ENCYSIVE

Title:	Document No.:	Revision No.:	Effective Date:
Label Control for Commercial Materials	Q1046	1	9/16/2009 3:17 PM DRAFT
	Type of Document: Standard Operating Procedure (SOP)		Page 1 of 5

1.0 PURPOSE

This procedure describes the process used by Encysive to generate, approve and maintain files for control of commercial labels.

2.0 RESPONSIBILITY

2.1 Quality Assurance (QA) reviews and approves labels for compliance with applicable SOPs and cGMPs and that all signatures have been properly obtained. QA also maintains the label files.

2.2 Global and Regional Regulatory Affairs (RA) and Medical Affairs must review and approve labels for content and compliance with regulatory filings.

2.4 Manufacturing reviews and approves the labels to assure an accurate representation of the product and consistency with the label requirements of the package

2.5 Global and Regional Marketing will review and approve to verify the labels meet the format, color, layout, etc., to achieve branding and marketing needs for to be marketed product.

3.0 REFERENCE

3.1 Form F9001 – Document Control

3.2 SOP G1005 – Language Translations for Regulatory and Medical Documents

4.0 DEFINITIONS

4.1 Proofs: A document generated by a printer or printed material manufacturer used to demonstrate size, color, content, print media (paper), and/or layout in preparation for the production of commercial materials.

4.2 Global Regulatory Affairs: Regulatory Affairs personnel, typically based at the corporate headquarters location, responsible for regulatory affairs on a global basis.

4.3 Regional Regulatory Affairs: Regulatory Affairs personnel, typically based at locations separate from corporate headquarters, responsible for regulatory affairs in one country or region of the world (Europe, for example). In some instances, particularly for the United States, the Regional Regulatory Affairs function is performed by Global Regulatory Affairs.

4.4 Global Marketing: Marketing personnel, typically based at the corporate headquarters location, responsible for marketing activities on a global basis.

4.5 Regional Marketing: Marketing personnel, typically based at locations separate from corporate headquarters, responsible for regulatory affairs in one country or region of the world (Europe, for example). In some instances, the Regional Marketing function is performed by Global Marketing.

5.0 PROCEDURE

5.1 Drafting and approval of label text for content only

5.1.1 A label is drafted containing the desired content and regulatory requirements.

5.1.2 A form F9001 is attached to the draft label. A label number and revision is assigned to the label by the Quality Assurance Document Control Coordinator (DCC). Every unique label must have a traceable and unique label number. Encysive label revisions are tracked by alpha character (not number).

5.1.3 The label at this stage must be reviewed for content by, at minimum, Regulatory Affairs, Manufacturing and Quality Assurance. Regulatory Affairs must verify the label complies with all regulatory filings. Manufacturing will verify the label represents the product. Quality Assurance will verify that appropriate SOPs have been followed and that all signatures have been obtained.

5.1.4 Approval of label content is indicated by signing or initialing and dating on the Form F9001.

5.1.5 Once the label content is approved as indicated by signatures in Part D of the Form F9001, the label can undergo further processing (i.e., professionally printed).

5.1.6 The original approved label and form is controlled by QA.

5.2 Approval of label text (content) and layout

5.2.1 A label is drafted containing the desired content and regulatory requirements and is configured in the proposed layout. This document will typically be a color pdf document.

5.2.2 A new form F9001 is attached to the draft label. If the label has been previously approved for content, and this review is for layout only, the layout approval will simply be considered an additional step under the same label revision number. The form F9001 is used in this case to simply track review signatures.

5.2.3 The label at this stage must be reviewed for content and layout by Global and Regional Regulatory Affairs, Global and Regional Marketing, Manufacturing, and QA.

5.2.3.1 Regulatory Affairs – verify that the labels comply with applicable regulatory filings.

5.2.3.2 Marketing – verify that the label format and layout met branding and marketing needs.

5.2.3.3 Manufacturing – verify that labels meet the requirements of the label manufacturer and the packager.

5.2.3.4 Quality Assurance – verify that requirements of procedures have been met and that all signatures are obtained.

5.2.4 QA must review the label to determine that it matches any previous approvals of the same revision number, incorporating all changes made along the way in the process.

5.2.5 Approval of label content and layout is indicated by signing or initialing and dating on the form F9001.

5.2.6 Once the label content and layout is approved, the label can undergo further processing (ie professionally printed).

5.2.7 The original approved label and form is controlled by QA.

5.3 Approval of proofs and professionally generated final labels

5.3.1 A sample of a proof or professionally generated final label is drafted containing the desired content, layout, colors, regulatory requirements, configuration, etc.

