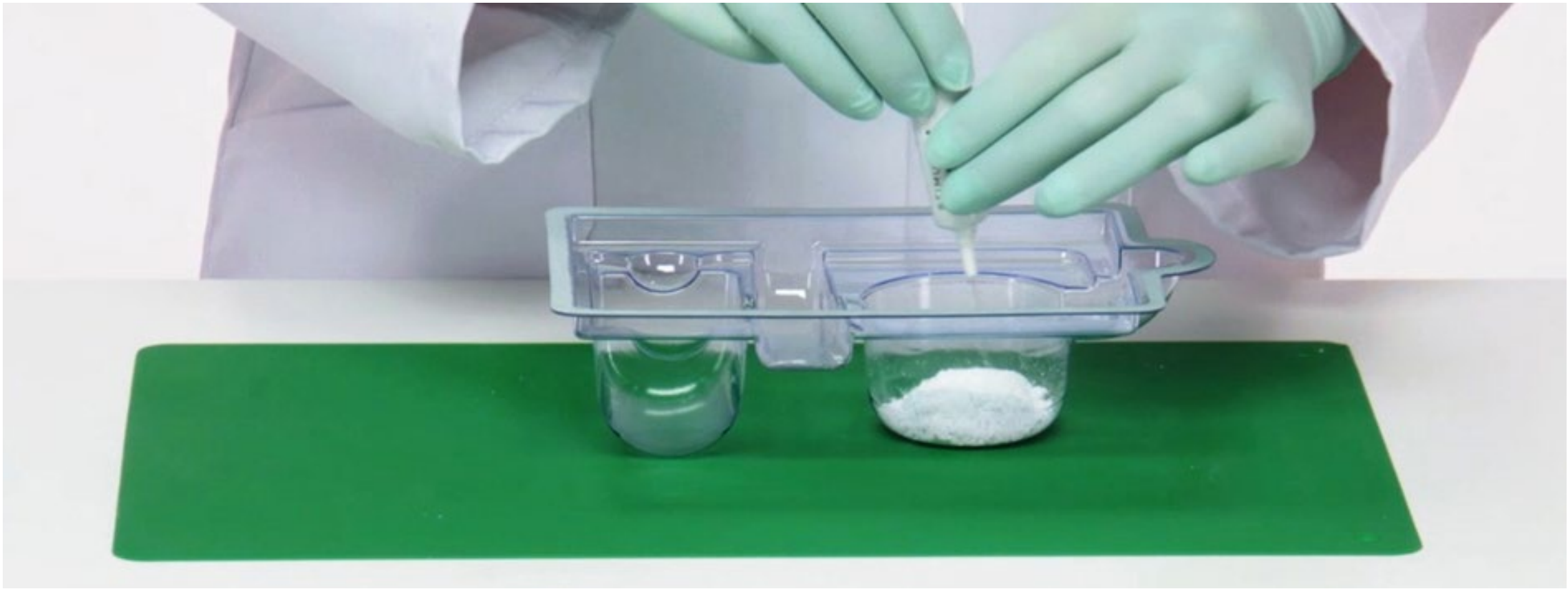

Unsolicited request process for Distributors

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Clearances

STIMULAN® clearance

- STIMULAN is cleared for use to fill a bone void or defect of the skeletal system
- STIMULAN is cleared for placement directly at the site of infection in bone voids and defects

genex® clearance

- genex is a bone graft substitute that is cleared for bony voids and defects that are not intrinsic to the stability of the bony structure

Requests for information

- Due to the demand to use STIMULAN and genex for purposes that fall outside the FDA cleared use of the products, you may receive unsolicited requests from customers for off-label information

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FDA clearance & guidance for responding to unsolicited requests

- Once a device has been approved or cleared by the FDA, it can be lawfully prescribed by healthcare professionals for uses or treatment indications that are not included in the device's statement of intended use
- The FDA recognizes that off-label uses may be important therapeutic options and may even constitute a medically recognized standard of care
- If a manufacturer responds to an unsolicited request for off-label information in accordance to current FDA guidance, the FDA does not consider these responses as evidence of the manufacturer's intent to use the product for an unapproved or uncleared use
- Biocomposites handles unsolicited requests using a carefully developed process in accordance with the FDA guidance for the industry

The process for handling unsolicited requests will now be explained. It is important you follow this process when asked for off-label information.

