



Combination Products:

A Regulatory Roadmap

Navigating the Regulatory Crossroads of Drug, Device, and Biologic

As innovation merges drugs, biologics, and devices into single therapies, the historical lines of regulatory separation are blurring. Combination products (CPs) bring the convenience of at-home self-administration, but they also bring a more complex regulatory landscape.

Here's what every sponsor needs to know.



What Is a Combination Product (CP)?

A CP is defined as one of three things:



Single Entity

Two or more regulated components physically, chemically, or otherwise combined and produced as one unit.



Co-Packaged

Two or more separate products packaged together in a single package or as a unit.



Cross-Labeled

A drug, device, or biologic packaged separately but intended for use only with another specifically identified product.

Each constituent part retains its individual regulatory status even after combination.

Who Reviews Your CP? It Starts with PMOA.

The **Primary Mode of Action (PMOA)** determines which FDA Center has jurisdiction.



If the PMOA is...	Lead Center is...	Example
 Drug	CDER	Drug-eluting ophthalmic implant
 Device	CDRH	Drug-eluting stent
 Biologic	CBER	Vaccine packaged with delivery device

When PMOA is unclear, file a Request for Designation (RFD) with FDA's Office of Combination Products. FDA must respond within 60 calendar days.

Regulatory Pathways at a Glance

Combination Product Agreement Meetings (CPAM)

— once the lead Center is clearly determined, sponsors can request a CPAM to reach FDA agreement on marketing authorization requirements, post-market modifications, and CGMP issues. Submit the full CPAM package with the initial request; FDA responds within 21 days and meets ~75 days after receipt. CPAMs aren't intended to resolve open scientific or regulatory questions — application-based meetings (below) remain the preferred route when an active application is under review.

CDER (Drug-led)

- NDA: 505(b)(1), 505(b)(2), 505(j)
- Standard review: 10 months / Priority: 6 months
- Meetings: Type A (30d), Type B (60d), Type C (75d)

CBER (Biologic-led)

- BLA under PHS Act §351
- Same review timelines as NDA
- 12-yr biologic exclusivity

CDRH (Device-led)

- 510(k), De Novo, PMA, HDE
- 510(k) Traditional: 90 days / Special: 30 days
- PMA: 180 days (320 with panel)

Two Paths to CGMP Compliance

(single-entity Cps and co-packaged Cps)

(21 CFR Part 4)

OPTION 1

Full Compliance

Comply with all CGMP requirements applicable to each constituent part.

OPTION 2

Streamlined Approach

Demonstrate compliance with either drug CGMPs (21 CFR 210/211) or device QMSR (21 CFR 820) — plus specified provisions from the other.

Biologics and HCT/Ps must always meet 21 CFR 600–680 / 1271, regardless of which streamlined path is chosen.

The Quality Management System Regulation (QMSR) took effect February 2, 2026, amending 21 CFR Part 820 to incorporate ISO 13485:2016 by reference — replacing the former device Quality System Regulation (QSR). FDA also made conforming edits to 21 CFR Part 4; CP CGMP requirements themselves are unchanged.

Development Done Right:

QbD Meets Design Controls

Drug and device constituents must develop in parallel, not in sequence.

Key integration points:

Target Product Profile	↔	User Needs
Specifications	↔	Design Outputs
Tech Transfer	↔	Design Transfer
Risk Management throughout (ICH Q9 + ISO 14971)		



Don't Forget the EU

The EU doesn't use the term "combination product"; it uses **Drug-Device Combination (DDC)**.



- **Integral DDCs** (Article 1(8)) and devices intended to administer a medicinal product (Article 1(9))
- **Article 117** requires Notified Body involvement for the device component of most drug-led DDCs
- MDD certificates expire on a tiered timeline through **2028** — sponsors must have applied to a NB by deadlines that have already passed for legacy devices.

Combination products don't fit into a single category—they require an integrated global strategy across drugs, devices, and biologics. Syner-G brings deep, cross-functional expertise across Regulatory and CMC to help sponsors de-risk jurisdictional pathways, align cGMP requirements, and deliver global submissions that support the next generation of combination therapies.