5.3.2 A form F9001 is attached to the sample label. A label number and revision is assigned to the label by the Quality Assurance Document Control Coordinator (DCC) if not previously done so by QA. Every unique label must have a traceable and unique label number. If the label has been previously approved for content and/or layout, this approval will be only for the proof or final professional sample and will be the same revision number.

5.3.3 The sample label must be reviewed for content and layout by, at minimum, RA, Manufacturing, and QA. RA must verify the label complies with all applicable regulatory filings and manufacturing must verify that the label meets the requirements of the packager. QA must review the label to determine it matches any previous approvals of the same revision number, incorporating all changes made along the way in the process.

5.3.4 Approval of this label is indicated by either signing or initialing and dating on the label copy, and/or the Form F9001.

5.3.5 Once the sample label is approved as indicated by signatures in Part D of the Form F9001 or equivalent, the label can undergo further processing (proofs) or used for commercial production (final labels).

5.3.6 The original approved label and form is controlled by QA.

5.4 Color Limit Samples

5.4.1 Once the final label has been approved and produced, the printer may provide color limit samples for approval. These samples define the acceptable limits of color variation that would be allowed for ongoing commercial label production. Approval of color limit samples (for color only) must be reviewed and approved by Marketing and QA. Marketing must verify that the color limit samples are acceptable for market presentation. QA must verify that the appropriate signatures have been obtained.

5.5 Language translations

5.5.1 Reference SOP G1005 for processing documents for translation into languages other than English.

5.5.2 Labels should be translated after label content has been approved.

5.5.3 Once the label text is translated (Section 5.2, for example) and a certificate verifying authenticity of the translation is received, additional Encysive approval of the translation for the purposes of content approval is not required as it is assumed that no inhouse Encysive employee is responsible for certifying label language translations. In this case, only a QA verification takes place to ensure the translation and certification are received.

5.5.4 Once the translation and certification are received and filed with the correct approved label revision in the controlled QA document file, the translated content label can be undergo further processing.

5.5.5 If the translation is used to generate an additional, further processed label under the same revision (such as is discussed in Sections 5.2 and 5.3, for example), that additional label must undergo review by, at a minimum, 2 separate Encysive individuals to verify the physical content (not meaning) of the further processed translated label matches the physical content previously received and certified from the translator. This verification is indicated by approval signatures in Part D of the Form F9001. If the generation of this label involves layout considerations, Marketing must also approve the label for layout (not for content or meeting). Following this verification, the label can undergo further processing (i.e., professionally printed for proof approval) or be used in commercial manufacturing (final labels).

5.5.6 The original approved label and form is controlled by QA.

5.6 <u>QA processing of label reviews and approvals</u>

When a new label is created or a label is revised, QA verifies that:

5.6.1 The Form F9001 is attached to the draft label and Parts A, B and C are completed by the originator;

5.6.2 The correctness of the information provided on the form. If a document number (label number) and revision have not been issued, QA issues them, and adds them to Part A and E of the form. This information is verified by a second individual in Part E of the form;

5.6.3 Appropriate review signatures have been obtained in Part D of the form per SOP G1001, and that they are complete;

5.6.4 A draft or sample label is attached to the form;

5.6.5 Dates of all review signatures in Part D of the form are on the same day as, or post date, any changes or comments made to the draft document;

5.6.6 All informational attachments or attached supporting documents are identified as informational only.

5.7 Completion of the label review and approval as described above will constitute approval to use the label. Therefore, the sections indicating "final draft review" and verification, "approval" and the "effective, posting, and release" dates under Part E of the Form F9001 will not be applicable to label approval for commercial materials. These sections will be lined through and identified as not applicable.

5.8 The release date for commercial labels controlled under this SOP is deemed to be the date of the last approval signature, as no further processing is done internally by Encysive QA.

5.9 When revisions are made to a label, the same processes are followed as described above with regard to the revised label.

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Title:	Document No.:	Revision No.:	Effective Date:
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	Type of Document: Standard Operating Procedure (SOP)		Page 6 of 6

DOCUMENT HISTORY:

REVISION	EFFECTIVE DATE	ORIGINATOR
0	31-Oct-06	Steve Pondell
SUMMARY OF CHANGE:		
New Procedure		

REVISION	EFFECTIVE DATE	ORIGINATOR
1	9/16/2009 3:17 PM DRAFT	Steve Pondell
SUMMARY OF CHANGE:		
Revised Procedure		

Originator: Steve Pondell	Title: Director, Manufacturing	Date:
Approved by: Robin LaBelle	Title: Director, Global Regulatory Compliance	Date:
Approved by: Barbara Thomas Smith	Title: Executive Director, Global Quality Assurance	Date: