Gateway Submissions and eCTD Validation

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FDA\CDER\OBPS
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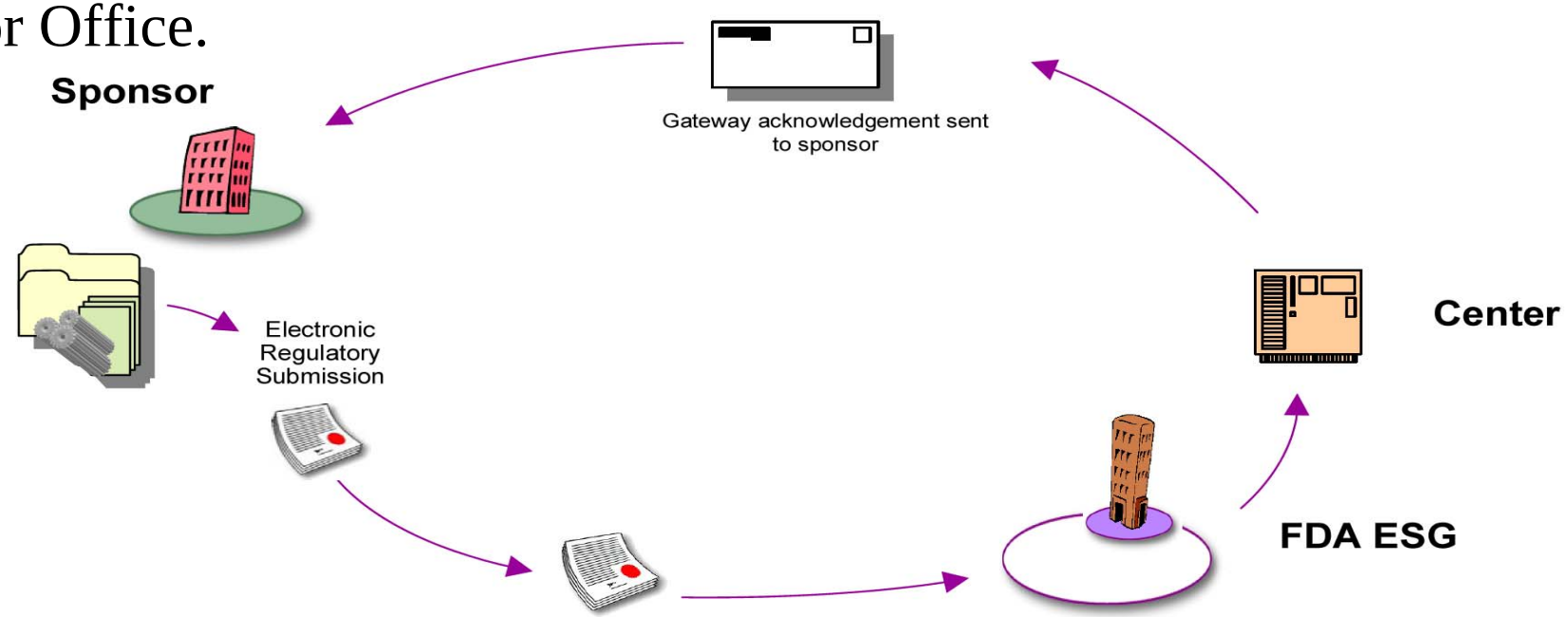
The Gateway

- What is the Gateway?
- Submission Options
- Gateway Cost
- Digital Signatures
- ESG Resources and Contact Information

What is the Gateway?

An Agency-wide solution and central transmission point for accepting secure electronic regulatory submissions over the Internet. The FDA ESG is a conduit, or "highway", along which submissions travel to reach their final destination. It does not open or review submissions; it automatically routes them to the proper FDA Center or Office.



Electronic Submissions Gateway Submission Options

- FDA ESG Web Interface (WebTrader)
  - Low cost option
  - Uses applet
- Gateway to Gateway (AS2)
  - Applicability Statement 2 (AS2) Gateway-to-Gateway
  - Requires an AS2 compliant gateway software

Gateway Facts

- The FDA does not charge for the use of ESG
- A company can have multiple WebTrader accounts
- Each account must send a guidance compliant test submission

Digital Signatures

- FDA does not require submission of a paper copy for electronic submissions submitted using the FDA ESG.
- FDA forms (e.g.,356h) and documents require a signature. Accepted signature methods by FDA are:
  - Scanned signatures
  - Digital signatures
  - Flattened digital signatures.
  - The Agency does not check electronic/digital signatures unless there is a directed inspection involving the submission transmission.

Digital Signatures (cont.)

