Bioventus
4721 Emperor Blvd., Suite 100
Durham, NC 27703
USA

1-919-474-6700
1-800-396-4325
www.Bioventus.com

Policies and Procedures

Medical Information Request Management Policy	SmartSolve #	POL-000082 [B]
	Effective Date:	See SmartSolve
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Purpose

The purpose of this policy is to define the management of unsolicited requests for off-label information in accordance with the Bioventus Code of Compliance and Ethics Policy.[1]

Scope

This policy applies to all Bioventus employees. Bioventus will not respond to any public questions, therefore, this policy pertains to non-public unsolicited requests only.

Definitions

HCP or Healthcare Professional or Healthcare Provider is defined as an individual or entity in a position to purchase, lease, recommend, use, arrange for the purchase or lease of, or prescribe Company's products or services. Examples include, but are not limited to practitioners, physicians, physician assistants, nurses, pharmacists, dentists, physical therapists, technologists, medical directors, investigators, researchers, account representatives employed by a customer, professional educators, hospitals, ambulatory surgical centers, group purchasing organizations, managed care organizations, insurers, employers, wholesalers, and any individual employed by such entities with responsibility or authority to purchase, prescribe, recommend, influence or arrange for the purchase or sale of a Company product or service. Third Party Representatives are not included in this definition of HCPs.

Unapproved Use is any indication, product form, treatment schedule, population, or other parameter for use of a product not mentioned in the approved labeling.

Approved Use is any use of the product within the current indications listed in the Instructions for Use and that takes into account information in the Contraindications, Warnings and Precautions sections of the Package Insert.

Unsolicited Requests are those initiated by persons or entities that are completely independent of the relevant firm. This may include many healthcare professionals, healthcare organizations, members of the academic community, formulary committees, and consumers such as patients and caregivers.

Solicited Requests are those for off-label information that are prompted in any way by a manufacturer or its representatives to be solicited. Such solicited requests may be considered evidence of a firm's intent that a drug or medical device be used for a use other than that specifically approved or cleared by FDA.

Medical Information Request (MIR) is a formal inquiry or request made by healthcare professionals, patients, or other stakeholders to obtain specific medical and scientific information about a particular drug

or medical device. This information may include details about a product's efficacy, safety, indications for use, dosing instructions, side effects, clinical trial data, or other related information.

Medical Information Request Form (MIRF) is the form utilized to submit a medical information request (MIR).

Medical Information Personnel should have a specialized background in responding to unsolicited requests for information, including important training, such as appropriately narrowing questions, tailoring responses only to the specific questions being asked, providing unbiased responses, and properly documenting responses.

Instructions For Use (IFU) is an FDA-approved label containing the official description of a drug product, including indication (what the drug is used for); who should take it; adverse events (side effects); instructions for uses in pregnancy, children, and other populations; and safety information for the patient.

Adverse Event is any untoward medical occurrence, unintended disease or injury, or any untoward clinical signs (including an abnormal laboratory finding) associated with the use of a drug or medical device in humans, whether or not considered drug or medical device related.

Product Quality Complaint is any malfunction or deterioration in the characteristics or performance of a device made available on the market, including use-error due to ergonomic features, as well as any inadequacy in the information supplied by the manufacturer and any undesirable side-effect. It comprises of any written, electronic or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a device after it is released for distribution to market or clinic by either: (1) Bioventus or (2) distributors or partners for whom Bioventus has partnered with. This includes all components distributed with the device, such as packaging, containers, delivery system, labelling, and inserts.

Policy

The Company will handle unsolicited medical information request(s) for approved and/or unapproved use information in accordance with the procedure set forth below. All responses to unsolicited medical information requests must be evidence-based and balanced, accurate, truthful, non-misleading, and non-promotional.[2]

Responsibilities

Medical Information is responsible for responding to and managing medical information requests. FDA recommends that the medical or scientific personnel should have specialized backgrounds in responding to unsolicited requests for information, such as appropriately narrowing questions, tailoring responses only to the specific questions being asked, providing unbiased responses, and properly documenting responses.

By contrast, because sales and marketing are focused by training and experience on promoting a firm's products, FDA recommends that sales and marketing personnel have no input on the content of responses to unsolicited questions or requests for off-label information.

