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CM-PharmE 1.0: A Business-Architecture-Informed and Ontology-Grounded Conceptual Model for Pharmaceutical Ecosystems

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ABSTRACT
Pharmaceutical ecosystems involve interdependent enterprises, regulators, healthcare providers, patients, and digital platforms whose interactions create substantial organizational, governance, and interoperability challenges. Existing contributions address important parts of this problem through domain ontologies, enterprise-architecture frameworks, process models, and digital-platform perspectives, but remain fragmented at the ecosystem level. This study presents CM-PharmE 1.0, a business-architecture-informed and UFO-grounded conceptual model expressed in OntoUML. A PRISMA-guided review identified 380 records, of which 17 studies were retained for qualitative thematic synthesis. The resulting modeling concerns were organized into five interrelated domains and translated into UFO/OntoUML constructs through an explicit concept- and relation-selection procedure. Assessment combined a scenario-based comparative benchmark, qualitative review by four experts, a focused manual inspection of eight selected OntoUML-informed anti-pattern categories, competency-question analysis, illustrative vaccine-distribution instantiation, and repository-supported computational checks. All eight competency questions were operationalized as executable queries and returned the predefined bounded results against the formalized model and machine-readable scenario; automated ROBOT/HermiT reasoning also completed without reporting a logical inconsistency or unsatisfiable named classes in the current axiom set. The resulting evidence provides preliminary support for the model's conceptual traceability, cross-domain coherence, ontological discipline, and bounded computational consistency, while reference-architecture adoption, contextual extensibility, operational interoperability, empirical completeness, and implementation effectiveness remain to be evaluated. CM-PharmE 1.0 is therefore positioned as an extensible conceptual baseline for governance reasoning, interoperability-oriented analysis, requirements engineering, and subsequent architectural development in regulated pharmaceutical ecosystems rather than as a complete or operationally validated ontology.

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KEYWORDS
Ecosystem-level Conceptual Modeling, Unified Foundational Ontology (UFO), Ontology Engineering, Enterprise Semantics, Interoperability Governance, Digital Health.

1. INTRODUCTION

Pharmaceutical ecosystems are regulated socio-technical systems in which enterprises, regulatory authorities, healthcare providers, patients, and digital infrastructures interact through organizational, governance, and digital arrangements. Beyond supply-chain coordination, they depend on institutional oversight and cross-organizational information exchange. Although technologies such as blockchain and large-scale analytics can improve transparency and operational efficiency [1], the organizational and semantic architecture connecting these actors remains insufficiently formalized.

Empirical studies report fragmented governance and persistent interoperability limitations that hinder ecosystem-level coordination [2]. Research on hybrid arrangements, including public-private partnerships and access initiatives, likewise highlights the need to align commercial, societal, and regulatory objectives [3]. Yet many contributions remain focused on process optimization, data integration, or sustainability without integrating organizational structure, inter-organizational collaboration, regulatory constraints, and digital enablement within a shared semantic framework [4].

To address this gap, the study presents CM-PharmE 1.0 (Conceptual Model for the Pharmaceutical Ecosystem), a business-architecture-informed and UFO-grounded conceptual artifact. It integrates organizational, collaborative, operational, regulatory, and digital concerns in a five-domain OntoUML representation [7], makes cross-domain dependencies explicit across concerns that prior work treats separately [4], [8]-[10], [12]-[23], and extends the initial model reported in [26] through stronger methodological traceability, comparative positioning, and multi-layer assessment. The guiding question is: How can business-

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architecture principles be systematically aligned with foundational ontology to conceptualize pharmaceutical ecosystem dynamics in a semantically rigorous and structurally coherent manner?

1.1. Motivation

Pharmaceutical ecosystems must coordinate multiple actors under strict governance while adapting to rapid digital change. Technologies such as blockchain, artificial intelligence, and big-data analytics can support transparency, traceability, and decision support, but their ecosystem-level value depends on coherent organizational and semantic foundations. CM-PharmE is motivated by the need for a shared conceptual structure that relates technological innovation to enterprise architecture and ecosystem governance rather than treating digital initiatives as isolated solutions.

1.2. State of the problem

Pharmaceutical ecosystem representation remains fragmented across partially overlapping research streams. OntoPharma supports clinical medication decisions but not ecosystem-level organizational modeling [8]; Sultanow et al. provide a pharmaceutical and healthcare reference architecture without foundational-ontology grounding [13]; Ilin et al. represent vaccine-lifecycle actors, processes, and digital concerns without UFO/OntoUML formalization [16]; and Ghadge et al. focus on blockchain-enabled pharmaceutical supply chains [21]. None of the reviewed approaches simultaneously provides foundational-ontology grounding, business-architecture-informed decomposition, ecosystem-level organizational representation, and cross-domain traceability. CM-PharmE therefore addresses the absence of an integrated artifact linking organizational, collaborative, operational, regulatory, and digital concerns within a shared ontological structure.

1.3. Research Aim

This study aims to develop and assess CM-PharmE 1.0 as a business-architecture-informed and ontology-grounded conceptual artifact for pharmaceutical ecosystems. It provides a unified representation of organizational, collaborative, operational, regulatory, and digital concerns grounded in UFO and intended to support ecosystem conceptualization, governance alignment, interoperability-oriented analysis, and downstream requirements and architectural work.

1.4. Outline of the manuscript

The manuscript proceeds as follows. Section 2 defines the conceptual foundations; Section 3 presents the research design, PRISMA-guided review, thematic synthesis, and UFO/OntoUML modeling procedure; Section 4 synthesizes the literature and research gap; Section 5 presents CM-PharmE and its illustrative instantiation; Section 6 reports the evaluation; Section 7 discusses implications and limitations; and Section 8 concludes the study.

Building on [26], the present study retains the five-domain architecture while strengthening its methodological and analytical basis. It makes the review, thematic synthesis, and domain derivation more explicit; refines semantics and cross-domain dependencies; broadens comparative positioning; and extends evaluation through expert review, OntoUML anti-pattern inspection with repository-supported reinspection, executable competency queries, scenario analysis, and logical reasoning. The contribution is therefore systematic refinement and substantiation of the existing architecture rather than its replacement. To reduce repetition with [26], overlapping foundational material has been condensed or cited to the conference paper where appropriate, while the present manuscript retains only the material needed to make the journal-level methodological, evaluation, and application extensions self-contained.

2. BASIC CONCEPTS

This section defines only the conceptual vocabulary needed to interpret CM-PharmE, leaving evidence synthesis to Section 4. The foundations cover (1) ecosystem and organizational concepts, (2) modeling and ontological concepts, and (3) digital-transformation and regulatory context.

2.1. Ecosystem and Organizational Foundations

A pharmaceutical ecosystem is a regulated network of interdependent enterprises, public authorities, healthcare providers, patients, and technology actors involved in the development, production, distribution, use, and governance of medicines [2], [3]. Business-ecosystem theory emphasizes their co-evolving roles, capabilities, and relationships [11]. In this study, business architecture is operationalized through organization design, capabilities, stakeholder participation and value delivery, strategy, and process, consistent with BACM [33]. These concerns serve as analytical lenses rather than a claim of complete BACM conformance; enterprise- and reference-architecture perspectives additionally connect business concerns with data, applications, technology, and interoperability [13], [15], [21].

2.2. Modeling and Ontological Foundations

Conceptual modeling abstracts domain entities, relations, and constraints for communication, analysis, and design, while ontology engineering makes their intended meanings and commitments explicit [8]-[10]. CM-PharmE uses UFO as its foundational reference and OntoUML as the corresponding modeling language [7]. UFO distinctions such as kinds, roles, relators, modes, and perdurants support disciplined stereotype and relation semantics, but foundational grounding alone does not establish empirical validity or operational interoperability. Semantic interoperability is therefore treated as a design objective supported by shared meaning rather than an automatically achieved system property [9], [10], [20].

2.3. Digital Transformation and Regulatory Context

Digital transformation and regulatory governance are interacting drivers of pharmaceutical ecosystems. Digital platforms, EHR systems, AI-enabled decision support, blockchain-based traceability, telemedicine, and real-world-evidence platforms can support information exchange and coordination [1], [12], [16], while regulatory authorities, policies, compliance requirements, and oversight mechanisms shape their permissible use [2], [3]. Public-private partnerships and real-world-evidence platforms illustrate how collaborative and digital infrastructures connect operational activity with access, pharmacovigilance, and regulatory decision-making [3], [16]. CM-PharmE therefore models these concerns as related ecosystem constructs rather than isolated technology categories.

These foundations establish the terminology used below; Section 3 explains the model-development procedure, and Section 4 presents the evidence synthesis and resulting gaps.

3. RESEARCH METHOD

This study adopts a qualitative, design-science-oriented conceptual research design centered on developing and preliminarily assessing a conceptual artifact rather than testing empirical hypotheses. The artifact, CM-PharmE 1.0, is an ontology-grounded conceptual model for representing organizational, collaborative, operational, regulatory, and digital concerns in pharmaceutical ecosystems. Its development combines systematic evidence synthesis, thematic abstraction, business-architecture-informed conceptualization, and UFO-based modeling. Design science provides the methodological orientation and reporting structure that links problem identification, artifact objectives, model development, demonstration, and evaluation [30].

The study does not report operational deployment or a fully iterative design–evaluation cycle; both remain subjects for subsequent empirical research.

3.1. Research Design and Design-Science Orientation

To make the design-science logic explicit, the completed research activities were aligned with the six activities of the Design Science Research Methodology (DSRM) proposed by Peffers et al. [30]: problem identification and motivation, definition of the objectives for a solution, design and development, demonstration, evaluation, and communication. This alignment serves as a retrospective framework for methodological reporting on how the conceptual artifact was developed and assessed. It does not imply that the study completed multiple operational build–evaluate iterations or deployed the artifact within a functioning pharmaceutical organization.

Problem identification and motivation are established in Sections 1 and 4 through evidence of structural fragmentation, limited ecosystem-level representation, and insufficient alignment between business architecture and foundational ontology. Section 1.3 states the research aim and guiding question. Design and development comprise the systematic literature review, thematic synthesis, translation of analytical concerns into five conceptual domains, and formalization using UFO and OntoUML, as described in Sections 3.2–3.4 and 5. Section 5.5 provides demonstration through the illustrative vaccine-distribution instantiation. Section 6 evaluates the artifact through comparative benchmarking, expert review, focused anti-pattern inspection, competency-question analysis, repository-supported semantic reinspection, executable competency queries, and logical-reasoning checks. Communication comprises the earlier report in [26] and the present study. Operational deployment remains outside the current scope; the computational assessment is intentionally bounded to the formalized ontology, executable competency queries, machine-readable scenario, and repository-supported validation procedures and should not be interpreted as a complete empirical design–evaluation cycle.

3.2. Systematic Literature Review

A systematic literature review was conducted to identify and integrate prior research on ontology development, business-architecture applications, and conceptual modeling in pharmaceutical and healthcare domains. The review followed PRISMA 2020 to support methodological transparency and reproducibility [5]. Its guiding question was: How have principles of ontology engineering and business architecture been employed to model organizational and ecosystem-level dynamics in pharmaceutical enterprises?

Electronic databases, including Scopus, Web of Science, PubMed, and IEEE Xplore, were searched using structured Boolean search expressions combining terms related to ontology engineering, business architecture, and pharmaceutical ecosystem modeling. Google Scholar and reference-list screening were used as supplementary identification sources to capture additional relevant studies not retrieved through the main database searches. To enhance methodological transparency, representative search strings included: (“ontology” OR “ontology engineering” OR “conceptual model”) AND (“business architecture” OR “enterprise architecture”) AND (“pharmaceutical” OR “healthcare”) AND (“ecosystem” OR “organizational interactions” OR “inter-organizational”); and (“pharmaceutical ecosystem” OR “healthcare ecosystem”) AND (“ontology” OR “OntoUML” OR “foundational ontology”) AND (“business architecture” OR “enterprise architecture” OR “conceptual modeling”). These strings are reported as representative expressions of the search logic rather than exhaustive reproductions of every database-specific query variant used during the review; database-specific adaptations were used where required to accommodate differences in search syntax and indexing behavior. The search covered peer-reviewed journal articles, conference proceedings, and book chapters published in English between 2018 and 2025. The initial combined identification process yielded 380 records.

The study-selection process was documented in accordance with PRISMA 2020 reporting guidance [5]. Identification, screening, eligibility assessment, and final inclusion were recorded to provide an audit trail. Figure 1 summarizes how records from database searches and supplementary sources were progressively refined into the final set included in the qualitative synthesis.

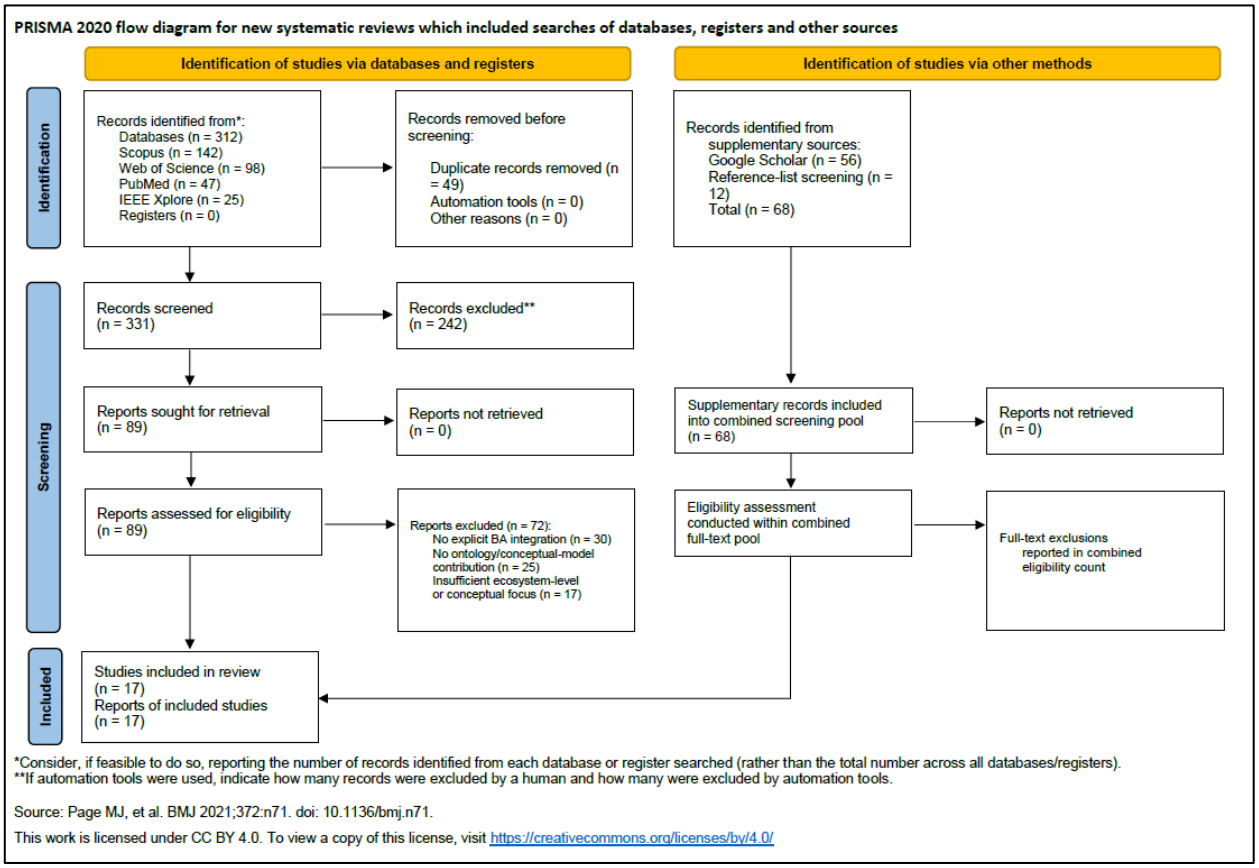


Figure 1. PRISMA 2020 flow diagram summarizing the identification, screening, eligibility assessment, and final inclusion of studies in the systematic literature review, adapted from Page et al. [5].

Studies were included if they (i) explicitly addressed ontology development, conceptual modeling, or business architecture in pharmaceutical or healthcare contexts, (ii) focused on organizational or ecosystem-level dynamics, and (iii) provided empirical, theoretical, or conceptual contributions. Studies concentrating solely on technical implementations or lacking explicit organizational or ecosystem perspectives were excluded. The inclusion and exclusion criteria applied during the study selection process are summarized in Table 1.

Table 1. Inclusion and Exclusion Criteria

Criteria Type	Inclusion Criteria	Exclusion Criteria
Domain	Pharmaceutical, healthcare, and closely related organizational ecosystems	Purely technical contributions (e.g., database design lacking an explicit organizational focus)
Topic	Ontology development, business architecture, and conceptual modeling	Not relevant to conceptual modeling or business architecture
Language	English-language publications	Non-English publications
Study Type	Peer-reviewed journal articles, conference proceedings, and book chapters	Editorials, commentaries, and theses lacking peer review

Two reviewers independently screened titles, abstracts, and full-text reports according to the predefined inclusion and exclusion criteria, with disagreements resolved through discussion to ensure consistency. The overall selection process is summarized using a PRISMA 2020 flow diagram (Figure 1). The identification process yielded 380 records in total: 312 records from electronic databases and 68 additional records from supplementary sources, including 56 records from Google Scholar and 12 records from reference-list screening. Supplementary records were incorporated into the combined screening pool before title and abstract screening. After removing 49 duplicate records, 331 records remained for title and abstract screening. Of these, 242 records were excluded, leaving 89 full-text reports for eligibility assessment. Seventy-two reports were excluded at the full-text stage because they lacked explicit business architecture integration, did not provide an ontology-development or conceptual-modeling contribution, or had insufficient ecosystem-level or conceptual focus. Ultimately, 17 studies satisfied all inclusion criteria and were retained for qualitative synthesis. For these selected studies, relevant data were systematically extracted into a structured form capturing research context, methodological approach, key findings, and explicitly reported knowledge gaps. This curated dataset provided the empirical foundation for the subsequent thematic synthesis and directly informed the construction of the proposed conceptual model.

A lightweight qualitative appraisal was also applied to the final study set to support analytical reliability. Because the review focused on conceptual rather than clinical evidence synthesis, no clinical scoring instrument was used. The appraisal considered four criteria aligned with the study objectives: (1) relevance to ontology engineering, business architecture, or conceptual modeling in pharmaceutical or healthcare contexts; (2) explicit treatment of organizational or ecosystem-level concerns; (3) conceptual richness and usefulness for identifying structural modeling gaps; and (4) clarity of methodological or conceptual reporting. It informed interpretive prioritization during synthesis but was not used as a rigid exclusion mechanism, thereby preserving conceptual breadth while improving transparency.

3.3. Thematic Synthesis

Following the three-stage thematic synthesis procedure of Thomas and Harden [31] and the applied approach reported in [6], the unit of analysis was an extracted textual statement describing a study's research focus, modeled concepts or relations, architectural scope, reported contribution, or explicit limitation. The analysis proceeded through line-by-line coding, development of descriptive categories, and generation of higher-order analytical themes. Representative initial codes included organizational structure, enterprise capability, strategic alignment, stakeholder collaboration, partnership, governance, compliance, clinical or business process, data integration, digital platform, traceability, and semantic interoperability.

Codes expressing related concerns were iteratively consolidated into descriptive categories covering enterprise structure and architecture, inter-organizational collaboration, operational and clinical process integration, governance and normative constraints, and digital enablement and semantic interoperability. These categories were compared across the 17 included studies and abstracted into the four analytical themes reported in Section 4. The synthesis was interpretive rather than frequency-based: a modeling concern was retained when it recurred across studies or was conceptually significant for ecosystem-level representation. For the present revision, the resulting evidence-to-domain mapping was retrospectively checked against the extracted study summaries to improve methodological traceability.

The four analytical themes and the five CM-PharmE domains should not be interpreted as a one-to-one classification. The themes organize related bodies of prior research, whereas the domains separate distinct modeling responsibilities within the proposed artifact. Table 2 documents a representative evidence-to-domain traceability chain by linking reviewed evidence, initial codes, descriptive categories, analytical themes, and the resulting modeling rationale. The table is intended as a transparent audit trail rather than an exhaustive qualitative codebook.

3.4. UFO/OntoUML Modeling Procedure

Building on the evidence-to-domain traceability established through the literature review and thematic synthesis, the extracted modeling concerns were translated into the current UFO/OntoUML representation through a documented concept-classification and relation-selection procedure [7], [32]. The procedure articulated and reviewed the ontological commitments of CM-PharmE 1.0 while preserving the five-domain architecture developed earlier in the research. It was not intended to establish that the resulting ontology is complete, uniquely correct, or optimal for every pharmaceutical ecosystem context.

For each candidate concept, classification began by considering its mode of existence and dependence. Kind was used for rigid, identity-supplying entity types, such as Pharmaceutical Enterprise, Organizational Unit Structure, Regulatory Authority Entity, and Digital Health Platform Component; Role was used for contingent, context-dependent classifications, such as Organizational Stakeholder, Ecosystem Actor, Individual Patient, and Prescribing Physician. Relator was used for reified social, contractual, governance, or coordination relations that depend on their participants, including Enterprise Governance Relator, Strategic Partnership Agreement, Regulatory Oversight, and Clinical Pathway. Mode represented dependent capabilities, signals, policies, or requirements, whereas Perdurant represented processes, activities, procedures, or sequences that unfold through time [7], [32].

Relation selection followed the ontological status of the connected concepts. Mediation connected a relator to the roles or entity types participating in the corresponding relationship; characterization connected a mode to its bearer; and part–whole relations were retained only when the intended domain meaning concerned structural composition or membership. Domain-specific associations such as enables, supports, constrains, informs, or coordinates were used when the available evidence supported a meaningful cross-domain dependency but not a stronger reified or mereological commitment [7], [32]. This conservative strategy limits ontological commitments to those required by the present conceptual scope.

Cardinalities were assigned as conceptual participation constraints based on the reviewed domain descriptions, the semantics of each relation, and the minimum commitments required by the selected UFO/OntoUML construct [7], [32]. Mandatory multiplicities were used only when the modeled relation presupposed participation for a concept to instantiate the intended role or relator. Optional or multiple participation was retained when the reviewed evidence did not justify a stronger restriction. Accordingly, the cardinalities are provisional conceptual constraints for the current model rather than empirically measured frequencies or universally applicable pharmaceutical-domain rules. Subsequent empirical deployment and broader data-grounded computational evaluation may identify context-specific refinements without requiring a change to the principal five-domain decomposition.

To support artifact traceability, computational assessment, and reproducibility, a version-controlled project repository accompanies CM-PharmE 1.0. The repository[1] contains the formal ontology source, stable semantic identifiers, model and mapping artifacts, a machine-readable vaccine-distribution scenario, executable competency queries, validation outputs, and reproducible build artifacts associated with the study. The competency questions were operationalized as executable queries consistent with their role as ontology-evaluation requirements [29], while automated ontology workflows and logical validation were performed using ROBOT [40] with the HermiT reasoner [41]. These repository-supported checks complement, rather than replace, the qualitative and scenario-based assessment reported in Section 6. During the revision, this repository layer was further engineered as a modular formal ontology and reproducible validation pipeline. The authoring source reconstructs the 1,086-triple canonical graph; generated artifacts include deterministic Turtle, RDF/XML, JSON-LD, N-Triples, and SHACL representations, with SHACL generation producing 76 node shapes and 76 property shapes. These engineering results are reported as repository-supported extensions to the assessment rather than as evidence that the original qualitative evaluation was itself fully formal.

4. LITERATURE REVIEW

This section synthesizes the 17 studies retained in the review, focusing on ontology development, business and enterprise

[1] CM-PharmE 1.0 — Project Repository: https://github.com/ArazSaieArasi3/CM-PharmE

architecture, ecosystem dynamics, and pharmaceutical or healthcare conceptual modeling. Four analytical themes summarize how prior work informed the scope of CM-PharmE.