If you are having trouble signing a fillable form:

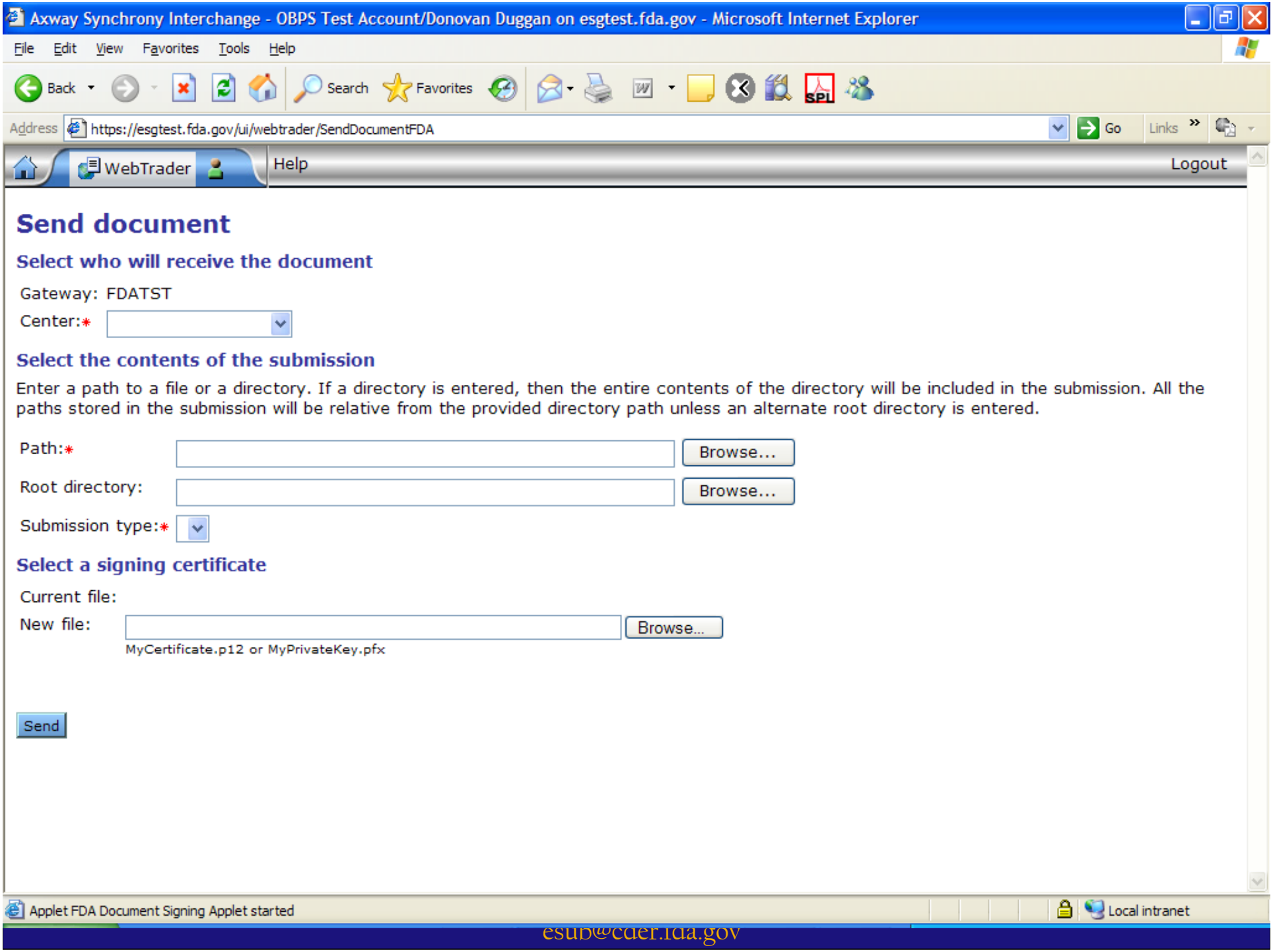
- Fill out the fillable form (356h) as you normally do – name it 356h.pdf
- Sign another 356h form and name it signed-form.pdf, form-continuation.pdf
- DO NOT USE 356 in the name of your signed form

