

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Unpublished Data	Not eligible as SIUU source material (SIUU requires published sources).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 published 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]
Format Examples	Distribution of reprints/CPGs/reference texts/digital resource materials or firm generated summaries of those sources to HCPs. [federalregister.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]
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Product Status Prerequisite	Applies only to approved/cleared products (for unapproved uses). Not for products with no approval/clearance at all. [hhs.gov]	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] , [fda.gov]



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 **January 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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