4.1. Theme 1: Ontology Development in Pharmaceutical Enterprises across Clinical, Core Business, and Data Domains

Pharmaceutical ontology research has largely emphasized clinical decision support and data semantics. OntoPharma supports medication decisions [8], ontology-based data management at Novo Nordisk advances FAIR data and semantic interoperability in pharmaceutical R&D [9], and related work structures pharmaceutical research outcomes [10]. These contributions demonstrate the value of ontology engineering but do not jointly represent organizational structures, governance constraints, and inter-organizational relationships within a business-architecture-informed ecosystem model.

4.2. Theme 2: Business Architecture Applications in Pharmaceutical Enterprises

Business- and enterprise-architecture research adds organizational and digital perspectives. Simonov describes more networked pharmaceutical business models [11]; Wedha et al. examine blockchain-enabled supply-chain transformation [12]; Sultanow et al. propose a pharmaceutical, healthcare, and life-sciences reference architecture [13]; and Solaimani et al. study implementation within a networked pharmaceutical enterprise [14]. Masuda et al. address adaptive digital-health platforms [15], while Ilin et al. model the vaccine lifecycle as a multi-actor ecosystem [16]. Together, these studies provide strong architectural insight but do not explicitly ground cross-domain ecosystem representations in a foundational ontology.

4.3. Theme 3: Business Architecture-Informed Ontology Development in Pharmaceutical Enterprises

Work at the intersection of organizational modeling, data architecture, and ontology engineering remains fragmented. Uzhakova and Fischer integrate business, data, and application concerns in pharmaceutical R&D architecture [17], while Spoladore and Pessot examine collaborative ontology engineering in healthcare [18]. Rahayu and Setiawan model substandard and falsified drugs through stakeholder and system-dynamics analysis [19], and Zhou et al. apply ontology-based semantic discovery to medical cloud logistics [20]. Together, these studies address complementary concerns without integrating them into a shared business-architecture-informed and foundational-ontology-grounded representation of the pharmaceutical ecosystem.

4.4. Theme 4: Business Architecture Applications in Conceptual Models of Pharmaceutical Ecosystem Enterprises

Several conceptual frameworks address ecosystem concerns without an integrated ontology-grounded representation. Ghadge et al. focus on blockchain-enabled pharmaceutical supply chains [21]; Elia and Margherita on cognitive-enterprise maturity and value drivers [22]; Flessa and Huebner on innovation diffusion in healthcare [4]; and Cavicchi and Vagnoni on sustainable community-pharmacy business models [23]. Their scopes remain centered on specific technological, organizational, innovation, or sustainability concerns. The remaining gap is a shared structure that relates organizational, collaborative, operational, governance, and digital concerns through explicit foundational-ontology commitments.

Table 2. Representative traceability from reviewed evidence and thematic synthesis to the five CM-PharmE domains.

CM-PharmE Domain	Representative Evidence and Initial Codes	Descriptive Category and Analytical Theme(s)	Modeling Rationale
Organizational/Structural	Organizational structures, business models, enterprise capabilities, strategic objectives, enterprise-architecture layers, and organizational decomposition reported in [11]–[17]. Representative codes: organizational unit, capability, strategy alignment, enterprise structure, and internal governance.	Enterprise structure and architecture; primarily Themes 2 and 3.	Prior architecture-oriented studies describe enterprise structures and capabilities but do not formally represent their identity, composition, roles, and strategic characteristics within an ecosystem-level ontology.
Ecosystem/Collaborative	Networked enterprises, stakeholder participation, access programs, partnerships, public–private arrangements, and ecosystem orchestration discussed in [3], [14], [16], [18], [19], and [24]. Representative codes: ecosystem actor, partnership, stakeholder network, collaboration, agreement, and value exchange.	Inter-organizational collaboration and ecosystem relations; Themes 2–4.	External ecosystem participation and relational coordination require explicit actor roles, relators, agreements, and collaboration mechanisms distinct from the internal structure of a single enterprise.
Operational/Process	Clinical decision support, supply-chain and logistics workflows, vaccine lifecycle activities, adverse-event reporting, surveillance, and operational traceability addressed in [8], [10], [12], [16], and [19]–[21]. Representative codes: business process, clinical activity, logistics, reporting, pathway, surveillance, and traceability.	Operational and clinical process integration; Themes 1–4.	Existing process-specific contributions seldom connect temporally unfolding activities to organizational roles, governance constraints, collaborative arrangements, and digital enablers within one model.
Governance/Regulatory	Regulatory oversight, policy, compliance, access, risk, sustainability, and governance arrangements discussed in [2]–[4], [16], [19], and [23]. Representative codes: regulatory authority, policy, compliance requirement, oversight, risk, and normative constraint.	Governance and normative constraints; Themes 2–4.	Governance concerns require explicit representation of authorities, policies, compliance requirements, oversight relations, and risk-related activities that constrain constructs across other domains.
Digital Transformation	Ontology-based data management, blockchain, reference architectures, healthcare platforms, cloud logistics, AI-enabled systems, and digitally mediated ecosystems examined in [1], [9], [10], [12], [13], [15], [16], and [20]–[22]. Representative codes: digital platform, semantic interoperability, blockchain, data integration, decision support, and digital infrastructure.	Digital enablement and semantic interoperability; Themes 1–4.	Digital technologies should be modeled as enabling ecosystem constructs connected to organizational, operational, collaborative, and regulatory concerns rather than as isolated technical artifacts.

The four analytical themes were translated into five modeling domains through design-oriented decomposition rather than direct relabeling. Organizational/Structural and Ecosystem/Collaborative were separated because internal composition and external participation involve different identity and mediation concerns. Governance/Regulatory and Digital Transformation were retained as distinct cross-cutting domains, while Operational/Process isolates temporally unfolding activities and participation structures. This decomposition preserves evidence traceability while improving modularity and ontological clarity [7].

Across the reviewed literature, the recurrent limitation is separation rather than absence: data ontologies rarely represent organizational semantics, architecture studies often omit foundational-ontology commitments, and ecosystem or process models seldom integrate governance, collaboration, operations, and digital enablement. CM-PharmE addresses this fragmentation by

connecting these concerns within one conceptual artifact [8]-[23].

Table 3 positions CM-PharmE against representative approaches to clarify the design space addressed by the model. The comparison is not intended to establish universal superiority, but to make differences in ontology grounding, business-architecture integration, ecosystem scope, and cross-domain representation explicit.

For Tables 3 and 8, ordinal labels were assigned through qualitative author assessment of each approach's reported scope and capabilities. Yes denotes explicit and substantive treatment; Partial denotes incomplete or secondary treatment; Limited denotes narrow or indirect support; and No denotes that no explicit evidence was identified. These labels are literature-based judgments rather than performance scores. Table 3 reports validation descriptively because the compared studies use qualitatively different assessment strategies.

Table 3. Comparative positioning of CM-PharmE 1.0 against representative prior approaches in pharmaceutical and healthcare ecosystem modeling.

Study	Primary Orientation	Explicit Foundational Ontology Grounding	Business Architecture Integration	Ecosystem-Level Organizational Scope	Cross-Domain Conceptual Integration	Formal / Structured Validation	Key Limitation Relative to CM-PharmE
[8] OntoPharma	Clinical decision support ontology	Partial / domain ontology only	No	No	Limited to clinical medication context	Not ecosystem-oriented	Operationally specific; does not represent organizational or ecosystem structures
[13] Sultanow et al.	Reference architecture for pharma, healthcare, and life sciences	No	Yes	Partial	Architectural integration without ontology-grounded ecosystem formalization	Architecture-oriented, not ontologically validated	Lacks explicit ontology-driven representation of ecosystem relations
[15] Masuda et al.	Adaptive enterprise architecture for digital healthcare platforms	No	Yes	Partial	Focused on enterprise and platform adaptation	Not designed as ontology-based conceptual validation	Does not formalize ecosystem-level ontology-informed structures
[16] Ilin et al.	Vaccine lifecycle ecosystem model	No	Partial	Yes	Covers multiple ecosystem concerns, but without explicit ontological formalization	Structurally informative but not ontology-centered	Lacks foundational ontology grounding and explicit ontological stereotypes
[17] Uzhakova and Fischer	Data-driven enterprise architecture in pharmaceutical R&D	No	Yes	Limited beyond enterprise boundary	Partial	Architecture-driven analysis	Does not provide a formal ecosystem-level conceptual ontology
[21] Ghadge et al.	Blockchain supply chain conceptual framework	No	Partial	Limited to supply chain context	Narrow operational focus	Conceptual framework only	Restricted to supply-chain traceability rather than integrated ecosystem conceptualization
CM-PharmE 1.0	Business-architecture-informed conceptual model for pharmaceutical ecosystems	**Yes (UFO / OntoUML)**	**Yes**	**Yes**	**Yes; five-domain decomposition with explicit cross-domain dependencies**	Structured qualitative assessment through expert review, focused anti-pattern inspection, competency questions, illustrative instantiation, and repository-supported executable-query and logical-reasoning checks	Empirical deployment, independent external validation, and broader data-grounded evaluation remain future work

Within the selected comparison set, CM-PharmE combines business-architecture concerns and foundational-ontology distinctions across five interrelated domains with explicit cross-domain dependencies. It is therefore positioned as an integrated conceptual scaffold for ecosystem-level analysis, not as evidence of universal superiority or implementation effectiveness.

5. CONCEPTUAL STRUCTURE OF CM-PharmE 1.0

CM-PharmE 1.0 represents the pharmaceutical ecosystem through a business-architecture-informed and ontology-grounded conceptual structure. This section presents the model's design logic, domain decomposition, core ontological constructs, and integrated representation.

Before presenting the formal OntoUML view, Figure 2 provides a simplified business-architecture perspective showing the principal actors, five domains, and main interaction pathways across organizational, collaborative, governance, operational, and

digital concerns.

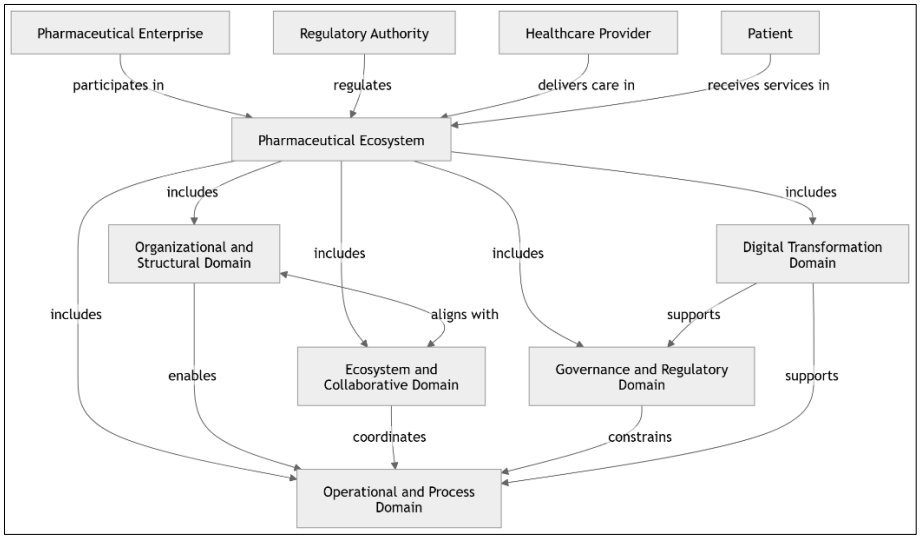


Figure 2. Simplified business-architecture view of CM-PharmE 1.0, showing the main actors, five conceptual domains, and their primary interaction logic.

Figure 2 presents the accessible business-architecture view, whereas Figure 4 makes ontological commitments explicit through stereotypes, relations, and cardinalities. Business architecture identifies what requires representation; UFO/OntoUML clarifies the identity, dependence, relational, and temporal characteristics of the selected constructs [7], [32], [33]. Table 4 documents this selective interpretive bridge and does not imply formal BACM-OntoUML conformance.

5.1. Conceptual Framing and Design Rationale

Within CM-PharmE, business-architecture-informed means that organization design, capabilities, stakeholder participation and value delivery, strategy, and process guided the model's scope and decomposition [33]. These concerns shaped the organizational, collaborative, strategic, value-delivery, and process constructs, while governance/regulatory and digital-transformation concerns were retained because of the regulated and digitally mediated pharmaceutical context. UFO and OntoUML then clarified the ontological status and relations of the selected constructs [7], [32]. This sequence provides architectural-to-ontological traceability without claiming formal equivalence, complete BACM conformance, or ontological completeness.