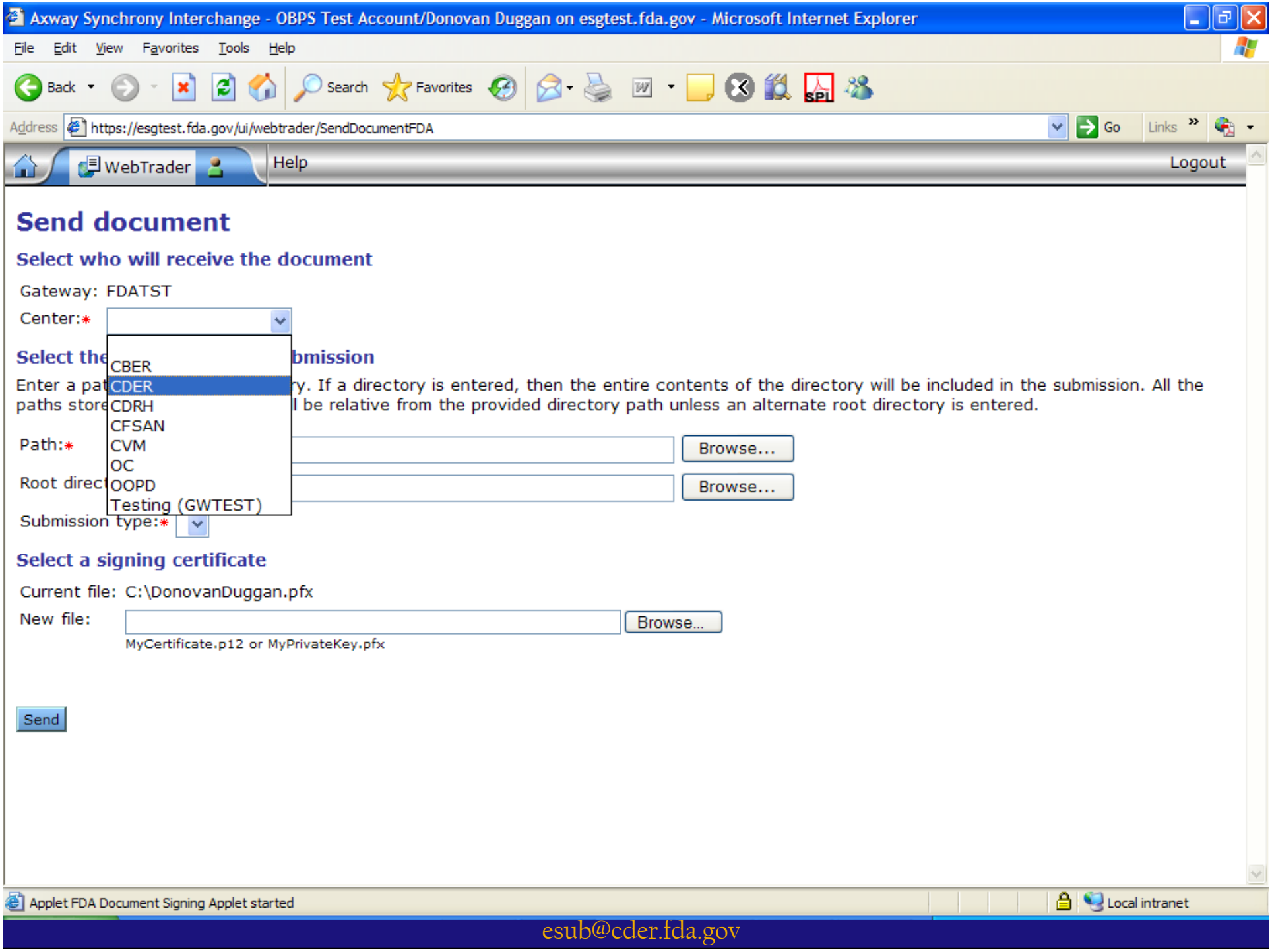
Electronic Submissions Gateway Process -Before You Register

- Submit a Letter of Non-Repudiation Agreement
- Obtain a Digital Certificate
- Determine Submission Method
- Understand Submission Guidelines

ESG resources and contact information

- Website: http://www.fda.gov/esg/
  - Registration Information
  - System Requirements
  - User Guide and Tutorials
  - Digital Signatures and Certificates
  - System Status and Help Desk
  - Links to submission guidelines
- Email for preparation/Registration/Policy: esgprep@fda.gov
  - This email is for question and help in setting up test and production accounts
- Email for technical issues: esgreg@gnsi.com
  - This email is for system and submission related issues


