SIUU vs. Unsolicited Off Label Requests:

A PRACTICAL COMPARISON

TOPIC	SIUU (Firm Initiated, Proactive)	UNSOLICITED OFF LABEL REQUESTS (HCP Initiated)
Scope Clarification	SIUU **does not cover** responses to unsolicited requests; it is strictly for **proactive** firm communications. [fda.gov]	Specifically addresses how to respond to **unsolicited** off label questions (non public and public settings). [kslaw.com], [fda.gov]
Eligible Source Material	Must be based on **published** "source publications": peer reviewed journal **reprints, CPGs, reference texts, or digital clinical practice resources.** 2025 final allows **firm generated summaries of any of these.** [hhs.gov]	No requirement to anchor to the four "SIUU sources." Response must be **accurate, balanced, and tailored** to the question; firms typically cite appropriate scientific evidence and labeling. [kslaw.com]
Data Stage Allowed	Standard is **"scientifically sound."** Early phase data (e.g., Phase 2) may qualify **if published** and presented with limitations. [federalregister.gov]	May discuss off label facts as needed to answer the **specific** question; ensure scientific accuracy, balance, and context. (No "proactive" promotion.) [kslaw.com]
Unpublished Data	**Not eligible** as SIUU source material (SIUU requires **published** sources). [hhs.gov]	Can sometimes be addressed **case-by-case** if directly responsive and handled per MI/SOPs, but firms exercise caution and maintain records; guidance emphasizes scientific accuracy and controlled channels. [kslaw.com], [govinfo.gov]
What FDA Offers (Enforcement Posture)	If a firm's SIUU communication **complies** with the guidance, FDA **does not intend** to treat it, **standing alone**, as evidence of a new intended use. [fda.gov], [federalregister.gov]	FDA provides a **pathway** for compliant responses; stresses non promotional tone and **record keeping** for responses, including for public vs. non public requests. [kslaw.com], [govinfo.gov]
Presentation & Balance Requirements	Must be **truthful, non-misleading**, include **material limitations**, and **make the source accessible** (e.g., link/attach reprint/CPG). Non promotional tone and clear separation from promotional materials. [federalregister.gov]	Response should be **scientific, balanced, non promotional**, narrowly tailored to the **specific** question, and (for public forums) direct the inquirer to **private channels** for detailed info. [kslaw.com]
Format Examples	Distribution of reprints/CPGs/reference texts/ digital resource materials or **firm generated summaries** of those sources to HCPs. [hhs.gov]	One-to-one medical information letters/emails, boothside verbal answers, or follow ups routed via Medical Information; for **public** posts, brief neutral reply with contact route, then respond privately. [kslaw.com]
Where It Applies (Use Case)	**Proactive** emails, mailings, booth handouts, or scientific exchange where the firm initiates off label scientific info distribution to HCPs. [fda.gov]	**Reactive** scenarios: HCP asks at a booth, via email/ phone, or on social media; firm responds under MI/MA procedures. [kslaw.com]
Product Status Prerequisite	Applies only to **approved/cleared** products (for **unapproved uses**). Not for products with no **approval/clearance** at all. [arnoldporter.com]	Same typical constraint in practice; questions about investigational products are handled under different R&D/MI procedures, not promotional pathways. (Unsolicited guidance focuses on off label for **approved/cleared** products.) [kslaw.com]
Internal Review/ Controls	Follow SIUU SOPs/MLR review, train MSLs, document what was shared, and ensure **separation** from promotional messaging. [fda.gov]	Follow Unsolicited SOPs: verify the request is **unsolicited**, route complex answers via Medical Information, **document** the request and response, and maintain records. [kslaw.com], [govinfo.gov]