Table 4. Operational mapping of business-architecture concerns to CM-PharmE domains and OntoUML constructs.

Business-Architecture Concern	CM-PharmE Domain Interpretation	Representative CM-PharmE Constructs	OntoUML Treatment
Organization design and stakeholder participation	Internal enterprise composition and contextual participation within and across organizations	Pharmaceutical Enterprise, Organizational Unit Structure, Organizational Stakeholder, Ecosystem Actor	Kinds and Roles connected through part–whole relations and mediation
Capability and strategy	Enterprise abilities and intentional direction characterizing organizational structures	Enterprise Capability, Strategic Resource Allocation	Modes connected to their bearers through characterization
Stakeholder value delivery and offerings	Coordination of ecosystem needs, available capacities, agreements, and service delivery	Ecosystem Demand Signal, Ecosystem Supply Capacity, Service Offering Specification, Ecosystem Relationship	Modes, Kinds, Relators, and domain-specific associations
Process and operating activity	Temporally unfolding pharmaceutical, clinical, reporting, and surveillance work	Pharmaceutical Business Process, Clinical Activity Sequence, Adverse Event Reporting Procedure, Post-Market Surveillance Activity	Perdurants with participating Roles and associated Relators
Governance, policy, and compliance	Normative constraints and oversight affecting organizations, collaborations, and processes	Regulatory Authority Entity, Regulatory Authority Role, Governance Policy Framework, Compliance Requirement, Regulatory Oversight	Kinds, Roles, Modes, Relators, mediation, characterization, and domain-specific associations
Digital enablement and information exchange	Technological support for ecosystem coordination, data exchange, and regulated workflows	Digital Health Platform Component, Electronic Health Record System, Real-World Evidence Platform, Blockchain-Based Supply Chain Ledger	Enabling Kinds connected through supports, enables, and informs associations

5.2. Domain Decomposition and Scope

CM-PharmE 1.0 organizes the pharmaceutical ecosystem through a five-domain architectural decomposition that analytically separates major modeling concerns while preserving explicit cross-domain dependencies. The decomposition is not merely thematic; it distinguishes modeling responsibilities whose interactions are represented through mediation, characterization, constraint, part–whole, and domain-specific associations where appropriate.

The Organizational/Structural domain captures the internal configuration of pharmaceutical enterprises, including organizational units, stakeholder roles, governance structures, and strategic capabilities. It formalizes how enterprise-level composition and authority structures are constituted and how stakeholder participation is mediated within institutional boundaries.

The Ecosystem/Collaborative domain extends the modeling scope beyond single-enterprise perspectives by representing inter-

organizational participation and relational coordination mechanisms. Actors assume contextual roles within partnership arrangements, contractual relators, and hybrid governance forms such as public–private partnerships. This domain models the relational infrastructure that sustains ecosystem-wide collaboration and value exchange.

The Operational/Process domain represents temporally unfolding pharmaceutical and clinical activities. It formalizes business processes, clinical pathways, and accountability structures as perdurants, explicitly capturing participation roles and process-level dependencies that connect enterprise capabilities to ecosystem service delivery.

The Governance/Regulatory domain represents normative constraints associated with regulatory authorities, including compliance requirements, oversight mechanisms, and risk-management structures. Its constructs capture how governance concerns influence operational execution and collaborative arrangements across domains.

Finally, the Digital Transformation domain represents enabling technological infrastructures that coordinate data exchange, interoperability, and digitally mediated governance. Rather than treating digital systems as isolated artifacts, this domain embeds them within the broader ecosystem structure as enabling kinds that interact with organizational, operational, and regulatory constructs.

Together, the five domains provide a modular but semantically integrated scaffold for ecosystem-level reasoning. Figure 3 summarizes their responsibilities and thematic separation.

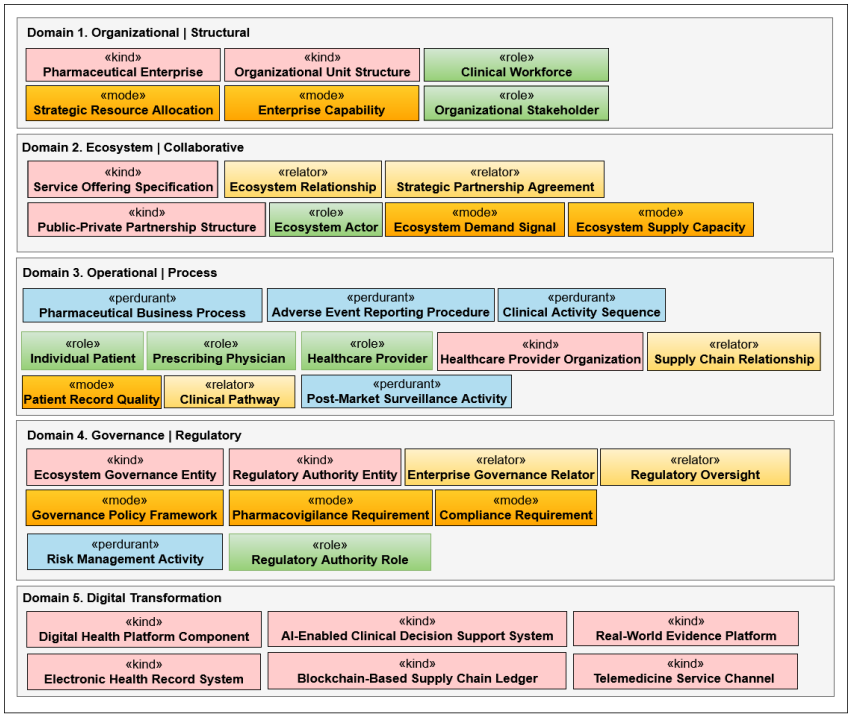


Figure 3. High-level view of the five business architecture–informed conceptual domains of CM-PharmE 1.0, illustrating their scope and thematic separation within the pharmaceutical ecosystem.

Figure 3 summarizes the five domain responsibilities: internal enterprise structure, inter-organizational collaboration, operational and clinical processes, governance and regulation, and digital enablement. Their interactions are represented explicitly in the integrated model rather than inferred from thematic proximity alone.

5.3. Core Ontological Constructs and Domain Semantics

At the organizational level, Pharmaceutical Enterprise (Kind) governs Organizational Stakeholders (Role) through the Enterprise Governance Relator. The enterprise comprises Organizational Unit Structures (Kind) and is characterized by Enterprise Capability (Mode) and Strategic Resource Allocation (Mode).

Within the broader ecosystem, Ecosystem Actors (Role) participate through Ecosystem Relationships (Relator) and Strategic Partnership Agreements (Relator), while hybrid collaboration is represented by Public-Private Partnership Structure (Kind). Demand-supply alignment is represented through Ecosystem Demand Signals (Mode), Ecosystem Supply Capacities (Mode), and Service Offering Specifications (Kind).

Operational dynamics are represented as Pharmaceutical Business Processes and Clinical Activity Sequences (Perdurants). Clinical Pathways (Relator) mediate roles such as Individual Patient and Prescribing Physician. Pharmacovigilance Requirements (Mode) constrain Post-Market Surveillance Activities, which are related to Adverse Event Reporting Procedures, while Real-World Evidence Platforms inform pharmacovigilance requirements and risk-management activities. These encoded relations distinguish formal dependencies from broader scenario interpretations [7], [32].

Governance and regulation are represented through Regulatory Authority Entity (Kind), Regulatory Authority Role (Role), and Regulatory Oversight (Relator), with Governance Policy Framework (Mode), Compliance Requirement (Mode), and Risk Management Activity (Perdurant) capturing normative and response concerns. Digital transformation is represented through Digital Health Platform Component, Electronic Health Record System, Telemedicine Service Channel, AI-Enabled Clinical Decision Support System, and Blockchain-Based Supply Chain Ledger, which connect digital capabilities to operational and

governance concerns.

5.4. Integrated Model View and Cross-Domain Coherence

Figure 4 integrates the model's concepts, relations, cardinalities, and stereotypes across the five domains. It makes selected cross-domain dependencies explicit, including pharmacovigilance requirements constraining post-market surveillance, digital constructs enabling or informing regulated work, and collaborative agreements structuring participation. The view applies the modeling procedure in Section 3.4 and documents the current commitments rather than an exhaustive or uniquely correct pharmaceutical ontology; empirical review and contextual extension remain possible.

5.5. Illustrative Ecosystem Instantiation

To examine representational plausibility, CM-PharmE was instantiated in a simplified vaccine-distribution scenario. Scenario-based instantiation is commonly used to determine whether an ontology can represent intended situations and support competency-oriented reasoning [29], and vaccine lifecycle research provides a suitable multi-actor, regulatory, operational, and digital context [16]. The scenario is illustrative rather than empirical and is used only to trace scenario elements to CM-PharmE constructs, stereotypes, and cross-domain relations.

Consider a simplified vaccine-distribution ecosystem in which a vaccine manufacturer instantiates Pharmaceutical Enterprise (Kind), while a national health authority is represented through Regulatory Authority Entity and its contextual Regulatory Authority Role. Strategic Partnership Agreement (Relator) represents coordinated participation, whereas Regulatory Oversight (Relator) represents supervision. Governance Policy Framework and Compliance Requirement provide the normative context, while distribution and cold-chain activities are Pharmaceutical Business Processes (Perdurants). This separates actors, agreements, oversight, normative conditions, and activities without asserting unencoded policy-to-process relations [7], [32].

At the clinical and post-market level, a vaccinated person instantiates Individual Patient (Role) and participates in a Clinical Activity Sequence coordinated through a Clinical Pathway (Relator). Adverse Event Reporting Procedure represents the reporting activity, while Pharmacovigilance Requirement constrains Post-Market Surveillance Activity, which is related to the reporting procedure. Real-World Evidence Platform is linked to the pharmacovigilance requirement and informs Risk Management Activity. Electronic Health Record System and Blockchain-Based Supply Chain Ledger remain digital enablers; information-exchange and traceability interpretations do not imply additional formal relations [16], [29].

Table 5. Traceability from the illustrative vaccine-distribution scenario to CM-PharmE constructs and relations.

Scenario Element	CM-PharmE Construct and Stereotype	Primary Domain(s)	Mapped Relation or Dependency	Interpretation in the Scenario
Vaccine manufacturer	Pharmaceutical Enterprise (Kind)	Organizational/Structural	Engages in a Strategic Partnership Agreement; distribution is modeled separately as a Pharmaceutical Business Process	Organizational bearer responsible for vaccine production and distribution activities
National health authority	Regulatory Authority Entity (Kind) and Regulatory Authority Role (Role)	Governance/Regulatory; Ecosystem/Collaborative	Regulatory Authority Entity is connected to Regulatory Authority Role; the role is mediated by Regulatory Oversight	Separates the institutional authority from its contextual oversight role
Distribution partnership	Strategic Partnership Agreement (Relator)	Ecosystem/Collaborative	Ecosystem Actor participation is mediated by the Strategic Partnership Agreement	Contractual or collaborative arrangement supporting distribution
Regulatory supervision	Regulatory Oversight (Relator)	Governance/Regulatory	Regulatory Authority Role is mediated by Regulatory Oversight	Formal oversight representation without adding unencoded regulated participants
Governance and compliance obligations	Governance Policy Framework and Compliance Requirement (Modes)	Governance/Regulatory	Governance Policy Framework characterizes Regulatory Oversight; Compliance Requirement characterizes Governance Policy Framework; Risk Management Activity mitigates Compliance Requirement	Normative context; no direct policy/compliance-to-process constraint is asserted
Cold-chain distribution	Pharmaceutical Business Process (Perdurant)	Operational/Process	Pharmaceutical Business Process situated in the scenario's governance and digital context	Temporally unfolding regulated distribution process
Vaccinated person and vaccination activity	Individual Patient (Role), Clinical Activity Sequence (Perdurant), and Clinical Pathway (Relator)	Operational/Process	Individual Patient is mediated by Clinical Pathway; Clinical Activity Sequence is represented within the associated business process	Clinical participation within the vaccine ecosystem
Adverse-event reporting	Pharmacovigilance Requirement (Mode) and Adverse Event Reporting Procedure (Perdurant)	Governance/Regulatory; Operational/Process	Pharmacovigilance Requirement constrains Post-Market Surveillance Activity, which follows the Adverse Event Reporting Procedure	Preserves the formal two-step path from requirement to reporting
Post-market evidence and risk analysis	Real-World Evidence Platform (Kind), Post-Market Surveillance Activity (Perdurant), and Risk Management Activity (Perdurant)	Digital Transformation; Operational/Process; Governance/Regulatory	Real-World Evidence Platform informs Pharmacovigilance Requirement and Risk Management Activity	Cross-domain pathway; surveillance interpretation extends beyond direct encoded relations
Digital traceability and information exchange	Electronic Health Record System and Blockchain-Based Supply Chain Ledger (Kinds)	Digital Transformation	Electronic Health Record System records Individual Patient and Patient Record Quality; Supply Chain Relationship mediates the Blockchain-Based Supply Chain Ledger	Application-level information-exchange and traceability interpretation; not a technical architecture

Table 5 maps the scenario to constructs and relations across all five domains using the ontological distinctions in Section 3.4 [7], [32]. It separates formally encoded relations from broader scenario interpretation, strengthening traceability without adding relations solely to fit the narrative. As a single constructed case, the scenario supports bounded representational plausibility and executable traceability but does not establish empirical validity, completeness, interoperability, or implementation feasibility

[29].

