

Facility Documents; Specialist Review, including Electronic Processing

I. BACKGROUND

The main objective in the Specialist's review and assessment of facility document submissions is to determine if the facility construction and arrangement, along with the established processes and procedures regarding preparation of licensed or permitted biological product, appear to effectively work together to ensure consistent manufacturing of products and to mitigate contamination of licensed or permitted product. The Specialist should become familiar with both title 9, *Code of Federal Regulations* (9 CFR), part 108, and Veterinary Services (VS) Memorandum 800.78 in order to conduct a meaningful review. The submitted document(s) should be reviewed in its entirety even though there may have only been a few changes.

II. SPECIALIST REVIEW (SECONDARY DOCUMENT REVIEW)

Below is a listing of some of the items each Specialist should consider when reviewing facility documents. Keep in mind that depending on the type of licensed/permitted product prepared at the facility and processes and procedures established to mitigate cross contamination of product will likely differ significantly. For example, licensed establishments preparing injectable vaccines will likely have established more safeguards to protect product against cross-contamination than the manufacturer of diagnostic test kits which do not require final sterility testing. In performing your review ask yourself the question – *Does the facility appear appropriate for the intended activities and use as described in the filed Outline(s) of Production?*

FACILITY DOCUMENT SUBMISSION TYPE (as determined by the Specialist)

New Address – sites not currently included on the establishment license

Prelicensing – self explanatory

1. Licensee – Has an APHIS Form 2001 been submitted to Policy, Evaluation, and Licensing (PEL)?
2. Permittee – Has an APHIS Form 2005 or a special outline been submitted?
3. Diluent – not technically required, but is site listed in a special outline?
4. Does the site require an inspection prior to adding it to the establishment license?
 - a. Prelicensing – requires an inspection
 - b. New Address for Production – requires an inspection unless there are extenuating circumstances. This will be at the discretion of the Section Leader, Inspection.

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- c. New Address for Testing or Distribution – depends, but can be approved without an inspection. There must be a statement from the firm indicating the personnel are trained (if new to the process) and equipment is adequate to provide similar results. May require technology transfer with testing by Center for Veterinary Biologics (CVB).

New Building – new construction on a site listed on the establishment license

Remodeled Facility – construction which moves walls, areas, or an addition

Does the building require an inspection prior to filing the facility documents?

1. Production – YES

Requires an inspection unless there are extenuating circumstances (rare). This is at the discretion of the Section Leader (SL), Inspection.

- a. New or remodeled facilities can be used AT RISK prior to an inspection.
 - b. Product made in a new or remodeled facility IS NOT eligible for consideration for marketing prior to assessment of the facility, equipment, personnel, and processes. Samples and APHIS Form 2008s should be held until after the inspection results are documented (unless an inspection was not required per SL, Inspection discretion)
 - c. Equipment and processes should be validated prior to an inspection.
2. Testing, Distribution – depends, but can be approved without an inspection as long as the personnel, equipment, and processes are the same.

Revision – usually due to an update from the firm or inspection findings.

III. REVIEW PROCESS

1. Process facility documents in order in which they are received in your queue. Exceptions may arise based on program priorities.
2. The Biologic Compliance Assistants (BCAs) will perform the preliminary review of the submitted documents using **ICWI0081**. Summary of changes will no longer be required for electronically submitted legends and addenda (once they have been filed electronically). The BCA preliminary review includes ensuring the documents submitted are identified correctly, the documents are complete in accordance with 9 CFR 108 and performing a document compare between the filed document and the submitted document for electronic submissions. The compare document will be identified as the type “Compare Document” and attached to the Mail Log (ML). The BCA may also attach a document titled

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“Facility Document Discrepancy” that informs the Specialist of any discrepancies identified in their preliminary review.

3. Check to see if the BCA had previously audited the documents back unprocessed and if so, were the proper correction made? Depending on the BCA’s concern(s) noted on the Facility Document Discrepancy document, the Specialist may need to identify those concerns on **ICTEM0045**, *Facility Document Correspondence* (hardcopy), or **ICTEM0049**, *Facility Document Correspondence* (for electronic submissions). If a portal submission, the previous ML should be informationally linked, if revisions were requested or if documents were unprocessed. This should be done by the submitter.
4. Review the Specialist’s response to the facility documents submitted immediately prior to the submission currently under review to see if the firm has addressed all of the concerns previously raised. If it is determined through your review that the overall quality of the submission is poor and/or the firm has not addressed issues needing correction as stated in the previous facility document correspondence, then the submitted documents may be returned unfiled along with the completed **ICTEM0045/ICTEM0049** form. In addition, communicate to the firm that compliance action may be taken if the next facility document submission does not provide complete and accurate information.
5. If there is to be a regulatory action based on the facility document submission, reference the date of the previous ‘blueprint’ letter(s) sent to the firm. The firm may be in violation of 9 CFR 114.1 if they have not addressed previous CVB requests to make revisions to one or more of the facility documents.
6. Facility documents “filed” with CVB as electronic are no longer eligible for page changes. Each submission needs to be a complete revision. The supersedes date does not need to be applied to or assessed for correctness for each document page. If the supersedes dates are provided, you do not need to check these against the filed facility documents.
7. For legends and addenda, evaluate the document compare report for electronic submissions or summary of changes for hard copy submissions to determine if the changes made are acceptable. For plot plans and blueprints, compare the summary of changes to the documents submitted. The two should be in agreement. If not, then contact the firm for clarification and/or return the documents unprocessed.
8. We will no longer be making pen-and-ink changes to the documents. Instead, make note of items needing revision in your response back to the firm. This is for both hard copy and electronic submissions.

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- a. **Rule of thumb**, if it was acceptable for a pen and ink change, most likely it is appropriate to request a revision rather than send back unfiled.
 - b. Hard copy – questions can be asked to clarify submissions. Document the conversation in a phone log and attach to the ML.
 - c. Electronic submissions – the Specialist can initiate a child loop, “Request info from Submitter” with specific questions. The firm can reattach or change documents to clarify. It is the Specialist’s responsibility to ensure they changed documents meet the specification in 9 CFR 108 as they will not be reviewed by the BCA.
 - d. Examples for clarifying questions are:
 - i. Information that PEL has approved the movement of organisms into a specific area.
 - ii. Disinfectants used (trade names vs. active agents)
9. The Facility Document Submission form (FDS) is used for hard copy submissions but is not used for electronic submissions.
10. Document all revisions or reasons for returning a document on the **ICTEM0045/ICTEM0049**. Only one template per ML should be used. Upload to ML as “Internally Routed”.

IV. PROCESSING OF THE FACILITY DOCUMENTS (SPECIALIST)

There will only be three possible outcomes for each facility document:

	Hard Copy – FDS Marked	Electronic Stamp	Electronic Nomenclature
Filed, No revisions or comments	Document Filed	Filed with the USDA-APHIS Biologics Program Blueprint/Legend	CVB
Filed with Revisions requested	Documents Filed, Revisions Requested	Filed with the USDA-APHIS Biologics Program with Revisions Requested Blueprint/Legend	REV
Returned, not filed	Documents Returned	No stamp	Not returned electronically

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After review, the Specialist will apply the appropriate stamp and date to each electronic document, see Section VII.

V. NOMENCLATURE FOR ELECTRONIC FACILITY DOCUMENTS

Specialist will be responsible for naming each electronic facility document attachment using a standard convention.

Example:

Est##_Primary Site_Ancillary Site_Document Type_Designation
[REDACTED]

Definitions:

- a. EST## – self explanatory
- b. Primary Site – designated name, usually city location where the primary inspection site is located for the document being reviewed. LSRTIS classification as manufacturing, testing, quarantine.
- c. Ancillary Site – designated name of the site that is associated with the primary site. LSRTIS classification of Ancillary site. – **may not be needed**
- d. Document Type

Document	Code
Plot Plan	PP
Plot Plan Legend	PPL
Plot Plan Legend Addendum	PPLA
Blueprint	BP
Blueprint Legend	BPL
Blueprint Legend Addendum	BPLA

- e. Designation – this includes building number or addendum designation.

EXAMPLES:

- A) If the document is for Building 2, the designation would be “Bld2”.

[REDACTED]

- B) If the document is addendum A for building 2, the designation would be “Bld2_A”.

[REDACTED]

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- C) If the document is an addendum A that covers multiple building, the designation would be “A”.

- f. Version – this will be a consecutive number for every submission of a revision to the facility document. This first electronic submission will be designated as Version 1. If the firm has not designated a version, the CVB will designate the version of CVB’s internal purposes. **Only filed documents will receive a version number. Documents sent back unfiled will not have a version number.**

VI. UNPROCESSED DOCUMENTS (SPECIALIST) NOTE: Documents returned unprocessed will not have a Stamp, Date, or Signature applied to the document.