Axway Synchrony Interchange - OBPS Test Account/Donovan Duggan on esgtest.fda.gov - Microsoft Internet Explorer
File Edit View Favorites Tools Help
Back Search Favorites
Address https://esgtest.fda.gov/ui/webtrader/SendDocumentFDA
Go Links
WebTrader
Help
Logout
Send document
Select who will receive the document
Gateway: FDATST
Center:*
Select the contents of the submission
Enter a path to a file or a directory. If a directory is entered, then the entire contents of the directory will be included in the submission. All the paths stored in the submission will be relative from the provided directory path unless an alternate root directory is entered.
Path:*
Browse...
Root directory:
Browse...
Submission type:*
Select a signing certificate
Current file:
New file:
Browse...
MyCertificate.p12 or MyPrivateKey.pfx
Send
Applet FDA Document Signing Applet started
Local intranet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Address https://esgtest.fda.gov/ui/webtrader/SendDocumentFDA
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Send document
Select who will receive the document
Gateway: FDATST
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CBER
CDER
CDRH
CFSAN
CVM
OC
OOPD
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Browse...
Submission type:*
Select a signing certificate
Current file: C:\DonovanDuggan.pfx
New file:
Browse...
MyCertificate.p12 or MyPrivateKey.pfx
Send
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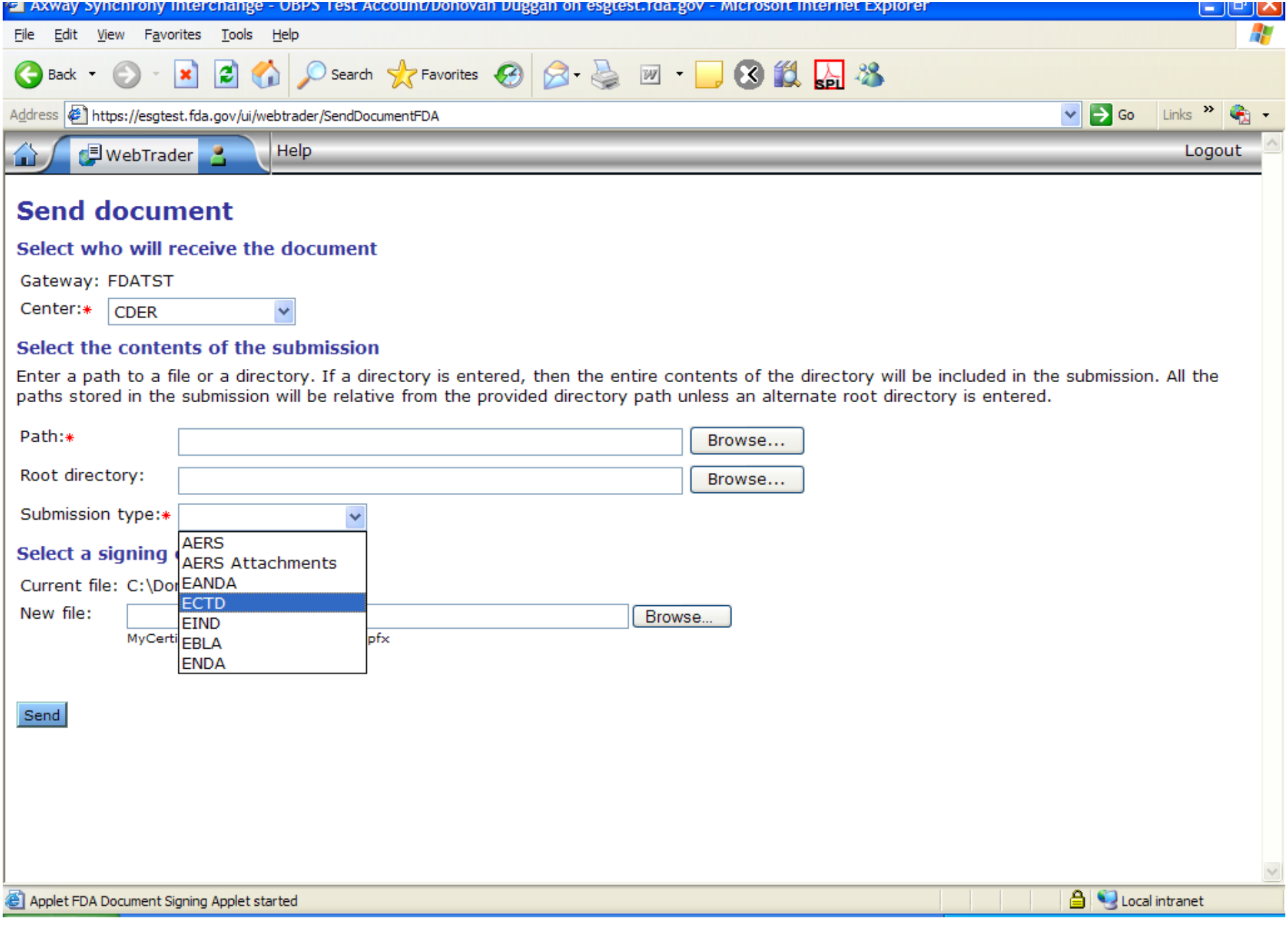
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Address https://esgtest.fda.gov/ui/webtrader/SendDocumentFDA
Go Links
WebTrader
Help
Logout
Send document
Select who will receive the document
Gateway: FDATST
Center:* CDER
Select the contents of the submission
Enter a path to a file or a directory. If a directory is entered, then the entire contents of the directory will be included in the submission. All the paths stored in the submission will be relative from the provided directory path unless an alternate root directory is entered.
Path:*
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Root directory:
Browse...
Submission type:*
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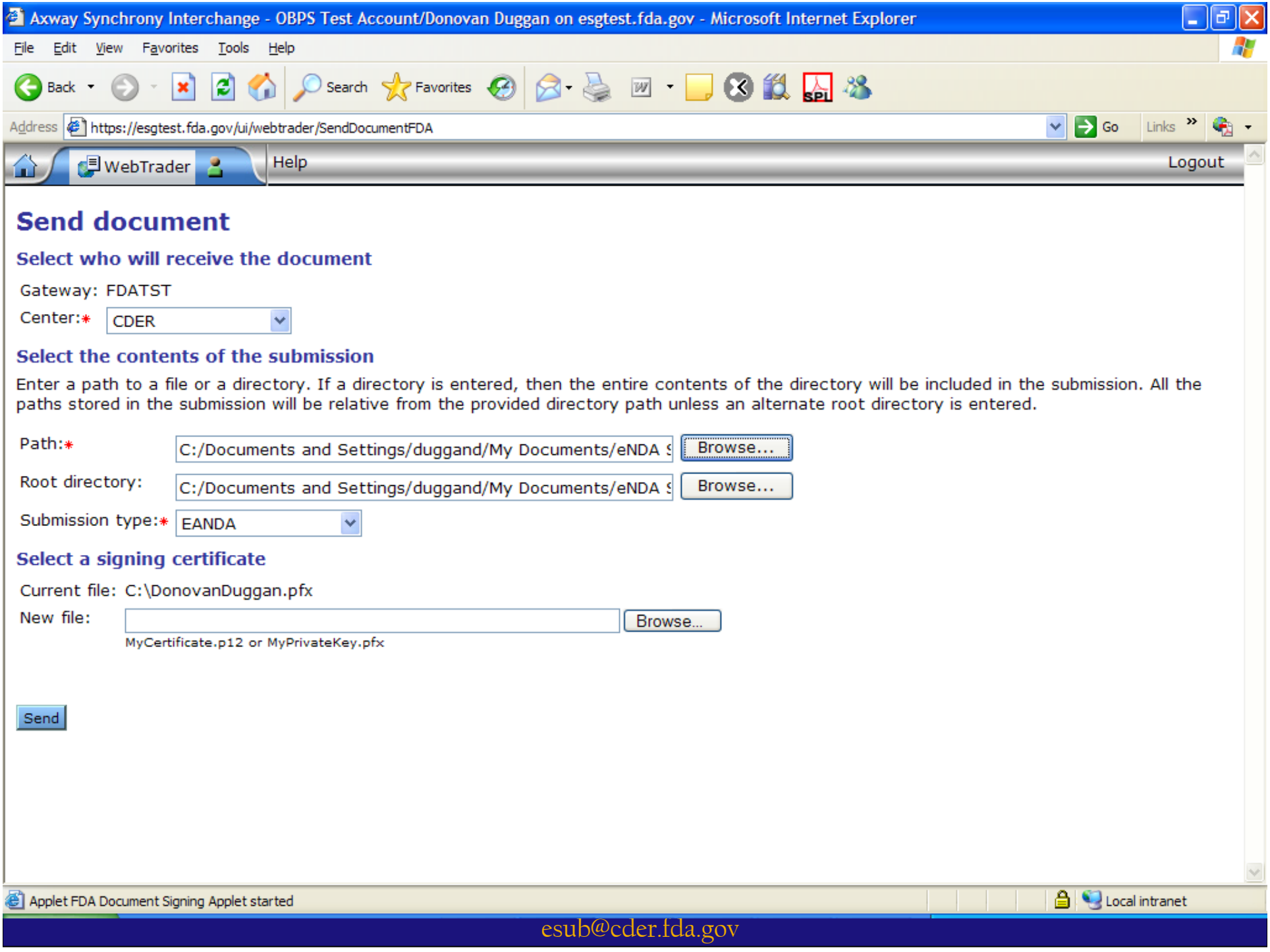