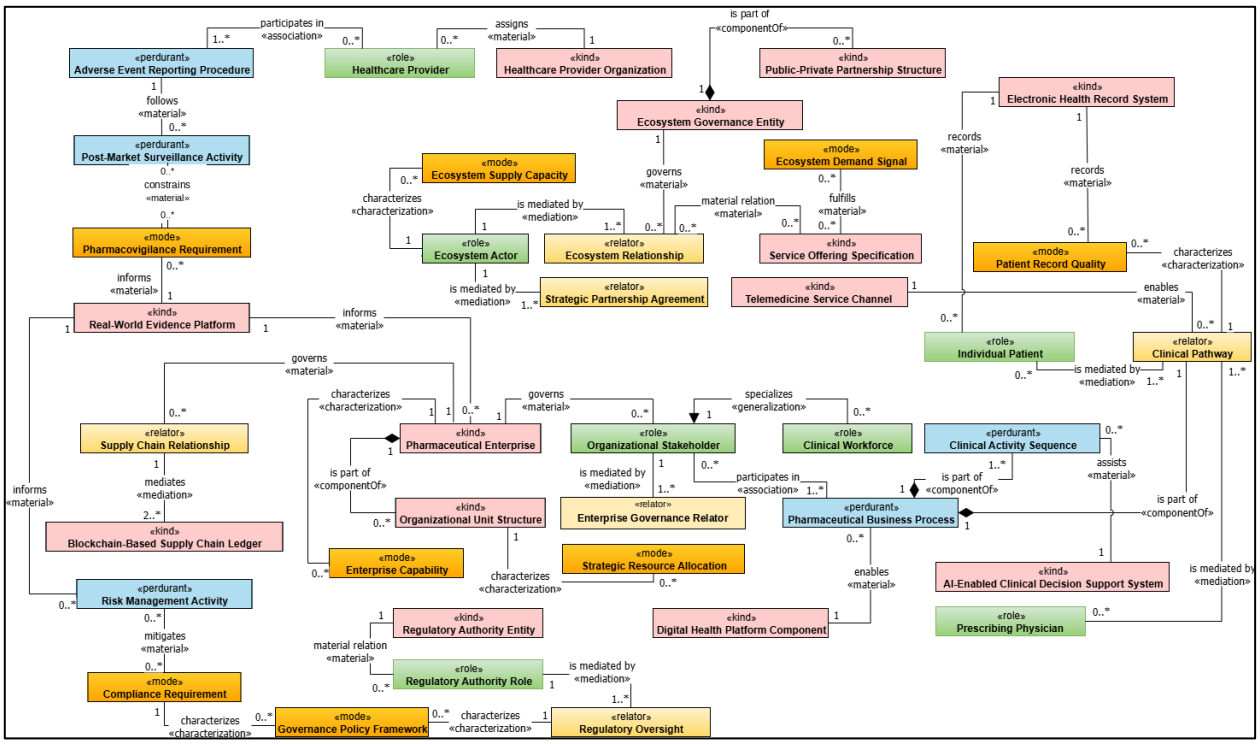


Figure 4. Integrated OntoUML-based conceptual model of the pharmaceutical ecosystem, depicting key concepts, relationships, cardinalities, and ontological stereotypes across organizational, collaborative, operational, regulatory, and digital domains.

The preceding sections establish CM-PharmE 1.0's structural and semantic basis and illustrate it in a representative ecosystem scenario. Section 6 evaluates conceptual coverage, ontological discipline, clarity, extensibility, and potential practical relevance through complementary qualitative and computational procedures. The resulting evidence is criterion-specific and preliminary; it does not constitute definitive formal validation, empirical proof of effectiveness, or evidence of universal applicability.

6. MODEL EVALUATION

The assessment of CM-PharmE 1.0 combines complementary qualitative procedures with bounded repository-supported computational checks addressing different aspects of the conceptual artifact. The qualitative procedures comprise a scenario-based comparative benchmark, expert review, focused manual OntoUML anti-pattern inspection, competency-question analysis, and illustrative ecosystem instantiation. The computational layer complements these procedures through executable competency queries over the formalized model and machine-readable scenario and through automated logical validation of the current ontology axiom set using ROBOT and HermiT [40], [41]. Because these procedures differ in scope and evidential strength, their results are interpreted criterion by criterion rather than aggregated into a single validation score. The assessment therefore distinguishes evidence of structural discipline, conceptual coverage, and bounded logical consistency from preliminary indications of clarity, adaptability, and potential practical value. For transparent synthesis, Section 6.7 organizes the complete evidence package into nine complementary repository-level evaluation layers (E1–E9), separating syntax, logic, structure, ontological review, semantic/expert evidence, data mapping, competency questions, application evidence, and reproducibility.

6.1. Evaluation Framework and Criteria

Given the qualitative and conceptual orientation of this study, the evaluation framework was adapted from established ontology-quality perspectives that distinguish structural or syntactic quality, semantic quality, pragmatic usefulness, and maintainability-related characteristics [34]–[36]. Five criteria were retained to match the principal claims made for CM-PharmE. Syntactic and Structural Correctness concerns stereotype use, relation semantics, and participation constraints; Semantic and Conceptual Accuracy concerns alignment with the intended pharmaceutical ecosystem meaning; and Conceptual Clarity concerns naming consistency, domain intelligibility, and interpretability. Adaptability and Modifiability concerns whether representative contextual extensions can be accommodated without restructuring the core domain decomposition, whereas Pragmatic Value concerns traceable support for governance, requirements, and architectural reasoning. All five criteria were used as qualitative analytical lenses rather than quantitatively weighted metrics.

Each criterion was operationalized through an evaluation indicator, an identifiable evidence source, a documented assessment procedure, and a bounded result, as summarized in Table 6. Only evidence from procedures reported in the manuscript was included. No composite score, statistical significance test, standardized usability instrument, or empirically measured implementation outcome was calculated. The assessment is therefore a transparent synthesis of preliminary qualitative evidence rather than a definitive measurement of overall ontology quality.

Table 6. Operationalization of the evaluation criteria applied to CM-PharmE 1.0.

Evaluation Criterion	Evaluation Indicator	Evidence Source	Assessment Procedure	Result and Evidential Boundary
Syntactic and Structural Correctness	Appropriate use of OntoUML stereotypes and relations; interpretable cardinalities; absence of critical issues among the selected anti-patterns	Section 3.4, Figure 4, and Tables 11–12	Focused manual inspection of eight anti-pattern categories relevant to the model, followed by repository-supported reinspection of the corresponding formalized concepts and relations	No critical issue was identified. The two previously reported minor issues and the low-risk observation were retained; repository-supported reinspection additionally identified one candidate role–relator issue and one additional part–whole relation requiring targeted semantic review. The assessment was neither an exhaustive OntoUML anti-pattern analysis nor the output of a complete automated detector.
Semantic and Conceptual Accuracy	Alignment of concepts, relations, and the five-domain decomposition with the intended pharmaceutical ecosystem meaning; ability to address the competency questions	Section 5.5, Section 6.3, Table 10, and Table 13	Qualitative expert review combined with traceability of competency questions to explicit model constructs and cross-domain relations	Preliminary support was obtained for domain relevance and conceptual coverage, with minor terminology and role-definition clarifications. The evidence is limited by the small expert panel and the absence of operational deployment.
Conceptual Clarity	Consistent terminology, readable domain descriptions, distinguishable stereotypes, and interpretable competency-question answers	Sections 5.2–5.4, Section 6.3, Figure 4, Table 10, and Table 13	Qualitative inspection of naming and domain explanations, supplemented by expert feedback concerning terminology and interpretability	The model was generally interpretable within the reviewed scope, although minor terminological clarification was required. No standardized usability scale or quantitative readability assessment was administered.
Adaptability and Modifiability	Ability to represent a context-specific scenario and accommodate extensions without changing the principal five-domain decomposition	Section 5.5, Figure 4, and the modular domain structure	Illustrative vaccine-distribution instantiation and qualitative inspection of whether the scenario required restructuring of the core domains	The scenario was represented without altering the core domain decomposition. This provides illustrative rather than experimental evidence because only one scenario was examined and no controlled extension test was conducted.
Pragmatic Value	Traceable pathways from model constructs to governance analysis, requirements derivation, reference-architecture interpretation, and system-design reasoning	Table 7, Table 13, Table 14, and Section 7.4	Analytical mapping of domains and constructs to representative use cases, competency questions, requirements concerns, and architectural activities	Plausible application pathways were identified. Practical value has not yet been confirmed through organizational adoption, measured user outcomes, or implementation-cost analysis.

As Table 6 shows, evidential strength varies across the five criteria. Structural and conceptual-coverage evidence draws on direct inspection of model constructs, repository-supported semantic reinspection, anti-pattern observations, competency-question traceability, executable-query results, and the illustrative instantiation. The reinspection helps distinguish stable modeling choices from issues requiring targeted semantic review, but it does not convert the selected anti-pattern assessment into exhaustive ontological validation. Adaptability and pragmatic value rely primarily on analytical and scenario-based evidence and therefore remain preliminary rather than demonstrated operational properties. This distinction prevents the combined assessment from being read as a claim of complete validation or proven organizational effectiveness.

Beyond the criterion-based assessment in Table 6, the five CM-PharmE domains can be interpreted in terms of potential reference-architecture applications. Table 7 presents this application-oriented view. Its rows correspond to the five model domains rather than the five evaluation criteria, and the listed uses are illustrative pathways derived from the model structure. They should not be treated as additional validation results or as evidence of deployment in pharmaceutical organizations.

Table 7. Application-oriented interpretation of CM-PharmE domains as a reference architecture.

CM-PharmE Domain	Reference-Architecture Application	Illustrative Pharmaceutical-Ecosystem Use
Organizational and Structural	Align organizational units, capabilities, and business goals with a unified reference architecture.	Support comparison of internal organizational structures with regulatory and supply-chain concerns.
Collaborative and Ecosystem	Establish a reference architecture for stakeholder collaboration (companies, regulators, insurers, patients).	Support analysis of public–private partnerships, alliances, and innovation networks.
Operational and Process	Map business processes to standardized operational flows within the reference model.	Support traceability analysis for processes such as adverse-event reporting and supply-chain activities.
Regulatory and Governance	Support alignment of regulatory policies and legal standards at national and international levels.	Support conceptual mapping and comparison of policies, compliance requirements, and oversight responsibilities.
Digital Transformation and Information Technology	Provide a coherent framework for information systems, enhancing interoperability and integration across technologies.	Support conceptual mapping of dependencies among digital platforms, EHR systems, blockchain-based solutions, and real-world-evidence platforms.

