI score is therefore neither necessary nor sufficient for advancement; what matters is whether the candidate remains defensible after evidence, consequences, and feasibility are considered together.

Pharmaceutical Development Implications

One implication is that manufacturability should enter formulation selection earlier than a conventional sequential workflow might suggest. Formulation choices made without scale-up in mind can create downstream difficulty that was not visible during initial laboratory optimization [22]. Machine-learning systems for manufacturing should therefore be positioned as evidence-generating components of development rather than as downstream tools that simply optimize a formulation already selected. Reviews of AI-enabled manufacturing show substantial opportunity for monitoring and control [16], while current process-modeling assessments continue to identify uncertainty, transfer, and scale as important limitations [24].

A second implication concerns the relationship between prediction and confirmation. Compatibility models can narrow experimental search [17], and release models can identify candidate formulations whose performance warrants further attention [18]. Orthogonal evidence can strengthen those judgments when it measures a property connected to the relevant formulation mechanism [19]. Development programs can consequently use AI to prioritize the next informative test rather than to eliminate testing. This changes the interpretation of automation: the useful loop is not prediction followed automatically by advancement, but prediction followed by evidence acquisition, reassessment, and an updated decision.

Patient-use evidence should be able to change the priority of technically promising candidates. Patient-centered development guidance supports incorporating such considerations into target product design [8], and qualitative evidence shows that handling and swallowability can matter materially for older users [11]. Multiparticulate approaches further demonstrate that dosage-form architecture may simultaneously influence release, flexible dosing, processing, and patient-facing characteristics [31]. These relationships argue against a workflow in which a technically optimized dosage form is treated as fixed before usability is considered.

Table 4 translates these principles into decision states without assigning unsupported numerical scores or universal thresholds.

Table 4. Decision states for selecting, revising, or rejecting formulations under multiobjective uncertainty

Decision state	Evidence configuration	Formulation interpretation	Appropriate development action	Evidence priority
Advance	No material feasibility violation; advantages persist across relevant uncertainty	Candidate is defensible across the objectives that matter for the intended product	Progress to the next development stage while maintaining planned verification	Confirm remaining stage-appropriate risks
Advance conditionally	Candidate appears favorable but one bounded uncertainty remains	Current preference is stable unless a specified assumption fails	Advance with a predefined confirmatory evidence requirement	Test the assumption most capable of invalidating advancement
Revise formulation	Attractive candidate contains a correctable compatibility, release, processing, or patient-use weakness	Product concept remains viable but present composition or architecture is not	Alter composition, dosage-form design, strength, or other formulation feature	Generate evidence targeted to the changed formulation
Revise process	Product concept is attractive but process robustness or quality control is inadequate	Formulation may remain viable under a different process strategy	Modify manufacturing route, process window, monitoring, or control approach	Demonstrate reproducibility and quality under revised conditions
Request discriminating evidence	Candidate ranking depends on unresolved uncertainty	Current evidence cannot defensibly distinguish options	Perform the experiment or analysis most likely to change the decision	Prioritize evidence with decision-changing potential
Redirect search	Current candidates occupy an unfavorable trade-off region	Local optimization is unlikely to solve the underlying conflict	Search a different formulation architecture or design region	Seek evidence from a materially different candidate class
Stop	Non-compensable compatibility, feasibility, quality, or use requirement is violated	Continuing development is not justified by gains elsewhere	Discontinue candidate or product concept	Document the decisive constraint; avoid unnecessary optimization

These states also suggest a different research agenda for AI-enabled formulation development. Comparative evaluation should not be restricted to which algorithm predicts a formulation property most accurately. Studies can also examine whether an AI-supported decision policy reduces late-stage reversals, whether it identifies manufacturing problems earlier, whether additional experiments are selected more efficiently, whether patient-use requirements alter candidate ordering, and whether candidate rankings remain stable as evidence moves from computational prediction to experimental confirmation. Structured formulation databases may provide useful priors for such work, but their composition and provenance must remain part of the interpretation [29].

The overall decision architecture is represented in **Figure 2**.

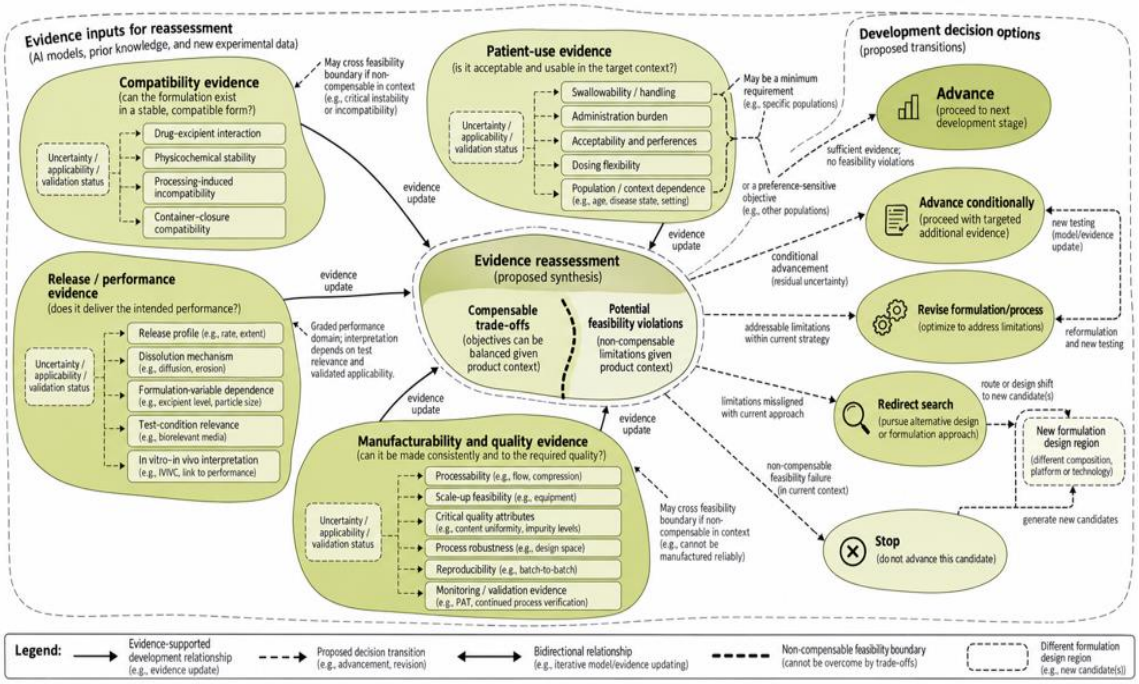


Figure 2. How evidence updates move an AI-guided formulation toward advance, revision, redirection, or stop.

Conclusion

AI-guided formulation development is most defensible when prediction is treated as evidence for a decision rather than as the decision itself. Excipient compatibility, release behavior, manufacturability, product quality, and patient use differ in evidentiary basis and consequence, and some limitations can become non-compensable constraints. The proposed decision-theoretic account therefore evaluates candidate formulations through objective-specific evidence states, context-specific feasibility boundaries, and the possibility that new evidence may reverse candidate ordering. Under low decision-relevant uncertainty, an admissible candidate can advance. Where uncertainty could change the preferred option, additional evidence is warranted; where limitations are correctable, revision or redirection may be appropriate; and where a consequential compatibility, manufacturing, quality, or patient-use requirement cannot be satisfied, development should stop. The central contribution is thus not another optimization score, but a way to preserve pharmaceutical trade-offs and consequences when AI is used to guide dosage-form choice.

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