A. Complete the correspondence with comments as to why the document is being returned unprocessed.

1. Hard copy
 - a. Comments returned on **ICTEM0045**. Attach document as “Internally Routed”.
 - b. On FDS (hard copy), check “Documents Returned” and sign in Block 10.A. (do not date).
2. Electronic Submission
 - a. Comments returned on **ICTEM0049**. Attach document as “Internally Routed”.
 - b. Unprocessed documents will not be uploaded as “IC Clean Copy”
 - c. Add a follow-up date that corresponds to the timeframe specified on the **ICTEM0049** in the ML.
 - d. Add tag “Returned Unprocessed” if the entire submission is returned.

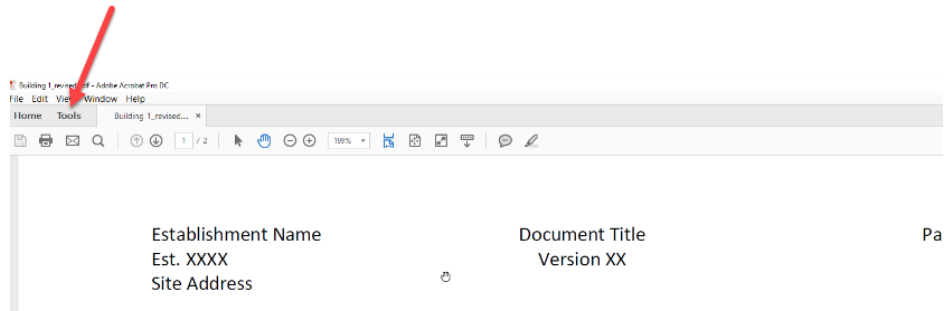
VII. DOCUMENTS PROCESSED – STAMPING/DATING (SPECIALIST)

Documents Filed with no revisions requested or Documents Filed with revisions requested.

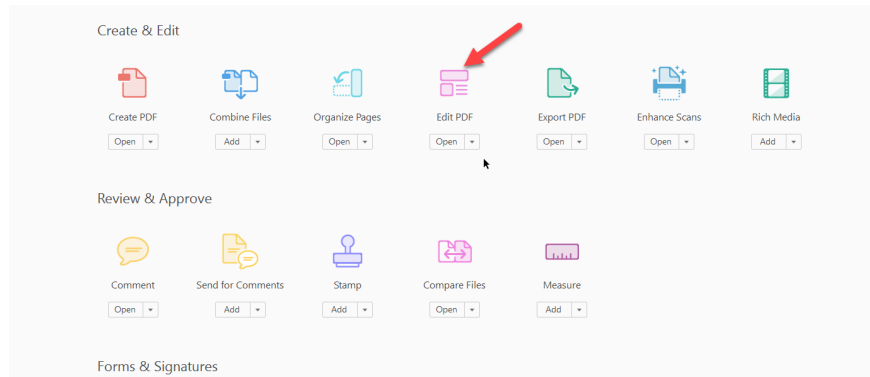
A. Apply STAMP

1. With the reviewed document open, select the tools tab.

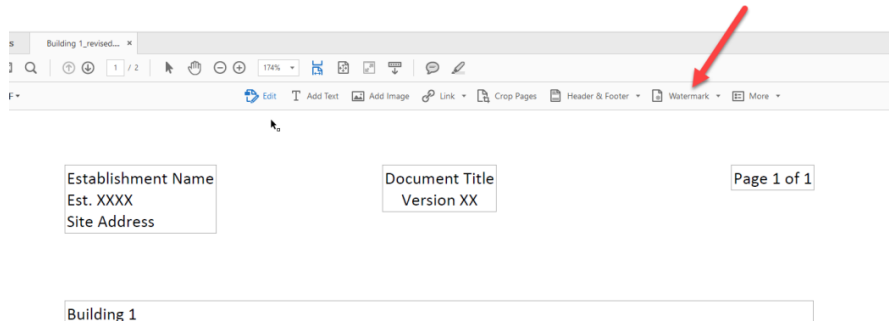
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2. Select Edit PDF



3. On tool bar, select Watermark



4. Select Add

5. On the position section, move vertical position to Bottom. Adjust the vertical distance so that the stamp does not hide any critical information. Adjust the vertical distance to 0.5 inches. This may need to be adjusted based on the margins of the submission.

6. On the position, move the horizontal position to Right. Adjust the horizontal distance so that the stamp does not hide any critical information. This may need to be adjusted based on the margins of the submission.

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7. Select File and browse to find the appropriate saved stamp that should be saved on each Specialist's H drive.



