

Regulatory Qualification of Photopolymer Combination Products Under the United States Framework: Device, Drug and Biological Constituents Across Lifecycle

Translational medical manufacturing

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Abstract

A photopolymer product that combines device, drug or biological functions must be qualified under a jurisdiction-specific regulatory framework. The controlled evidence for this review is United States material: the combination-product definition in 21 CFR 3.2(e), FDA final guidance on premarket pathways for combination products, and the Office of Combination Products guidance environment. This review is explicitly limited to the United States framework and treats constituent identity, primary mode of action, premarket pathway, manufacturing controls and lifecycle change as connected regulatory questions. It does not make European Union claims. A proposed product-configuration map links constituent function, evidence and change assessment without making a regulatory determination for a real product.

Keywords: photopolymer combination products · United States framework · device · drug · biological constituents · lifecycle qualification

1. Jurisdiction and scope

ER-470 is a United States regulatory qualification review. It is not a global or EU regulatory review. The controlled source set consists only of FDA/US instruments, so every conclusion is bounded to that jurisdiction.

2. Combination-product definition

The starting point is the United States definition of a combination product under 21 CFR 3.2(e) [1]. A photopolymer product may contain or integrate device, drug or biological constituents, but its regulatory treatment cannot be inferred from the manufacturing process alone. Qualification begins by identifying the constituent functions and the basis on which the product is regulated.

3. Premarket pathway

FDA final guidance on principles of premarket pathways for combination products is the controlling source class for pathway logic [2]. The regulatory question is not simply which constituent is present; it is how the combined product is evaluated and which evidence must bridge the constituent functions within the intended use.

4. Material and manufacturing state

Photopolymerisation creates a delivered material state through formulation, exposure, cleaning and post-cure. For a combination product, those manufacturing steps can affect the device structure and, where a drug or biological constituent is present, can also affect identity, release, stability or activity. The regulatory dossier therefore needs a state definition that links manufacturing history to the constituent-specific evidence rather than treating the print step as a generic fabrication detail.

5. Lifecycle qualification

A regulatory qualification must remain valid when material, supplier, process, geometry, post-processing or constituent configuration changes. The evidence burden for a change depends on what function may be altered and on the governing pathway. This review does not assign a universal requalification threshold; it requires each change to be assessed against the product's constituent functions and approved state.

6. Evidence architecture

The proposed engineering dossier would identify constituent parts, intended use, primary mode of action where applicable, material and process state, relevant chemistry and release controls, mechanical or functional verification, biological evidence, stability where relevant, and the change-control logic that preserves the approved configuration.

7. What this review does not cover

It does not interpret Regulation (EU) 2017/745 or EU drug-device combination rules. The absence of EU instruments in the evidence base is why this article is restricted to the United States framework. A future EU companion article would require its own controlled evidence base.

8. An evidence map for a product with several functions

The proposed regulatory-analysis record starts with the complete product configuration and its intended use. It identifies each constituent, its intended role, how it is supplied and how the constituents act together. Material identity alone cannot describe that arrangement. For example, a photopolymer structure carrying an active substance poses different questions from the same structure used only as a manufacturing aid. This is an analytical distinction, not a classification of a real product.

A worked dossier would separate the stated therapeutic purpose from the mechanisms proposed to achieve it. It would then map each mechanism to the evidence supporting that account and identify the question requiring an authoritative regulatory determination. The record should distinguish a producer's proposed classification from an agency decision and preserve the exact object and configuration to which a decision applies.

The manufacturing evidence would remain linked to the marketed configuration. A test on the unfilled polymer would not automatically represent a device after loading, sterilisation and storage. A test on an active constituent alone would not establish its behaviour in the combined product. The review can identify those evidence joins without deciding a submission pathway for a particular commercial product.

9. Trace the consequence of a configuration change

A proposed change assessment would compare the before and after configurations across constituent identity, intended function, mode of action, manufacture and delivered performance. It would record which existing evidence is still representative and why. Where a change alters a constituent's role, merely updating a material specification may leave the product-level rationale incomplete.

Consider a hypothetical polymer component initially used for a structural function and later modified to deliver an active substance. The analytical question is no longer confined to whether the geometry remains accurate. The dossier would need to revisit the combined purpose and the evidence supporting the newly introduced function, then resolve the relevant regulatory questions through the applicable official process. No conclusion about the route follows from this example alone.

A useful output is therefore a table connecting each regulatory question to the official source or decision, the product facts on which it depends, and the supporting evidence. Dates and document versions matter because a later decision or configuration may supersede an earlier rationale. This structure adds an auditable application to the jurisdictional overview while retaining the distinction between published guidance and a binding decision for a specific object.

10. Regulatory interpretation boundary

The official definition and the introduction and selected combination-product sections of the FDA guidance were examined. This is not a complete legal assessment. The guidance contains nonbinding recommendations and does not address postmarket policy. The material-state dossier and lifecycle discussion here are proposed engineering structures, not a complete statement of regulatory requirements. Application-specific pathway and change obligations require separate assessment against the applicable instruments.

11. Evidence ownership and change-control logic for combination products

A combination-product dossier should be organised around the product's constituent functions and principal mode of action rather than around the manufacturing method alone. The fact that a photopolymer is used does not determine jurisdiction, lead regulatory centre or submission pathway. A review must distinguish binding regulatory definitions and decisions from nonbinding guidance or examples. Product-specific classification remains a matter for the competent authority when the facts support uncertainty.

Manufacturing changes should be assessed through the risks they may alter, not simply recorded as a new resin batch or a new printer model. A changed formulation, post-cure, cleaning route or contact geometry may modify extractables, mechanical function, drug distribution or biological exposure. The change-control argument should map each change to its potentially affected constituent function, the measurement able to detect the effect and the evidence needed before use or submission.

The review should separate device performance, drug delivery and biological response into distinct evidence layers before arguing that the combined product functions as intended. General guidance can structure this argument but cannot substitute for results on the final configuration. The appropriate conclusion is therefore a traceable regulatory evidence strategy, not an assertion that a particular hypothetical product meets a regulatory requirement.

12. Formal and preliminary jurisdiction requests

The FDA distinguishes an RFD from a Pre-RFD. Under the 2011 RFD guidance, a formal Request for Designation requests classification and/or assignment of the reviewing FDA component; an FDA designation letter provides a binding determination within the conditions specified by applicable law. By contrast, the FDA final Pre-RFD guidance revised in November 2025 describes preliminary, informal and non-binding feedback. A sponsor must therefore not treat a favourable Pre-RFD discussion as an approved classification or an authorisation to market a product [3,4].

A source-based review should retain four separate records: the sponsor's original description of the marketed configuration, its analysis of constituent modes of action, the exact request submitted to FDA and the agency response. For a photopolymer scaffold that also releases an active substance, the manufacturing designation alone cannot identify the primary mode of action. Geometry and polymer cure state are necessary facts, but the classification question also depends on the intended therapeutic action and relative contribution of the constituents. The RFD guidance identifies intended use, formulation, manufacturing processes, developmental results, dose or route of administration where relevant and the rationale for the proposed primary mode of action among the pertinent information [3].

13. Manufacturing-system requirements versus proposed engineering controls

Combination-product manufacturing requirements are a separate regulatory layer from product classification. FDA lists final guidance on current good manufacturing practice for combination products, associated with 21 CFR Part 4, among its official combination-product guidance documents [5]. This layer should not be collapsed into a general assertion that an ISO-certified printer or a resin supplier's quality system by itself establishes combination-product compliance. The applicable manufacturing requirements must be determined from the specific combination product and its constituent regulatory status.

For photopolymer components, a technically useful but proposed control matrix would link material incoming acceptance, exposure conditions, washing, post-curing and storage to functions that could be affected. Measurements could include cure-state-sensitive mechanical performance and geometry, chemical characterisation, release behaviour or biological activity where relevant. These are candidate engineering controls, not a list of universally mandated tests. Their relevance and acceptance criteria must be justified against the actual product, its claimed function and applicable regulatory requirements; the reviewed FDA sources do not prescribe one generic photopolymer process window [2,5].

14. Evidence boundaries and implications for research

The cited FDA documents establish classification mechanisms, the difference between binding designation and preliminary feedback, and manufacturing regulatory frameworks. They do not supply clinical performance evidence for any particular photopolymer combination product. Future case-based research should publish, where disclosure permits, the constituent-function map, the exact production configuration, a traceable change matrix and the relationship between measured endpoints and intended use. Without these data, apparent similarity in resin chemistry or print resolution cannot establish equivalence of regulatory evidence.

An important limitation of this Engineering Review is its jurisdictional concentration on the United States and its absence of a systematic search of published combination-product cases. It consequently provides a structured interpretation and qualification framework rather than a comprehensive meta-analysis or a legal determination for any marketed product.

Source access limitation: the cited publications were not systematically verified against their complete primary texts. The evidence appraisal is therefore restricted to the accessible records and reported findings; bibliographic identification does not constitute full-text verification.

15. Conclusions

Photopolymer combination-product qualification must be jurisdiction-specific. Under the United States framework, constituent identity, regulatory pathway, manufacturing state and lifecycle change must remain linked. The print process does not replace constituent-specific regulatory evidence, and this review makes no EU claim.

Competing interests

The author is Founder, CEO and CTO of 3Dresyns by Resyner Technologies S.L. The company develops and supplies photoresins and related process materials. No proprietary formulation, manufacturing sequence, process window or comparative product recommendation is disclosed.

Data availability

No new experimental dataset was generated.

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