Procedure

1. Receipt of Unsolicited Medical Information Request(s)

1.1. Unsolicited medical information request(s) related to Bioventus products are received through the Medical Information Request Form (MIRF), accessible via the Bioventus Corporate website, Okta Tile, or mobile application.

Requestors may directly access, complete, and submit a MIRF via the Bioventus Corporate website. Bioventus employees may also direct Requestors to the website to submit a MIRF directly OR submit the request(s) on behalf of Requestors.

1.2. The following fields of the MIRF must be completed for all unsolicited medical information requests:

- Requestor's First and Last Name
- Contact Information of Bioventus employee (if submitting on behalf of the Requestor)
- HCP Institution/Office Name, if applicable
- Requestor's Province/State, Zip/Postal Code, and Country
- Requestor's Preferred Method of Contact
- Product Name
- Product Inquiry Details

2. Assessment of Medical Information Request(s)

2.1. The Medical Information Personnel will confirm that the request is unsolicited in nature by ensuring that the unsolicited request acknowledgement checkbox is complete.

Request(s) that are not in accordance with the above procedure (i.e., solicited requests or requests where the employee submitting the form does not check the disclaimer box) will not be fulfilled with a medical information response.

2.2. The Medical Information Personnel will ensure that all pertinent background data are obtained to be able to determine what information is being requested before providing a

response. If an unsolicited question is broad in nature or unclear, an attempt to contact the Requestor will be made via the preferred method of contact.

2.3. Unsolicited medical information request(s) will be classified as:

2.3.1. Approved/On-Label – Data in IFU

- Request(s) which relate to an approved/indicated use and can be handled by any Bioventus employee trained and qualified to respond to approved use request(s) (e.g. Sales Representative). This does not preclude the submission of an approved use inquiry to Medical Information as deemed necessary by the initial Bioventus employee who received the inquiry.

2.3.2. Approved/On-Label - Data not in IFU

- Request(s) which relate to an approved/indicated use for which data is not discussed within the IFU and requires additional assistance from a medical information personnel.

2.3.3. Unapproved/Off-Label – Routine

- Request(s) for frequent non-indicated use for which data is not discussed within the IFU and requires additional assistance from medical information.

2.3.4. Unapproved/Off-Label – Complex

- Request(s) for unique, non-frequent, and non-indicated use for which input is required from the supervisor to identify approach in responding to the request.
- Escalation may be required in instances where consult with a subject-matter expert outside of Medical Affairs is necessary (e.g., Research & Development, Regulatory Affairs, Compliance, Legal).

2.3.5. Non-MIR (Quality)

- Request(s) for non-MIR (i.e. Off-Label product stability questions) will be forwarded to the Quality Team.

2.3.6. Non-MIR (Customer Service)

- Request(s) for non-MIR (i.e. cost-related questions) that do not require dissemination of medical information will be forwarded to Customer Service.

2.3.7. Non-MIR (Legal)

- Request(s) for Legal support that do not require dissemination of medical information will be forwarded to the Legal Team.

2.3.8. Non-MIR (Research)

- Request(s) for research or participation in clinical studies that do not require dissemination of medical information will be handled on a case-by-case basis.

2.3.9. Potential AE/PC

- Any potential adverse event(s), product quality complaint(s) or potential safety concern that are identified during the management of a medical information request will be handled in accordance with Bioventus' Complaint's Policy (TRN-000779 [B]) by notifying the Complaints department via email (complaints@bioventus.com) within 24 hours of notification of the event.[3]

3. Preparation of Response(s) to Medical Information Request(s)

3.1. Information distributed in response to an unsolicited request should be accompanied by the following:

3.1.1. A copy of the FDA-required or local labeling, if any, for the product (e.g. Prescribing Information or Instructions For Use).

3.1.2. A prominent statement notifying the recipient that the FDA, or local authority, has not approved or cleared the product as safe and effective for the use addressed in the materials provided, when appropriate.

3.1.3. A prominent statement disclosing the indication(s) for which FDA, or local authority, has approved or cleared the product.

3.1.4. A prominent statement providing all important safety information including, if applicable, any boxed warning for the product.

3.1.5. A complete list of references for all of the information disseminated in the response (e.g., a bibliography of publications in peer-reviewed medical journals or in medical or scientific texts; citations for data on file, for summary documents, or for abstracts).