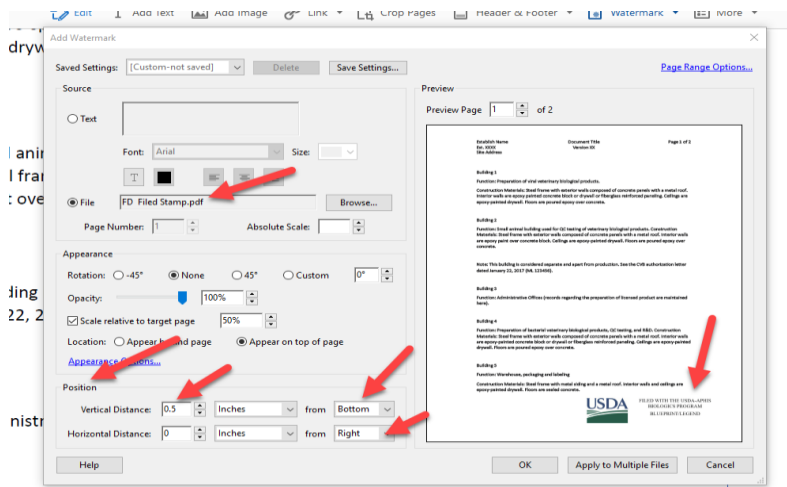
FILED WITH THE USDA-APHIS
BIOLOGICS PROGRAM
BLUEPRINT/LEGEND

Filed with no revisions



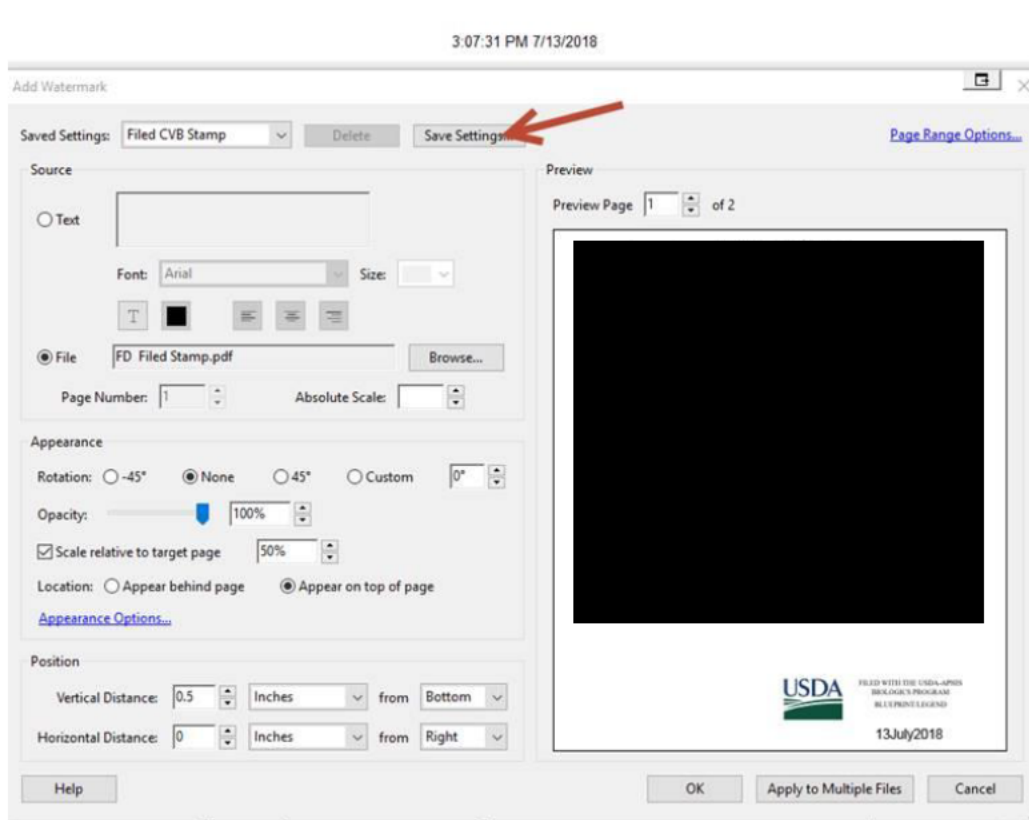
FILED WITH THE USDA-APHIS
BIOLOGICS PROGRAM WITH
REVISIONS REQUESTED
BLUEPRINT/LEGEND