As indicated in Table 7, the five domains provide a structured basis for interpreting organizational, collaborative, operational, regulatory, and digital concerns in a reference-architecture context. The table identifies potential uses such as organizational mapping, collaboration analysis, process alignment, compliance structuring, and digital-system coordination. These uses remain prospective and application-oriented: they illustrate how stakeholders may employ the conceptual model, but they do not establish implementation feasibility, organizational adoption, transition cost, or measurable operational benefit. The Discussion therefore treats these applications as pathways for subsequent empirical and engineering-oriented research.

6.2. Scenario-Based Comparative Benchmark

A lightweight scenario-based benchmark was used to complement the internal model assessment by comparing representational coverage within a common illustrative setting. The vaccine-distribution scenario was examined across six concerns: organizational actors, inter-organizational collaboration, governance and compliance constraints, operational processes, digital enablers, and cross-domain traceability. Table 8 applies the qualitative rubric defined for Table 3: Yes denotes explicit and substantive representation, Partial denotes explicit but incomplete representation, Limited denotes narrow or indirect representation, and No denotes the absence of explicit evidence for the assessed capability. The ratings are literature-based comparative judgments within the selected scenario rather than quantitative measures of model performance.

Table 8. Scenario-based comparative benchmark of CM-PharmE 1.0 against representative prior approaches using a simplified vaccine distribution ecosystem scenario.

Approach	Organizational Actors	Inter-Organizational Collaboration	Governance / Compliance Constraints	Operational Process Representation	Digital Enablers	Cross-Domain Traceability
[8] OntoPharma	Partial	No	Limited	Yes	Partial	No
[13] Sultanow et al.	Partial	Partial	Partial	Partial	Yes	Limited
[16] Ilin et al.	Yes	Yes	Partial	Yes	Yes	Limited
[21] Ghadge et al.	Limited	Partial	Limited	Yes	Yes	No
CM-PharmE 1.0	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**

As shown in Table 8, most prior approaches cover the benchmark scenario only partially because they focus on clinical ontology, architectural structuring, supply-chain conceptualization, or ecosystem process framing in relative isolation. CM-PharmE represents the same scenario within a unified structure that combines organizational actors, collaborative arrangements, governance constraints, operational workflows, digital infrastructures, and explicit cross-domain dependencies. This finding does not replace empirical validation, but it provides comparative evidence of broader representational coverage within the selected scenario and comparison set.

Building on this comparative benchmark, the following subsections examine the proposed model through qualitative expert review, focused OntoUML anti-pattern inspection, and competency-question analysis. These complementary procedures address different aspects of the artifact and are interpreted according to their respective evidential boundaries rather than as equivalent forms of formal validation.

6.3. Expert Review

A small-scale qualitative expert review complemented the model-centered assessment by eliciting informed feedback on domain relevance, conceptual intelligibility, cross-domain coherence, and potential applicability. The review provided preliminary qualitative evidence rather than statistically representative validation. Its purpose was to identify conceptual ambiguities and refinement needs and to assess whether professionals with relevant domain and architectural experience could interpret the principal model structure.

The review involved four experts purposively recruited through the authors' professional network to provide complementary perspectives on CM-PharmE. Selection reflected the relevance of each expert's academic or professional experience to one or more model areas, including pharmaceutical-enterprise operations, healthcare information systems, regulatory or governance concerns, and enterprise or business architecture. Given the small, nonrepresentative panel, experts are reported anonymously as E1–E4. Table 9 summarizes the professional characteristics used to establish panel relevance while avoiding unnecessary personal identification.

Table 9. Anonymized professional profiles of the experts involved in the CM-PharmE review.

Expert ID	Professional Context	Primary Relevant Expertise	Basis of Relevant Experience	Rationale for Inclusion
E1	Academic researcher and enterprise-architecture practitioner	Enterprise and business architecture, conceptual modeling, and ontology-informed systems analysis	Academic and professional experience in enterprise architecture and conceptual-model development.	Assessment of the architectural coherence of the five-domain decomposition, the relationship between business-architecture concerns and OntoUML constructs, and the clarity of cross-domain dependencies
E2	Healthcare information-systems and digital-health professional	Health informatics, healthcare information systems, semantic interoperability, and digital-health platforms	Professional experience in the analysis, design, or implementation of healthcare information systems.	Assessment of the Digital Transformation domain, interoperability-oriented concepts, information-system constructs, and the relationship between digital enablers and regulated ecosystem processes
E3	Pharmaceutical-industry or pharmaceutical-enterprise professional	Pharmaceutical operations, organizational structures, value-chain processes, and inter-organizational coordination	Professional experience in pharmaceutical-enterprise operations or pharmaceutical ecosystem activities.	Assessment of pharmaceutical-domain relevance, organizational and operational constructs, ecosystem actors, business processes, and the practical intelligibility of the model
E4	Regulatory, governance, or health-ecosystem professional	Regulatory governance, compliance, policy, oversight mechanisms, and ecosystem collaboration	Academic or professional experience in regulatory, governance, or health-ecosystem responsibilities.	Assessment of the Governance/Regulatory and Ecosystem/Collaborative domains, including policies, compliance requirements, oversight relations, partnerships, and cross-organizational coordination

To preserve anonymity, Table 9 reports only the professional context, relevant expertise, and experience basis used to establish

each expert's relevance to the review. Age, gender, institutional affiliation, and exact experience duration are omitted because these variables were not used as formal eligibility criteria.

The review covered the integrated model, its five-domain decomposition, principal concepts and relations, and major cross-domain dependencies. Four dimensions were considered: semantic appropriateness, intelligibility and perceived domain coverage, coherence of cross-domain dependencies, and potential usefulness for ecosystem-level analysis. No standardized psychometric instrument or quantitative scoring scale was used. Feedback was obtained through individual discussions and subsequent written exchanges and retained as narrative observations for author review.

The authors reviewed the expert feedback qualitatively and consolidated it according to the four assessment dimensions rather than subjecting it to statistical aggregation or frequency-based scoring. No inter-rater reliability coefficient, consensus threshold, or quantitative content-validity index was calculated. The analysis aimed to identify observations requiring clarification, refinement, or reconsideration and to record the corresponding author decision. Table 10 summarizes the principal feedback-to-action traces that informed the revision.

Table 10. Traceability between documented expert feedback and corresponding author actions.

Feedback Category	Summary of Documented Observation	Author Decision	Revision / Response	Effect on Core Model
Terminology precision	Some model terms required clearer wording to reduce potential ambiguity in interpretation.	Accepted	Terminology and explanatory definitions were clarified in the corresponding domain descriptions and methodological explanation.	No structural change
Role-definition clarity	Selected contextual roles required clearer explanation to distinguish role-based classification from rigid entity types.	Accepted	Role definitions and the UFO/OntoUML decision rationale were clarified in Sections 3.4 and 5.3.	No structural change
Five-domain structure	The documented review did not identify feedback requiring redesign of the principal five-domain decomposition.	Retained	The five-domain architecture was preserved while explanatory material and traceability were strengthened.	No structural change

The documented expert feedback provided preliminary support for the model's relevance and intelligibility within the panel's scope. The principal refinement needs concerned terminology and clarification of selected role definitions; none required redesign of the five-domain architecture. Given the small, purposively assembled panel and qualitative review design, these findings constitute expert-informed feedback for conceptual refinement rather than conclusive evidence of semantic validity, conceptual completeness, or practical effectiveness. Broader expert panels and empirical deployment studies are needed to assess the model across additional organizational and regulatory contexts.

6.4. Focused Manual OntoUML Anti-Pattern Inspection

A focused manual OntoUML anti-pattern inspection was conducted on the refined CM-PharmE model, informed by the UFO/OntoUML foundations in [7], [32] and the anti-pattern literature in [37]. The authors examined eight categories relevant to roles, relators, modes, perdurants, part–whole relations, and cross-domain associations. During the present revision, these observations were rechecked against the formalized repository representation using structural heuristics and targeted semantic inspection of the corresponding concepts and relations. This second stage examined whether the formalized graph exposed issues not apparent in the earlier diagram-centered review. No exhaustive OntoUML anti-pattern detector, model simulator, or OCL-based verification mechanism was applied. Accordingly, the results constitute a strengthened but still selective diagnostic assessment rather than exhaustive formal verification or proof of ontological correctness. Table 11 summarizes the selected categories and their relevance to CM-PharmE.

Table 11. Selected OntoUML-informed inspection categories used in the focused manual review of CM-PharmE 1.0 [7], [32], [37].

Anti-Pattern	Description	Relevance to CM-PharmE
Type–Role Confusion	Modeling roles as rigid types (kinds) or modeling kinds as roles	Relevant due to extensive use of organizational, clinical, and ecosystem roles
Role without Relator	Role defined without mediation through a contextual relator	Relevant for governance, clinical, and ecosystem participation roles
Relator without Mediation	Relator defined without explicit mediation to role instances	Relevant for partnership, governance, and supply chain relations
Event as Object	Modeling events or processes as kinds	Relevant due to multiple clinical and business processes
Mode vs. Attribute Confusion	Modeling qualities, dispositions, or requirements as independent entities	Relevant due to modeling of capabilities, requirements, and signals
Part–Whole Misuse	Incorrect or semantically weak use of componentOf or partOf relations	Relevant for organizational and ecosystem structures
Relation as Class	Representing relations as kinds instead of relators	Relevant for contractual, governance, and collaborative relations
Overloaded Association	Single association used with multiple or ambiguous semantics	Relevant for governance and information-related relations

Each category was initially applied manually to the relevant concepts, stereotypes, relations, and cardinalities represented in Figure 4, after which the corresponding formalized structures were reexamined in the project repository. The resulting observations were classified as Clean, Minor issue, Candidate minor issue, or Low risk. Clean indicates that no apparent issue was identified in the inspected fragment and that repository reinspection did not introduce a contradictory finding. Minor issue denotes a previously identified modeling concern that remains supported by the formalized representation. Candidate minor issue denotes a newly exposed concern that merits targeted semantic review but is not treated as a confirmed modeling defect. Low risk denotes an acceptable current representation for which further elaboration may improve semantic precision. Because the assessment remains selective and does not cover the complete OntoUML anti-pattern catalog through a dedicated automated

detector, these classifications are diagnostic judgments rather than formal verification results [7], [32], [37]. The resulting classifications and observations are reported in Table 12.

Table 12. Results of the focused OntoUML anti-pattern inspection and repository-supported reinspection of CM-PharmE 1.0.

Anti-Pattern	Inspection Result	Observations	Implications for Future Versions
Type–Role Confusion	Clean	No type–role conflation was identified among the inspected constructs; for example, Individual Patient is represented as a Role and Pharmaceutical Enterprise as a Kind.	No action required
Role without Relator	Candidate minor issue	Repository-supported reinspection identified Healthcare Provider (Role) as lacking an explicit or inherited mediation relation in the current formalized graph. Other inspected roles retain an identifiable contextual mediation basis.	Targeted semantic review of the Healthcare Provider participation context
Relator without Mediation	Minor issue	The previously identified mediation-specificity issue remains: Supply Chain Relationship does not yet expose sufficiently explicit mediation to the participant role types expected of the relator in the current formalized representation.	Targeted refinement of mediation semantics in a subsequent model revision
Event as Object	Clean	The inspected clinical and business processes are represented as perdurants rather than as rigid object types.	No action required
Mode vs. Attribute Confusion	Clean	The inspected capabilities, requirements, and demand/supply signals are represented as modes within the current model.	No action required
Part–Whole Misuse	Minor issue	The previously identified Public–Private Partnership Structure–to–Ecosystem Governance Entity relation remains semantically debatable as structural composition. Repository-supported reinspection additionally identified the "Clinical Pathway is part of Pharmaceutical Business Process" relation as requiring targeted mereological review because it connects constructs with distinct ontological categories.	Reconsider the semantics of both part–whole relations before stronger ontological-validation claims
Relation as Class	Clean	The inspected social, contractual, and governance relationship constructs are represented as relators.	No action required
Overloaded Association	Low risk	No material semantic overloading was identified among the inspected governance and information associations within the current scope.	No immediate action required

The combined inspection did not identify a critical issue requiring redesign of the five-domain architecture. Repository-supported reinspection confirmed four clean categories, retained the previously reported low-risk observation, and confirmed two earlier minor concerns involving mediation specificity and part–whole semantics. It also identified Healthcare Provider as a candidate Role-without-Relator concern and a second part–whole relation, involving Clinical Pathway and Pharmaceutical Business Process, for targeted mereological review. These distinctions separate confirmed observations from review candidates rather than treating every concern as a model defect. The evidence remains bounded: the inspection was selective, no complete automated OntoUML anti-pattern detector was used, and the observations do not establish exhaustive ontological soundness. Logical consistency was assessed separately through the ROBOT/HermiT procedure in Section 6.5 [40], [41]; such reasoning complements but does not resolve the semantic modeling issues identified here. Broader tool-supported anti-pattern analysis and targeted semantic review remain appropriate for subsequent model evolution [7], [32], [37].