3.2. A Standard Response Letter may be created for frequent unsolicited off-label questions in accordance with the phactMI™ Code of Practice [APPENDIX II], indicating the requested

search using PubMed or other scientific literature database utilized by Bioventus (e.g. PubMed etc).[4]

3.2.1. Summaries of published articles may be included in a response provided that the information is scientifically accurate, non-promotional, scientifically balanced, and evidence-based.

3.2.2. Internet links to recognized databases of Published Scientific Information should be used. In the event a DOI link or other sufficient internet link is unavailable, the article citation will be provided in a standardized format (e.g. American Medical Association [AMA]-style citation).

3.2.3. Competitor product information may not be supplied except where it includes data relevant to the Bioventus product.

4. Notification of Medical Information Request(s) Response Status

4.1. Responses to unsolicited requests for information should be generated by the Medical Information personnel independent of the sales or marketing departments.

4.2. The Medical Information Personnel will notify the Bioventus employee who submitted the Medical Information Request(s) on behalf of the requestor once a response has been provided to the requestor, however, the content of the response will not be communicated with the employee.

5. Documentation

5.1. Each medical information request, defined as a communication delivered via MIRF, and subsequent responses will be documented and retained by the Medical Information Personnel. Each communication received will be assigned a unique ID in a chronological and traceable format.

5.2. A firm should maintain the following records:

5.2.1. The nature of the request for information, including the name, address, and affiliation of the requestor;

5.2.2. Records regarding the information provided to the requestor;

5.2.3. Any follow-up inquiries or questions from the requestor

5.3. A medical information request repository software with an integrated platform may be used to house medical inquiry records and produce the corresponding metrics.

References

1. POL-000074 [E]: Code of Compliance and Ethics
2. *US Food and Drug Administration*. 2011. Dec, [2017-11-21]. Guidance for industry: responding to unsolicited requests for off-label information about prescription drugs and medical devices [draft guidance] https://www.fda.gov/downloads/drugs/guidances/ucm285145.pdf
3. TRN-000779 [B]: Quality/Complaints Training
4. Hermes-DeSantis ER, Johnson RM, Redlich A, et al. Proposed best practice guidelines for scientific response documents: a consensus statement from phactMI. *Ther Innov Regul Sci*. 2020 Nov;54(6):1303-1311. Doi: 10.1007/s43441-020-00151-1. Epub 2020 Apr 20. PMID: 33258092.

APPENDIX I:

EXAMPLES OF SOLICITED RQUESTS (From FDA Guidance[2]):

If a firm's sales representative mentions a use of a product that is not reflected in the product's approved labeling and invites a health care professional to request more information, resulting requests would be considered solicited requests.

If a representative of a firm, such as a medical science liaison or paid speaker (e.g., key opinion leader), presents off-label use data at a company-sponsored promotional event (e.g., a dinner) and attendees then ask or submit requests for more information, these requests would be considered solicited requests.

If a firm's sales representative mentions a use of a product that is not reflected in the product's approved labeling and invites a health care professional to request more information, resulting requests would be considered solicited requests. Example 5: If a representative of a firm, such as a medical science liaison or paid speaker (e.g., key opinion leader), presents off-label use data at a company-sponsored promotional event (e.g., a dinner) and attendees then ask or submit requests for more information, these requests would be considered solicited requests.

EXAMPLE OF UNSOLICITED REQUESTS (From FDA Guidance[2]):

An individual calls or e-mails the medical information staff at a firm seeking information about off-label use.

APPENDIX II:

SUGGESTIONS ON SCIENTIFIC RESPONSE FORMAT and LEVELS OF EVIDENCE (From phactMI™ Code of Practice[4])

Table 2. Adaptation of PRISMA Checklist for Scientific Response Documents [10].

Elements of a Scientific Response Document	PRISMA Elements
Restatement of unsolicited request	Title
Summary of information (required if document longer than 2 pages)	Abstract Structured summary
Introduction/background Approved product indication Appropriate black box warnings, important safety information Company information Background information on the topic or disease state, when appropriate	Introduction Rationale Objective
Search strategy Literature search information Date of search Databases searched (should be reliable and credible databases only) Search terms utilized (including any limitation, subheadings, etc.) Study selection	Methods Protocol registration Eligibility criteria Information sources Search Study selection Data collection process Data items Risk of bias in studies Summary measures Synthesis of results Risk of bias across studies Additional analysis
Literature summary Publication status Clinical trials Study design Study population Interventions and duration Efficacy results (including all relevant numbers, i.e., absolute/relative risk, p values, 95% confidence interval) Safety results Subgroup analysis Author conclusions Meta-analysis; Case reports; Real World Evidence, other	Results Study selection Study characteristics Risk of bias within studies Results of individual studies Synthesis of results Risk of bias across studies Additional analysis
Treatment guidelines (if applicable and available)	Discussion Summary of evidence Limitations Conclusion
Additional information Disclaimer Company contact information	Funding
Citations	Citations

Table 4. Levels of Evidence and Comments [13–16].