Filed with revisions requested



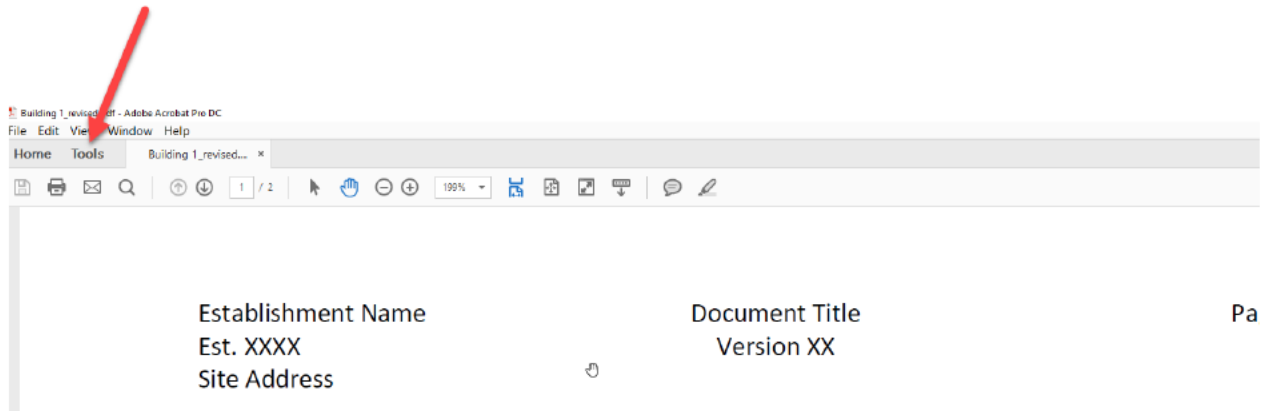
8. This should place the stamp in the lower right corner of every page of the document.
9. Option to save setting for future use: Go to Save Settings. Name it for the specific stamp type, Choose OK. It will appear in Saved Settings next time in water marks.

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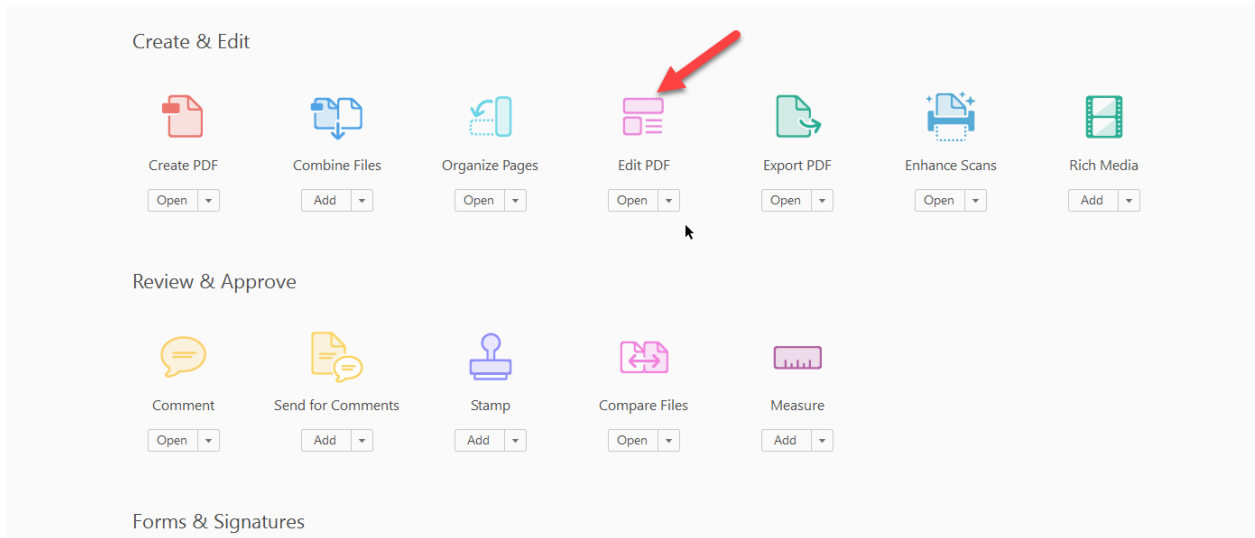
B. Apply DATE