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Solicited vs. unsolicited requests

Solicited request

- Prompted by a manufacturer or its representatives
- Responding to solicited off-label questions can be considered evidence of an unapproved new intended use or misbranding
- Soliciting off-label questions must be avoided

Unsolicited request

- Initiated by persons completely independent of the manufacturer or its representatives
- To respond to a customer with an off-label question, the process shown on the next slide must be followed

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Standard requests

Respond to standard requests using the following procedure:

1 A request is received

- An unsolicited request/question for off-label information is received from customer

2 Explain how response will be obtained

- As the request pertains to off-label information, explain to customer that due to FDA regulations, the request will be routed to Biocomposites' Compliance unit for response

3 Route information to Biocomposites for response

- Route information to Biocomposites' representative or send directly to Biocomposites' Compliance unit via Distributor Hub app
- Required information: requestor's name, credentials, affiliated institution, contact details, specific question & request

4 Biocomposites to fulfill/ respond to request

- Biocomposites' Compliance unit will respond directly to the requestor in a personal e-mail communication

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Urgent requests

Respond to urgent requests using the following procedure:

1 Clearly respond to the customer

- State that the question is in regard to a use of the product that is not currently cleared/approved by the FDA

2 Only respond within your sphere of knowledge

- "I am aware that Dr. X at Hospital Y does _____."
- "I believe the addition of X may extend the setting time by N minutes."

3 If you must respond by text or e-mail

- State that the question is in reference to product use not cleared or approved by the FDA
- State that the question will be routed to the manufacturer's Compliance unit for formal follow-up

4 After responding to the customer

- Forward correspondence to Biocomposites' representative or Compliance unit
- Required information: requestor's name, credentials, affiliated institution, contact details, specific question & request

Respond verbally whenever possible

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Template for responding to an urgent request

If you must respond to an urgent unsolicited request by text or e-mail, utilize the following template:

Dear Doctor,

The question you have posed relates to a use of the product that is not currently cleared or approved by the FDA. I will forward your question to Biocomposites' Compliance unit via the company's unsolicited request process. You should expect to receive an email response containing a list of any existing well-balanced, relevant medical literature.

However, since you have requested an immediate response related to emergency patient care, I would like to inform you that I am aware of the following:_____.

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Guidelines

- Phrase requests as closely as possible to requestor’s actual verbal request
- Always avoid interpreting and elaborating
- Provision of full text copies of papers with associated copyright costs are subject to Physician Payments Sunshine Act reporting requirements

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Capturing the question: Common elements

Each question must contain enough detail for a specific response to be provided in return

Product information

- Company device name
- Component of company device

Data type

- Clinical data
- Efficacy data
- Elution data

Product use

- Indication
- Procedure name

Remember to include the off-label element

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References

FDA Draft Guidance for Industry:

Responding to Unsolicited Requests for Off-Label Information about Prescription Drugs and Medical Devices

FDA Guidance for Industry:

Good Reprint Practices for the Distribution of Medical Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices

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Compliance

Find out more at **biocomposites.com**

Patents granted: EP 1390086 B1, US 8632796, CN ZL02809194.9, US 8496955, GB2367552, EP 1204599 B1, US 6780391, EP 1436019 B1, US 8563024, CN ZL02825134.2, EP 2594231 B1, US 88883063, CN ZL201210466117.X, GB2496710, EP 3058899 B1, US 10390954

Patents Pending: GB1502655.2, US 15/040075, CN 201610089710.5, GB1704688.9, EP 18275044.8, US 15/933936, CN 108619579A

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