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Send document
Select who will receive the document
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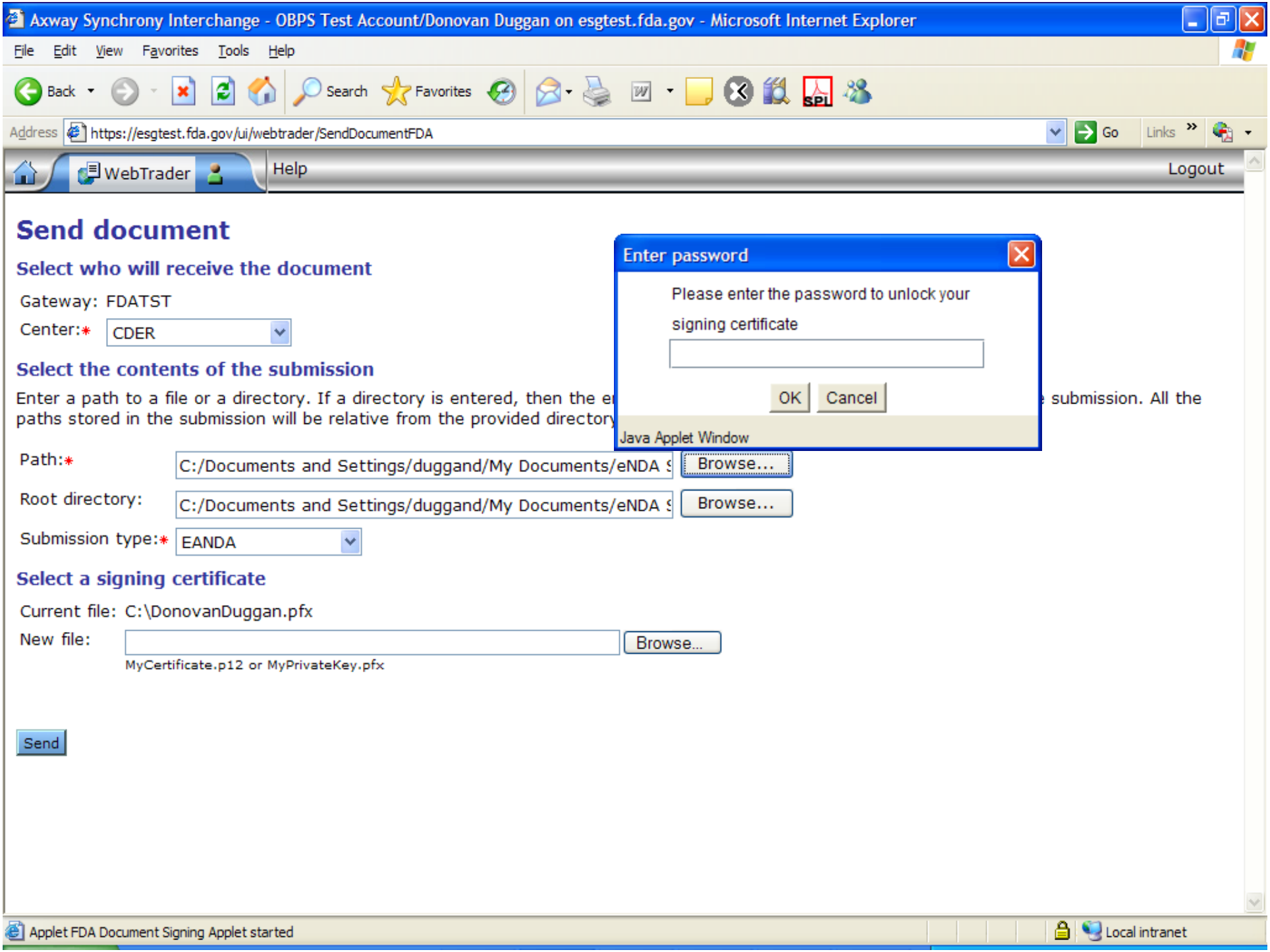
Center:* CDER
Select the contents of the submission
Enter a path to a file or a directory. If a directory is entered, then the entire contents of the directory will be included in the submission. All the paths stored in the submission will be relative from the provided directory path unless an alternate root directory is entered.
Path:* C:/Documents and Settings/duggand/My Documents/eNDA S
Browse...
Root directory: C:/Documents and Settings/duggand/My Documents/eNDA S
Browse...
Submission type:* EANDA
Select a signing certificate
Current file: C:\DonovanDuggan.pfx
New file:
Browse...
MyCertificate.p12 or MyPrivateKey.pfx
Send
Applet FDA Document Signing Applet started
Local intranet
esub@cder.fda.gov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Go Links
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Send document