1. Select the Tools tab.

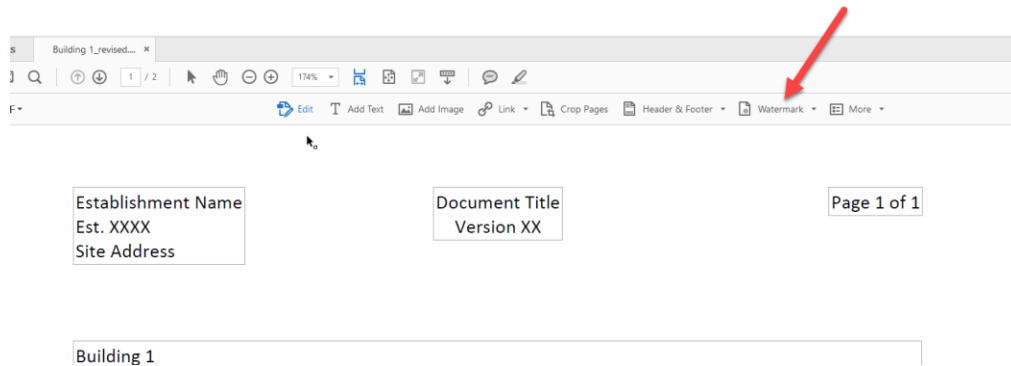


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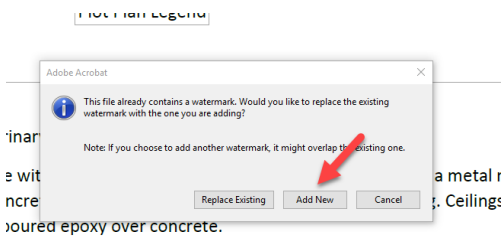
2. Select Edit PDF



3. On tool bar select Watermark



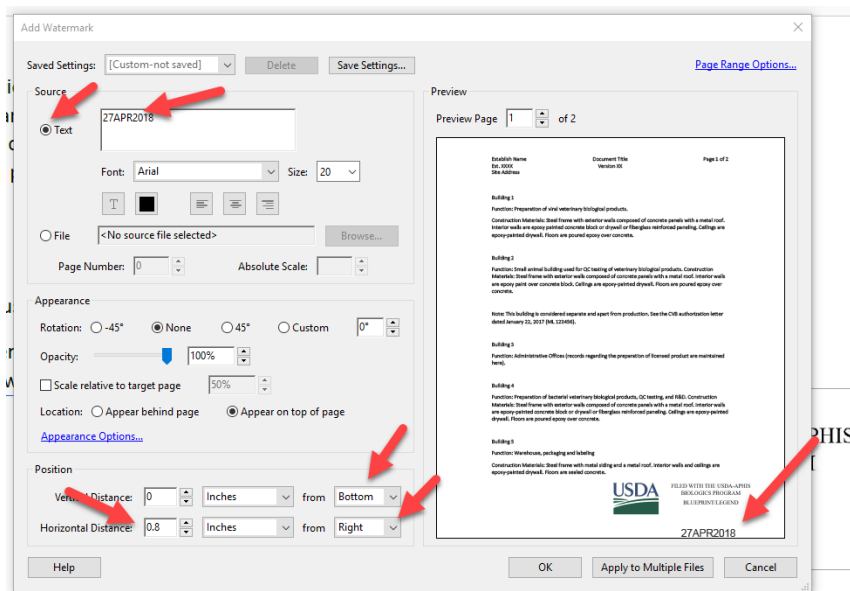
4. Select Add – Select Add New



5. Select Source as Text

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6. Enter File Date (date the document is signed) – Date Format DDMMYYYY, i.e., 27APR2018
7. Change the Font Size to 20
8. Adjust Vertical Distance to be 0 inches from bottom. Adjust the vertical distance so that the stamp does not hide any critical information.
9. Adjust Horizontal Distance to be 0.8 inches from right. Adjust the horizontal distance so that the stamp does not hide any critical information.
10. Select OK



C. Name document, see Section VII.

FILED (example) Example: [REDACTED] **2_CVB**

REVISIONS (example) Example: [REDACTED] **_REV**

D. Upload the stamped/dated facility document(s) to the mail log item as “**IC Clean Copy**”

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VIII. DOCUMENT REVIEW (SECTION LEADER)

Once all of the documents have been reviewed, processed, and uploaded to the ML, the ML item will be sent to the Facilities Manager or Section Leader, Inspections for policy review.

1. The Specialist will send the ML item using “Section Leader Review(IC)”. Assign either the Facilities Manager or Section Leader, Inspection.
2. The SL assigned will review the documents for consistent policy. This is also an opportunity to review the **ICTEM0045/ICTEM0049** document, assure the appropriate stamp has been applied to the document, and assure the file is named in accordance with naming convention described in See Section V and Section VII.C above.
3. After SL review there are two options.
 - a. If the SL has determined all the documents in the ML item conform to the process and policy, the SL will forward the ML item to the appropriate BCA for finalization.
 - b. If the SL has determined that items need clarified by the Specialist prior to moving forward, the SL will make comments on the **ICTEM0045/ICTEM0049** and attached a revised copy to the ML item.
 - 1) If the SL determines that a further SL review of the documents is required after the Specialist has made corrections, the SL leader would not approve the documents when sending back to the Specialist by selecting “Cancel” in the pop up. If a Specialist applied the wrong stamp, the Specialist will need to redo the stamp. Go to edit PDF watermark. Remove. This will remove both the stamp and date that was previously applied.
 - 2) If the SL determines that they do not need to review the documents again after the Specialist has made corrections, the SL leader would approve the documents when sending back to the Specialist. Once the Specialist makes appropriate corrections, they send to the appropriate BCA for finalization.