Trigger & Applicable Guidance

TOPIC	SIUU (Firm Initiated, Proactive)	UNSOLICITED OFF LABEL REQUESTS (HCP Initiated)
Trigger	Firm **proactively** initiates communication to HCPs about **unapproved uses** of an **approved/cleared** product. [fda.gov], [federalregister.gov]	HCP **asks first** (verbal, email, online). Firm responds **only after** receiving a **bona fide unsolicited** request. [kslaw.com], [lw.com]
Primary Governing Document	FDA final guidance **"Communications from Firms to HCPs Regarding Scientific Information on Unapproved Uses"** (Jan **2025**). [fda.gov], [federalregister.gov]	FDA **"Responding to Unsolicited Requests for Off Label Information…"** (Draft Guidance, **Dec 2011**; still posted/relied upon). [kslaw.com], [foleyhoag.com]
Audience	**HCPs** involved in prescribing/administration; not patients/lay audiences. [fda.gov]	Typically, **HCPs**: responses to public requests must be handled carefully (e.g., move to non public channels). [kslaw.com]
Scope Clarification	SIUU **does not cover** responses to unsolicited requests; it is strictly for **proactive** firm communications. [fda.gov]	Specifically addresses how to respond to **unsolicited** off label questions (nonpublic and public settings). [kslaw.com], [fda.gov]
Eligible Source Material	Must be based on **published** "source publications": peer reviewed journal **reprints, CPGs, reference texts,** or **digital clinical practice resources.** 2025 final allows **firm generated summaries** of any of these. [federalregister.gov]	No requirement to anchor to the four "SIUU sources." Response must be **accurate, balanced, and tailored** to the question; firms typically cite appropriate scientific evidence and labeling. [kslaw.com]
Data Stage Allowed	Standard is **"scientifically sound."** Early phase data (e.g., Phase 2) **may** qualify **if published** and presented with limitations. [fda.gov]	May discuss off label facts as needed to answer the **specific** question; ensure scientific accuracy, balance, and context. (No "proactive" promotion.) [kslaw.com]
Unpublished Data	**Not eligible** as SIUU source material (SIUU requires p**ublished** sources). [federalregister.gov]	Can sometimes be addressed **case-by-case** if directly responsive and handled per MI/SOPs, but firms exercise caution and maintain records; guidance emphasizes scientific accuracy and controlled channels. [kslaw.com], [fda.gov]
What FDA Offers (Enforcement Posture)	If a firm's SIUU communication **complies** with the guidance, FDA **does not intend** to treat it, **standing alone,** as evidence of a new intended use. [fda.gov], [federalregister.gov]	FDA provides a **pathway** for compliant responses; stresses nonpromotional tone and **record keeping** for responses, including for public vs. nonpublic requests. [kslaw.com], [fda.gov]
Presentation & Balance Requirements	Must be **truthful, non-misleading,** include **material limitations**, and **make the source accessible** (e.g., link/attach reprint/CPG). Nonpromotional tone and clear separation from promotional materials. [fda.gov]	Response should be **scientific, balanced, non promotional,** narrowly tailored to the **specific** question, and (for public forums) direct the inquirer to **private channels** for detailed info. [kslaw.com]
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Content Requirements & Evidence Standards

TOPIC	SIUU	UNSOLICITED OFF LABEL REQUESTS
Source material allowed	Must be **published**: peer reviewed journal articles, **CPGs, reference texts, or digital practice resources.**	
2025 final allows firm generated summaries of these sources. [ropesgray.com]	No SIUU source restrictions. Content must be **scientifically accurate, balanced,** and directly responsive. [federalregister.gov]	
Use of early phase data	Allowed **only if published** and scientifically sound. Standard is **"scientifically sound."** [fda.gov]	Permitted when directly responsive; must remain scientific and non promotional.
Unpublished Data	**Not eligible** as SIUU source material. [ropesgray.com]	May sometimes be referenced in MA/MI controlled answers but handled with heightened caution. [federalregister.gov], [lw.com]

How Information May Be Delivered

TOPIC	SIUU	UNSOLICITED OFF LABEL REQUESTS
Mode of communication	Proactive distribution of reprints, CPGs, texts, digital resources, or compliant firm generated summaries. [ropesgray.com]	Reactive responses: MI letters, booth scientific exchange, 1:1 emails, private follow up. Public requests must be directed into private channels. [federalregister.gov]
Tone and presentation	Must be **non promotional, balanced**, include study limitations, and provide access to source publications. [fda.gov]	Must be **scientific, factual, and narrowly tailored** to the question; no promotional language.
Audience	**HCPs only**, not patients or consumers. [fda.gov]	Typically HCPs: public inquiries require special handling to avoid promotional appearance

Regulatory Protections & Expectations

TOPIC	SIUU	UNSOLICITED OFF LABEL REQUESTS
FDA enforcement posture	If communication meets SIUU criteria, FDA does not intend to treat it alone as evidence of a new intended use. [fda.gov], [downloads....ations.gov]	FDA provides a compliant pathway but requires documentation and care—especially for public requests. [lw.com]
Recordkeeping	Must follow SIUU SOPs; maintain documentation of distributed materials. [fda.gov]	FDA expects firms to document unsolicited questions and responses. [lw.com]
Product eligibility	Only for **approved/cleared** products with **unapproved uses**. Not for products with no approval. [fda.gov]	Also typically applies to approved/cleared products; investigational questions follow separate R&D pathways.

Key Sources

FDA's J**anuary 2025 final SIUU guidance** and notice (and multiple reputable summaries), plus FDA's **2011 draft guidance on unsolicited requests** (still referenced by FDA/HHS and widely followed operationally).

1. FDA SIUU guidance page
2. Federal Register notice for SIUU (Jan 7, 2025)
3. King & Spalding summary of SIUU changes
4. FDA Unsolicited Requests (draft, Dec 2011) – FDA page / PDF

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