Select who will receive the document
Gateway: FDATST
Center:* CDER
Select the contents of the submission
Enter a path to a file or a directory. If a directory is entered, then the e
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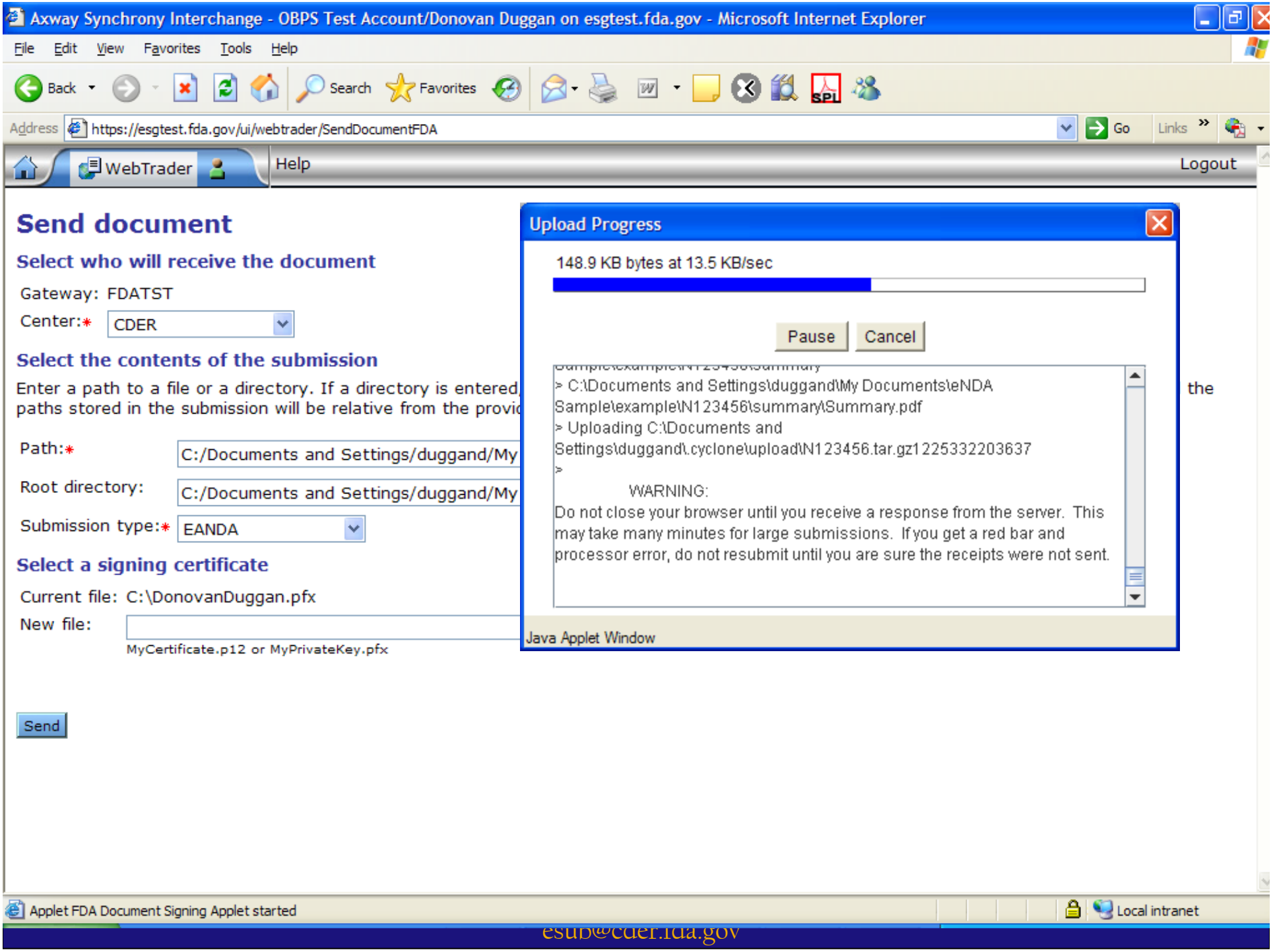
Path:* C:/Documents and Settings/duggand/My Documents/eNDA S
Browse...
Root directory: C:/Documents and Settings/duggand/My Documents/eNDA S
Browse...
Submission type:* EANDA
Select a signing certificate
Current file: C:\DonovanDuggan.pfx
New file:
Browse...
MyCertificate.p12 or MyPrivateKey.pfx
Send
Enter password
Please enter the password to unlock your
signing certificate
OK
Cancel
Java Applet Window
Applet FDA Document Signing Applet started
Local intranet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Logout
Send document
Select who will receive the document
Gateway: FDATST
Center:* CDER
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Enter a path to a file or a directory. If a directory is entered,
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Path:* C:/Documents and Settings/duggand/My