IX. FINALIZATION – BCA role, ICWI0084

X. SIGN CORRESPONDENCE (IC) - SPECIALIST

A. Hard copy

1. Ensure the **ICTEM0045** has been dated.

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- a. The FDS form should be “Outgoing General Correspondence
- b. The **ICTEM0045** should be “Outgoing Enclosure
- c. The ML should be tagged “SUPPRESS Response from Portal”

2. Click on Sign Correspondence

3. Move to Section Leader – Final Authorization

B. Electronic Submission

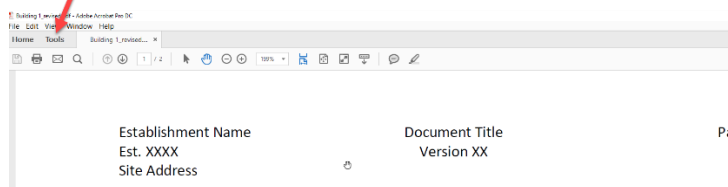
1. If needed, digitally sign **ICTEM0049**

Attach to Document Tab as “Outgoing General Correspondence”

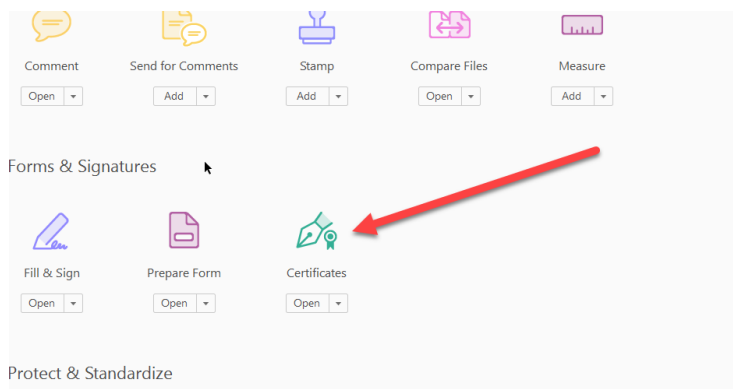
2. If documents are to be filed with or without revisions requested, sign each facility document – use invisible digital signature.

3. For documents that are not going to be filed, do not sign them and add a follow-up date in the Follow-Up section of the ML. Go to 4 below

a. Select Tools tab

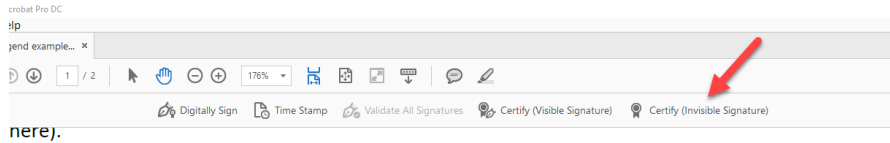


b. Select Certificates



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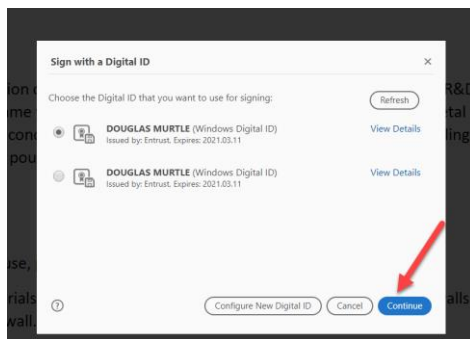
- c. On certificates tool bar select Certify (Invisible Signature)



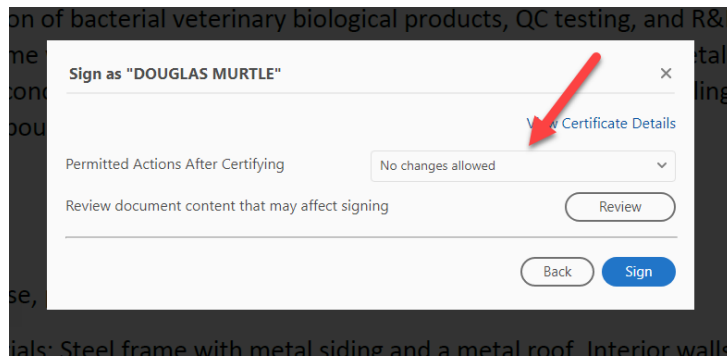
Building 4

Function: Preparation of bacterial veterinary biological products, QC testing, and R&D. Construction Materials: Steel frame with exterior walls composed of concrete panels with a metal roof. Interior wall are epoxy-painted concrete block or drywall or fiberglass reinforced paneling. Ceilings are epoxy-paint

- d. Select Continue



- e. Make sure the field “permitted Actions after certifying states No changes allowed.