Following this focused manual inspection, the next subsection examines the conceptual coverage of CM-PharmE 1.0 through competency questions linked to the model's intended ecosystem concerns, explicit constructs, and cross-domain relations.

6.5. Competency-Question Assessment

Competency questions were used as traceability-based checks of whether CM-PharmE contains the concepts and relations needed to address its intended ecosystem concerns. Consistent with ontology-development methodologies [29], the eight questions were derived from the guiding research question, five-domain scope, evidence-to-domain traceability in Table 2, and intended analytical uses of the model. CQ1–CQ5 examine domain-specific coverage, CQ6 examines cross-domain alignment between business-architecture concerns and UFO/OntoUML constructs, and CQ7–CQ8 address prospective reference-architecture use and contextual extension. The eight questions were also operationalized as executable queries over the formalized ontology and machine-readable vaccine-distribution scenario in the project repository. This computational layer tests whether the formal representation can retrieve the structures required by each question rather than relying only on narrative inspection.

For each competency question, the manuscript-level assessment remains traceability-based. Addressed denotes an explicit and traceable conceptual response; Addressed conceptually denotes conceptual support without implementation-level confirmation; and Partially addressed denotes dependence on prospective application, adaptation, or evidence beyond the current assessment. These qualitative categories were not converted into a numerical score and are retained in Table 13 because successful query execution does not by itself demonstrate organizational adoption, reference-architecture effectiveness, or contextual extensibility. The executable queries were assessed separately against predefined bounded expectations, and all eight returned the expected results for the current formalized model and scenario. Because both the questions and computational tests were authored within the study, they provide internal computational traceability rather than independent external validation.

Table 13. Traceability-based competency-question assessment of CM-PharmE 1.0.

Competency Question	Explicit CM-PharmE Evidence	Domain(s)	Assessment Result and Boundary	Supporting Sources
CQ1. How are organizational structures and capabilities of pharmaceutical enterprises represented within the ecosystem?	Pharmaceutical Enterprise and Organizational Unit Structure are represented as Kinds; Enterprise Capability and Strategic Resource Allocation as Modes; and stakeholder participation through the Enterprise Governance Relator.	Organizational/Structural	Addressed. The current model contains explicit constructs for enterprise identity, composition, capability, strategic resource allocation, and governance participation.	Sections 3.4 and 5.3; Figure 4; [7], [11], [17]
CQ2. How does the model capture inter-organizational collaboration and partnerships across the pharmaceutical ecosystem?	Ecosystem Actor roles are mediated by Ecosystem Relationship and Strategic Partnership Agreement relators; collaborative arrangements also include Public-Private Partnership Structure.	Ecosystem/Collaborative	**Addressed.** Explicit role and relator constructs support a traceable conceptual representation of collaboration.	Sections 5.2–5.3; Figure 4; [3], [16], [24]
CQ3. How are business and clinical processes connected to ecosystem-level participation?	Pharmaceutical Business Process and Clinical Activity Sequence are represented as Perdurants; Clinical Pathway represents the coordination context through which relevant roles participate.	Operational/Process; Ecosystem/Collaborative	**Addressed.** The model explicitly connects temporally unfolding processes with participating roles and relational contexts.	Sections 5.3 and 5.5; Figure 4; [8], [10], [14]
CQ4. How are regulatory governance and compliance constraints represented across pharmaceutical ecosystems?	Regulatory Authority Entity, Regulatory Authority Role, Regulatory Oversight, Governance Policy Framework, Compliance Requirement, Pharmacovigilance Requirement, and Risk Management Activity represent oversight, normative constraints, and governance response.	Governance/Regulatory; Operational/Process	**Addressed.** The current model contains explicit constructs and constraining relations for the principal governance concerns examined.	Sections 5.3 and 5.5; Figure 4; [2], [4], [19]
CQ5. How are digital technologies conceptually connected to ecosystem governance and operations?	Digital Health Platform Component, Electronic Health Record System, Real-World Evidence Platform, AI-Enabled Clinical Decision Support System, and Blockchain-Based Supply Chain Ledger are connected through the formal cross-domain associations represented in the current model.	Digital Transformation; Cross-Domain	**Addressed conceptually.** The model represents digital enablement and cross-domain dependencies, but no technical interoperability or system-integration test was conducted.	Sections 5.3–5.5; Figure 4; [1], [12], [15]
CQ6. How are business-architecture concerns aligned with foundational ontology at the ecosystem level?	Table 4 maps organization design, capability, strategy, stakeholder value delivery, process, governance, and digital enablement to CM-PharmE domains and UFO/OntoUML treatments.	Cross-Domain	**Addressed conceptually.** An explicit analytical mapping is provided, without claiming formal equivalence or BACM metamodel conformance.	Sections 2.1, 3.4, and 5.1; Table 4; [7], [32], [33]
CQ7. In what way can CM-PharmE function as a reference architecture for pharmaceutical ecosystems?	Table 7 and Section 7.4 identify potential uses for organizational mapping, collaboration analysis, compliance structuring, requirements derivation, and architectural reasoning.	Cross-Domain	**Partially addressed.** Analytical application pathways are provided, but organizational adoption, implementation feasibility, transition cost, and measurable benefit have not been evaluated.	Table 7; Section 7.4; [13], [16], [21], [27]
CQ8. How can the model be adapted or extended to different pharmaceutical contexts?	The modular five-domain structure and the vaccine-distribution instantiation demonstrate one context-specific mapping without alteration of the principal domain decomposition.	Cross-Domain	**Partially addressed.** The evidence is based on one illustrative scenario; no controlled extension experiment, multi-case comparison, or deployed adaptation was conducted.	Section 5.5; Table 5; Figure 4; [15], [22], [23], [29]

Table 13 shows that CQ1–CQ4 are addressed through explicit organizational, collaborative, operational, and regulatory constructs and relations. CQ5 and CQ6 are supported conceptually, although no technical interoperability test or formal BACM/OntoUML metamodel-conformance assessment was performed. CQ7 and CQ8 remain partially addressed because reference-architecture adoption and contextual extensibility have not been examined through operational deployment, controlled extension experiments, or multi-case evaluation. All eight executable competency queries returned their predefined bounded results against the formalized ontology and machine-readable vaccine scenario. ROBOT/HermiT reasoning completed without reporting a logical inconsistency or unsatisfiable named class in the current axiom set [40], [41]. Together, these checks strengthen evidence for computational traceability and bounded logical consistency but do not establish ontology completeness, standards conformance, operational interoperability, practical effectiveness, or universal applicability. Future evaluation should extend the competency-question set through broader stakeholder elicitation and execute it against representative pharmaceutical-ecosystem datasets [29].

6.6. Practical Guidelines for Utilizing the Conceptual Model

Table 14 translates CM-PharmE 1.0 into a staged analytical workflow rather than a prescriptive implementation method. Each stage specifies the required conceptual input, recommended model-based activity, expected analytical output, and a short illustrative example. The workflow is intended for enterprise architects, domain analysts, regulatory and governance specialists,

requirements engineers, and digital-health or information architects, depending on the application context. Technical implementation, standards conformance, data migration, organizational change, and deployment planning remain separate engineering activities and are not implied by use of the conceptual model.

Table 14. Operational guidelines for applying CM-PharmE 1.0 as a conceptual reference in pharmaceutical ecosystems.

Guideline	Required Input	Recommended Activity	Expected Output and Boundary	Short Example
1. Establish the application scope	Target ecosystem, organizational context, regulatory context, and analysis objective	Identify which of the five CM-PharmE domains and cross-domain concerns are relevant to the intended analysis.	A bounded conceptual-analysis scope; not a complete enterprise-architecture specification.	For vaccine distribution, select organizational, operational, governance, collaborative, and digital concerns relevant to distribution and surveillance.
2. Map organizations and contextual roles	List of participating organizations, authorities, professionals, and user groups	Map actors to Pharmaceutical Enterprise, Regulatory Authority Entity and Regulatory Authority Role, Ecosystem Actor, Individual Patient, Prescribing Physician, or other corresponding constructs.	An actor-and-role map with explicit distinctions between rigid entity types and contextual roles.	Represent a manufacturer as Pharmaceutical Enterprise and distinguish a national health authority as Regulatory Authority Entity acting through Regulatory Authority Role.
3. Map capabilities and strategic concerns	Business capabilities, organizational objectives, and strategic concerns	Relate Enterprise Capability and Strategic Resource Allocation to the organizational structures that bear them.	A conceptual capability-and-strategy view; not a quantified capability-maturity assessment.	Associate distribution capability and supply continuity objectives with the responsible pharmaceutical enterprise.
4. Trace collaborative arrangements	Partnerships, contracts, coordination mechanisms, and participating actors	Identify Ecosystem Relationships, Strategic Partnership Agreements, and relevant coordination or governance relators.	A collaboration map showing how ecosystem participation is structured.	Represent a manufacturer–authority distribution arrangement through a Strategic Partnership Agreement.
5. Map processes and participation	Key pharmaceutical or clinical activities and responsible participants	Associate processes with participating roles, pathways, capabilities, governance constraints, and supporting entities.	A cross-domain process traceability view; not an executable workflow model.	Link adverse-event reporting to the reporting procedure, patient participation, responsible organizations, and pharmacovigilance requirements.
6. Map governance and compliance constraints	Applicable policies, regulations, compliance obligations, oversight mechanisms, and risk concerns	Relate Governance Policy Framework, Compliance Requirement, Regulatory Oversight, and risk-related activities to affected actors and processes.	A conceptual governance-and-compliance traceability map; not evidence of legal conformance.	Map a pharmacovigilance requirement to the post-market surveillance activity it constrains and trace the related reporting procedure.
7. Identify digital enablers	Existing or planned information systems, platforms, data services, and digital technologies	Relate digital constructs to the processes, actors, information flows, and governance concerns they support or inform.	A technology-to-domain dependency map; not a detailed solution architecture.	Relate Electronic Health Record System to patient-record constructs and use Real-World Evidence Platform to trace pharmacovigilance and risk-management dependencies.
8. Align with implementation standards where required	Target information exchanges, medicinal-product information, and applicable interoperability requirements	Use CM-PharmE concepts as a semantic reference when defining implementation-specific mappings to standards such as HL7 FHIR and ISO IDMP [38], [39].	A candidate semantic mapping layer; CM-PharmE itself does not establish standards conformance.	Map relevant clinical exchange concepts to FHIR-based interfaces while aligning regulated medicinal-product identifiers with IDMP structures.
9. Derive downstream requirements and architecture concerns	Validated actor, process, governance, and digital-dependency mappings	Translate identified responsibilities and constraints into candidate functional, non-functional, data, integration, and governance requirements using established requirements-engineering practices [27].	Traceable candidate requirements and architecture concerns requiring engineering validation.	Derive a requirement that adverse-event reports remain traceable to the responsible actor, reporting procedure, and governing compliance requirement.
10. Review extensions and transition implications	Target-state mappings, legacy-system information, identified gaps, and organizational constraints	Identify missing concepts, legacy mappings, migration dependencies, organizational changes, and required model extensions.	An extension and transition backlog; cost and adoption impact must be estimated in the target organization.	Record a legacy terminology mismatch as a semantic-mapping task rather than modifying the five-domain architecture prematurely.