Level	Examples	Comments
1	Systematic reviews of randomized controlled trials	The most reliable of all literature Systematic reviews are recognized as the highest standard in evidence-based care
2	Randomized trial or observational study with dramatic effect	Very reliable/gold standard Randomized controlled trials are able to quantify the effects of intervention
3	Non-randomized controlled cohort/follow-up study	Becoming more reliable Observational studies are good for prognosis, diagnosis, frequency and etiology, but not efficacy
4	Case-series, case–control studies, or historically controlled studies	Slightly more reliable but potential for recall bias and quality may be affected if data is collected retrospectively
5	Mechanism-based reasoning Expert opinion without explicit critical appraisal	Least reliable. Basically anecdotal Unscientific reports and observations

Document Detail

Type: Policies

Document No.: POL-000082[B]

Title: Medical Information Request Management

Owner: MONICA.RAI Monica Rai

Status: RELEASED

Effective Date: 23-Jan-2024 **Expiration Date:** 23-Jan-2027

Reference

Document No.	Content Type	Relation	Fixed Rev	Status
TRN-000779 [B]	DOCUMENT	Related	No	RELEASED

Title:Quality/Complaints Training

Revision Notes

Document Build No.	Access Activity	Accessed By	Accessed Date
1	Check In	MONICA.RAI	29-Dec-2023
Note:			
4	Check In	MONICA.RAI	08-Jan-2024
Note:			

Review

Build No.: 4 **Closed Date:** 1/23/2024 10:16:57PM

Review: Standard Release Review

Review Purpose: This Review verifies all basic documents and has the typical reviewers attached.

Review Note: SYSTEM AUTO CLOSE REVIEW

Level	Owner Role	Actor	Sign-off Date	Sign-off By
0	BV Configuration Analyst BV Configuration Analyst	AMBER.PLOTNER Amber Plotner	09-Jan-2024 9:39 pm	AMBER.PLOTNER

Note To Reviewer:

Note From Reviewer:Approved as CA

Level	Owner Role	Actor	Sign-off Date	Sign-off By
1	BV Doc Owner / Author BV Doc Owner / Author	MONICA.RAI Monica Rai	09-Jan-2024 9:40 pm	MONICA.RAI

Note To Reviewer:

Note From Reviewer:Approved

Level	Owner Role	Actor	Sign-off Date	Sign-off By
1	BV Doc Approver BV Doc Approver	MARY.KOTTKE Mary Kottke	09-Jan-2024 9:48 pm	MARY.KOTTKE

Note To Reviewer: MK will be both the Medical and Regulatory reviewer for this Policy.

Note From Reviewer:approved

Level	Owner Role	Actor	Sign-off Date	Sign-off By
1	BV Doc Approver BV Doc Approver	KATRINA.CHURCH Katrina Church	23-Jan-2024 4:23 pm	KATRINA.CHURCH

Note To Reviewer: Katrina will be the Compliance review for this Policy.

Note From Reviewer:BV1958

Level	Owner Role	Actor	Sign-off Date	Sign-off By
1	BV Doc Approver BV Doc Approver	LAURA.ELLIOTT Laura Elliot	23-Jan-2024 9:36 pm	LAURA.ELLIOTT

Note To Reviewer: Tom Brady was the Legal approver of this document in the past, however, as per Tony's email, Laura has been added on his behalf as the Legal approver of this Policy.

Note From Reviewer:Approved by Legal

Level	Owner Role	Actor	Sign-off Date	Sign-off By
2	BV Configuration Analyst BV Configuration Analyst	AMBER.PLOTNER Amber Plotner	23-Jan-2024 10:16 pm	AMBER.PLOTNER

Note To Reviewer:

Note From Reviewer:Approved as CA