- f. Sign and save. See Section V and VII.C for nomenclature – should not have to change.
- g. Upload the signed document to the ML as “Outgoing Enclosures.”

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- h. Add the “Version #” to the Version Field on the Create Attachment screen.

Create Attachment

Mail Log #	Establishment	Product Code	Brief Description	Type	Date Submitted
177943	999		Test on adding documents	Facility Document	February 09, 2018

Attachment 177943-3 created

Select File Location: Uploaded File Hard Copy

Select File to Upload: H:\RENEEFY 2018 Documents\999_Ames_BP_Bld2-CVB.pdf

Type:

Version #:

Tags:

Comments:

- i. Once all documents have been dated, signed, and uploaded, move the ML item to Section Leader Final Authorization.
4. If a document is not being filed, ensure the Tag “Returned Unprocessed” is added to the document and add the comment “returned unprocessed”. This can be done by editing the attachment as follows:

A. Click on Doc ID

Show 50 entries Search:

Doc ID	Type	File Name	Create Date	Comments	Hard Copy
201908 - 1	Blueprint	2018_0614_Sub to CVB_BP_Building A_2nd floor.pdf	07/05/2018		
201908 - 2	Summary of Changes (Required)	2018_0614_Sub to CVB_BP_Building A_2nd floor_SOC.pdf	07/05/2018		
201908 - 3	IC Clean Copy	2018_0614_Sub to CVB_BP_Building A_2nd floor-CVB.pdf	07/12/2018		

Showing 1 to 3 of 3 entries


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B. Click on Edit

Show Attachment

MailLog #	Establishment	Product Code	Brief Description
201908	██████	NA0000	Revision to Blueprint, Building A, 2nd floor with corresponding summary of change

Attachment ID	201908 - 1
File	Show 2018_0614_Sub to CVB_BP_Building A_2nd floor.pdf
Type	Blueprint
Create Date	2018-07-05 11:47:23 CDT
Create User	NCAH-Portal, NCAH-Portal
Last Modified Date	
Last Modified User	
Comments	
Tags	




C. Choose the tag Returned Unprocessed and click Add.

Edit Attachment

MailLog #	Establishment	Product Code	Brief Description
201908	██████	NA0000	Revision to Blueprint, Building A, 2nd floor with corresponding summary of change

Attachment ID	201908 - 1
Current File	2018_0614_Sub to CVB_BP_Building A_2nd floor.pdf
Type	Blueprint
Tags	Returned Unprocessed - Doc <input type="button" value="+ Add"/>
Comments	



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D. Add returned unprocessed to comments and click update.

Edit Attachment

MailLog #	Establishment	Product Code	Brief Description	Type
201908		NA0000	Revision to Blueprint, Building A, 2nd floor with corresponding summary of changes.	Facility Do

Attachment ID	201908 - 1
Current File	2019_0814_Sub to CVB_BP_Building A_2nd floor.pdf
Type	Blueprint
Tags	<input type="checkbox"/> + Add Returned Unprocessed - Document ✖
Comments	returned unprocessed

E. Once completed, send to Section Leader Final Authorization.

XI. SECTION LEADER FINAL AUTHORIZATION

A. Hard copy

1. Review attachments to ensure they are complete – make sure the signed FDS form has been scanned and uploaded. If needed, make sure the **ICTEM0045** is complete.
2. Move Forward to “Certified Receipt” to the responsible BCA.
3. If being returned unprocessed, ensure the Tag “Returned Unprocessed” is added.

B. Electronic Submission - This is the final IC step prior to the ML item being returned to the firm via the NCAH Portal.

1. Each document should be opened and reviewed to assure:
 - a. The proper stamp and date are shown on each page of the document.
 - b. There is a statement in a blue box stating “Certified by (Specialist).”
 - c. The **ICTEM0049** is digitally signed by the Specialist.
 - d. The file name has the appropriate status (“CVB” or “REV”).
2. If all the documents in the ML are not being filed, then ensure the Tag “Returned Unprocessed” is added to the ML.
3. If all is satisfactory, then the SL approves the ML.
4. This moves the document to records management. (See work instruction)

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Electronic Submission Flow Chart