Table 14 positions CM-PharmE as a conceptual reference that precedes, rather than replaces, implementation-specific architecture and standards engineering. Adoption may proceed incrementally: organizations can first establish a bounded ecosystem scope and conceptual mappings, then identify governance and process dependencies, and subsequently derive implementation requirements and standards-specific mappings. For healthcare information exchange, HL7 FHIR Release 5 provides an implementation-oriented specification for electronic healthcare data exchange [38]. ISO 11615:2017, within the Identification of Medicinal Products (IDMP) standards family, defines structured concepts and data elements for identifying and exchanging regulated medicinal-product information [39]. CM-PharmE may provide a higher-level semantic context for such mappings, but no FHIR or IDMP conformance is claimed or evaluated in this study. Transition cost cannot be estimated generically from the conceptual artifact because it depends on legacy-system heterogeneity, data and terminology alignment, regulatory context, organizational change, integration scope, and the extent of model customization required in a specific deployment.

6.7. Integrated Multi-Layer Evaluation and Reproducibility

The manuscript-level evaluation procedures described above were subsequently organized in the project repository into a nine-layer evidence architecture so that qualitative, formal, computational, application-oriented, and reproducibility claims could be inspected separately. This organization was introduced during repository engineering and should therefore be interpreted as a structured synthesis and strengthening of the available evidence, not as a claim that all nine layers were predefined as independent components of the original study protocol.

Table 15 summarizes the resulting E1–E9 evaluation architecture and its current status. The strongest repository-executed evidence concerns syntax, logical consistency, structural integrity, bounded data/mapping checks, executable competency questions, and reproducibility. Ontological soundness remains conditional because targeted semantic findings are still open; semantic/expert evidence and application evidence remain partial or illustrative because they have not been independently replicated or operationally deployed.

Table 15. Integrated repository-supported evaluation architecture for CM-PharmE 1.0.

Layer	Evaluation focus	Repository evidence / method	Status	Interpretive boundary
E1	Syntax validation	Parsing and serialization-equivalence checks over the canonical RDF/OWL artifacts	**PASS**	Syntactic and graph-serialization validity; not semantic completeness.
E2	Logical consistency	ROBOT v1.9.10 with the HermiT reasoner in GitHub Actions	**PASS**	No logical inconsistency or unsatisfiable named class was reported for the current logical axiom set; this does not establish domain completeness.
E3	Structural integrity	Automated repository cross-checks of stable IDs, concepts, relations, domains, cardinalities, lifecycle records, and formal-graph alignment	**PASS — 28/28 checks**	Structural consistency and traceability only; not semantic adequacy by itself.
E4	Ontological soundness	Focused OntoUML-informed anti-pattern inspection plus repository-supported semantic reinspection and finding disposition	**CONDITIONAL**	No redesign-level defect was found, but targeted role–relator and part–whole refinements remain open.
E5	Semantic / expert evidence	Qualitative four-expert evidence and feedback-to-action traceability	**PARTIAL**	Small, nonrepresentative qualitative evidence; no independent replication is claimed.
E6	Data / mapping validation	Machine-readable vaccine-distribution sample and schema/mapping checks	**PASS — bounded**	33 individuals, 32 existing core classes, all five domains, 34 relation assertions, and no unknown classes/properties or explicit domain/range violations in the constructed sample.
E7	Competency questions	Eight versioned SPARQL queries with predefined bounded expectations	**PASS — 8/8**	Internal computational traceability; CQ6–CQ8 do not establish BACM conformance, organizational adoption, or general extensibility.
E8	Application evidence	Illustrative vaccine-distribution instantiation and application-oriented analysis	**PARTIAL / illustrative**	No deployed reference architecture, operational interoperability test, user outcome, or empirical transition-cost evidence.
E9	Reproducibility	Deterministic ontology build, graph fingerprints, generated serializations and SHACL, checksums, repeated clean builds, CI regression gates, and deterministic release bundle	**PASS**	Reproducibility of the current repository artifact; not evidence of empirical usefulness or standards conformance.

The formal and reproducibility layers provide additional evidence beyond the earlier diagram- and prose-centered assessment. Repository validation records 28/28 structural and traceability checks as passing; the current formal inventory contains 39 concept classes, 39 OWL object properties plus one generalization record, five domains, and 42 qualified OWL cardinality restrictions. The machine-readable vaccine scenario contains 33 individuals instantiating 32 existing core classes across all five domains with 34 CM-PharmE relation assertions and no unknown classes or predicates. All eight executable competency queries returned their predefined bounded results.

Reproducibility was strengthened further through the deterministic build pipeline. The modular source reconstructs the 1,086-triple canonical graph; SHACL generation yields 574 triples, 76 node shapes, and 76 property shapes; generated serializations are checked for graph equivalence; repeated clean builds and release bundles are required to be byte-identical; and ROBOT/HermiT logical validation is enforced as a CI gate. These results establish reproducibility, structural traceability, and bounded logical consistency for the current repository artifact, but they do not resolve the open ontological-semantic findings or demonstrate domain completeness, standards conformance, empirical effectiveness, or organizational adoption.

7. DISCUSSION

CM-PharmE 1.0 integrates organizational, collaborative, regulatory, operational, and digital concerns within one ontology-grounded structure. Relative to the initial proposal, the present study strengthens evidence synthesis, modeling traceability,

comparative positioning, and qualitative and computational assessment. The resulting alignment with UFO/OntoUML improves ecosystem-level conceptual traceability without implying complete ontology validation or operational interoperability.

7.1. Interpretation

The findings support complementary roles for business architecture and foundational ontology. Business architecture identifies structures, capabilities, stakeholder concerns, processes, and value-delivery responsibilities requiring representation; UFO/OntoUML clarifies their identity, dependence, relational, and temporal characteristics [7], [32], [33]. CM-PharmE operationalizes this alignment through five domains and explicit cross-domain relations. Executable-query and ROBOT/HermiT checks add bounded evidence of computational traceability and logical consistency [29], [40], [41], but do not establish unique correctness, semantic completeness, empirical validity, or universal suitability. The E1–E9 synthesis makes this evidential asymmetry explicit: syntax, logic, structure, bounded data/mapping, competency-question execution, and reproducibility satisfy their defined repository checks, whereas ontological soundness remains conditional and expert-semantic and application evidence remain partial.

Moreover, CM-PharmE provides a structured lens for regulated digital ecosystems, where conceptual fragmentation can constrain interoperability and governance coherence. By representing governance, operational, collaborative, and digital constructs with explicit cross-domain dependencies, it contributes to discussions on platform-based ecosystems and digitally mediated capabilities [21], [24]. Distinguishing formal dependencies from application-level interpretations supports semantic traceability without implying unencoded implementation behavior.

7.2. Comparison

Tables 3 and 8 position CM-PharmE relative to selected approaches rather than establishing universal superiority. Those approaches contribute important clinical, architectural, vaccine-lifecycle, R&D, and supply-chain perspectives, but each emphasizes a subset of ecosystem concerns. Within the study's qualitative rubric and vaccine scenario, CM-PharmE represents organizational actors, collaboration, governance, operations, digital enablers, and cross-domain dependencies in one artifact. This finding supports broader representational coverage within the selected comparison set, but not superior empirical performance or suitability for all applications.

7.3. Limitations

Several limitations bound these findings. CM-PharmE remains a conceptual artifact without longitudinal deployment or controlled empirical evaluation. The expert review, anti-pattern inspection, competency questions, comparative benchmark, illustrative instantiation, and repository-supported checks provide complementary but limited evidence. The model's abstraction supports cross-context use but may reduce immediate operational specificity. Executable queries and ROBOT/HermiT reasoning support traceability and logical consistency for the current axiom set [40], [41], but not the correctness of every ontological commitment, exhaustive anti-pattern clearance, or standards interoperability; standards-specific mappings require separate validation [38], [39]. Migration effort, organizational adoption, legacy-system impact, temporal evolution, reasoning over representative real-world data, and broader independent empirical evaluation remain open research areas. The nine-layer repository organization should not be interpreted as nine statistically independent validation studies: several layers reuse common model, scenario, and repository evidence, and E4, E5, and E8 explicitly remain conditional or partial.

7.4. Practical Implications

CM-PharmE may support downstream requirements and architectural analysis by tracing actors, governance constraints, processes, collaboration, and digital enablers within one structure. Table 14 provides a staged analytical workflow, while requirements derived from these mappings still require validation through established requirements-engineering practices [27].

A pharmacovigilance reporting scenario illustrates this transition. An analyst can identify the responsible actors, trace Pharmacovigilance Requirement to Post-Market Surveillance Activity and then to Adverse Event Reporting Procedure, identify relevant digital enablers, and derive candidate reporting and compliance requirements. These are downstream engineering interpretations rather than additional formal relations. Implementation-specific interoperability still requires separate mappings to HL7 FHIR and to applicable IDMP standards such as ISO 11615:2017 [38], [39].

CM-PharmE may also inform domain-driven design by exposing candidate responsibility and semantic boundaries [28]. The five model domains should not, however, be interpreted as predefined bounded contexts or microservice boundaries. Such architectural decisions require additional domain analysis, organizational decomposition, and implementation-level validation.

7.5. Managerial Implications

From a managerial perspective, CM-PharmE provides a common structure for examining ecosystem orchestration and platform-based business models [24], [25]. It offers a way to relate digital initiatives such as AI-enabled decision support and real-world evidence integration to governance, compliance, inter-organizational coordination, resilience, supply-chain agility, and public-private collaboration rather than treating these as isolated strategic concerns.

7.6. Future Research Scenarios

Future evaluation should move from the current computational baseline toward empirical and data-grounded assessment. Multi-case studies should examine interpretation, adaptation, governance traceability, interoperability coordination, and organizational adoption. Computational work should extend to broader tool-supported OntoUML anti-pattern analysis, formal constraint validation, knowledge-graph transformation, reasoning over representative datasets, and systematic analysis of coverage and semantic gaps [7], [29], [37], [40], [41].

Engineering research should examine governance and risk extensions, standards alignment, requirements derivation, and candidate architectural boundaries. Priorities include implementation-specific mappings to healthcare and medicinal-product standards [38], [39], validated requirements-engineering processes [27], and dedicated domain-driven design analysis of candidate bounded contexts and service responsibilities [28].

8. CONCLUSION

This study examined how business-architecture principles can be aligned with foundational ontology to model pharmaceutical ecosystem dynamics. The resulting two-stage logic uses business architecture to identify organizational, collaborative, operational, governance, and digital responsibilities requiring representation, and UFO/OntoUML to make their identity, dependence, relational, and temporal commitments explicit [7], [32], [33]. CM-PharmE 1.0 operationalizes this logic through five interrelated domains and explicit cross-domain dependencies.

Methodologically, the study extends the initial foundation reported in [26] without replacing its architecture. The PRISMA-guided review and thematic synthesis trace the five-domain structure to evidence, while the UFO/OntoUML procedure makes stereotype, relation, and cardinality decisions explicit. Evaluation combines comparative benchmarking, qualitative review by four experts, focused anti-pattern inspection with repository-supported reinspection, competency-question traceability, scenario instantiation, executable queries, and automated logical reasoning. Reinspection identified targeted role-relator and part-whole refinement candidates without requiring domain redesign; all eight competency queries returned the predefined bounded results, and ROBOT/HermiT reported no logical inconsistency or unsatisfiable named classes in the current axiom set [7], [29], [32], [37], [40], [41]. These results support conceptual coverage, traceability, ontological discipline, and bounded logical consistency, not empirical completeness, exhaustive correctness, operational interoperability, or universal applicability. At repository level, the evidence is now organized into nine complementary layers: syntax, logic, structural integrity, bounded data/mapping validation, competency-question execution, and reproducibility pass their defined checks, while ontological, expert-semantic, and application evidence retains conditional or partial status. This multi-layer synthesis strengthens transparency about what has been formally checked and what remains a subject for further semantic and empirical evaluation.

CM-PharmE 1.0 therefore contributes an integrated conceptual baseline rather than a complete or uniquely optimal pharmaceutical ontology. It provides a shared structure for reasoning across actors, ecosystem relationships, processes, governance constraints, and digital enablers. Implementation still requires context-specific standards mappings, organizational tailoring, engineering validation, and transition planning; no HL7 FHIR or ISO IDMP conformance is claimed [38], [39].

Future work should prioritize multi-case deployment, broader expert review, tool-supported OntoUML inspection, reasoning and executable queries over representative datasets, standards alignment, and controlled contextual extensions. It should also examine knowledge-graph and relational-data implementations, as well as downstream requirements and architectural analysis, to support stronger claims about interoperability, adaptability, adoption, empirical adequacy, and practical value.

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