Root directory: C:/Documents and Settings/duggand/My
Submission type:* EANDA
Select a signing certificate
Current file: C:\DonovanDuggan.pfx
New file:
MyCertificate.p12 or MyPrivateKey.pfx
Send
Upload Progress
148.9 KB bytes at 13.5 KB/sec
Pause
Cancel
> C:\Documents and Settings\duggand\My Documents\eNDA Sample\example\N123456\summary\Summary.pdf
> Uploading C:\Documents and Settings\duggand\.cyclone\upload\N123456.tar.gz1225332203637
>
WARNING:
Do not close your browser until you receive a response from the server. This may take many minutes for large submissions. If you get a red bar and processor error, do not resubmit until you are sure the receipts were not sent.
Java Applet Window
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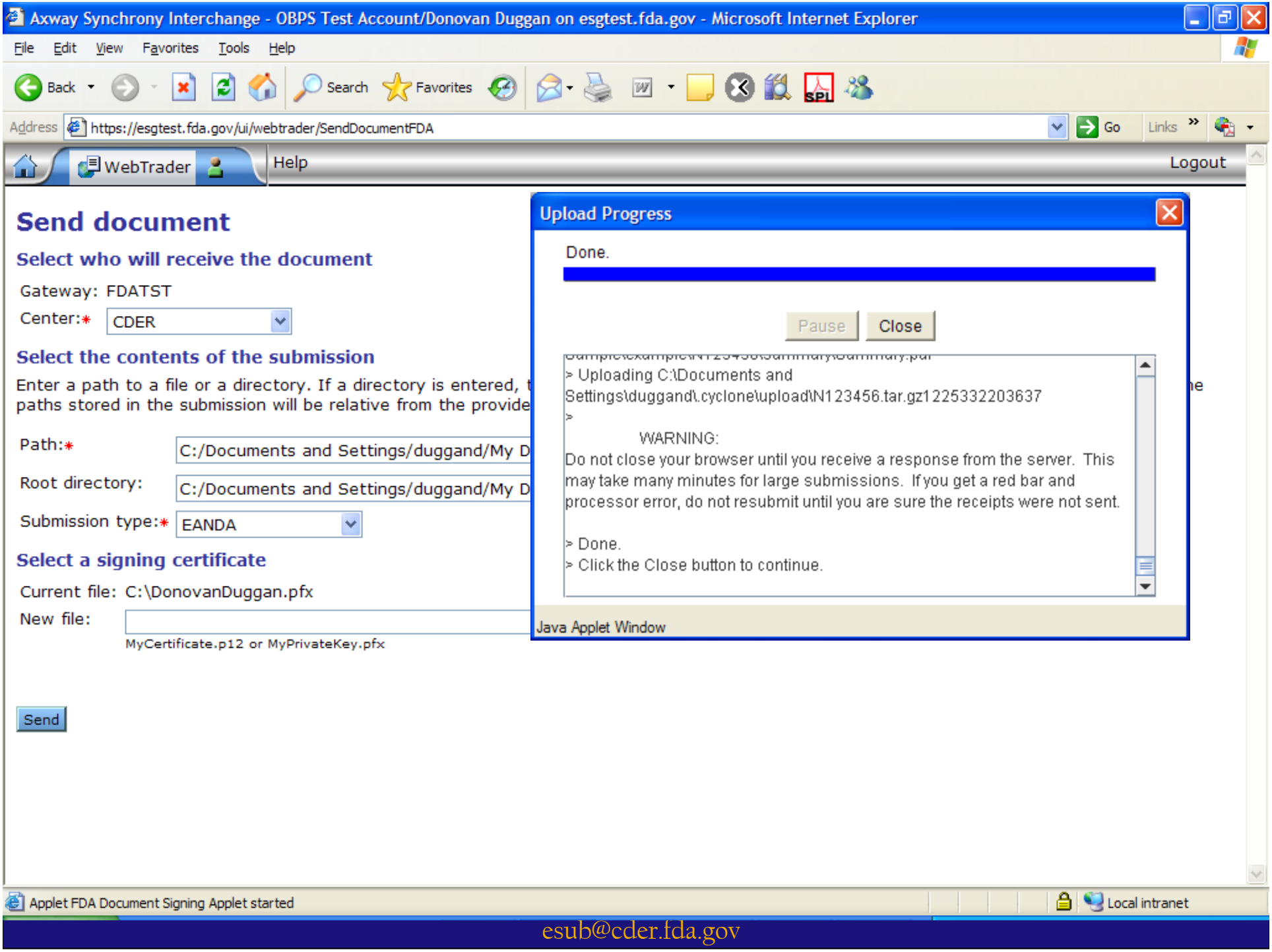
Local intranet
esub@cder.fda.gov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Send document
Select who will receive the document
Gateway: FDATST
Center:* CDER
Select the contents of the submission
Enter a path to a file or a directory. If a directory is entered, t
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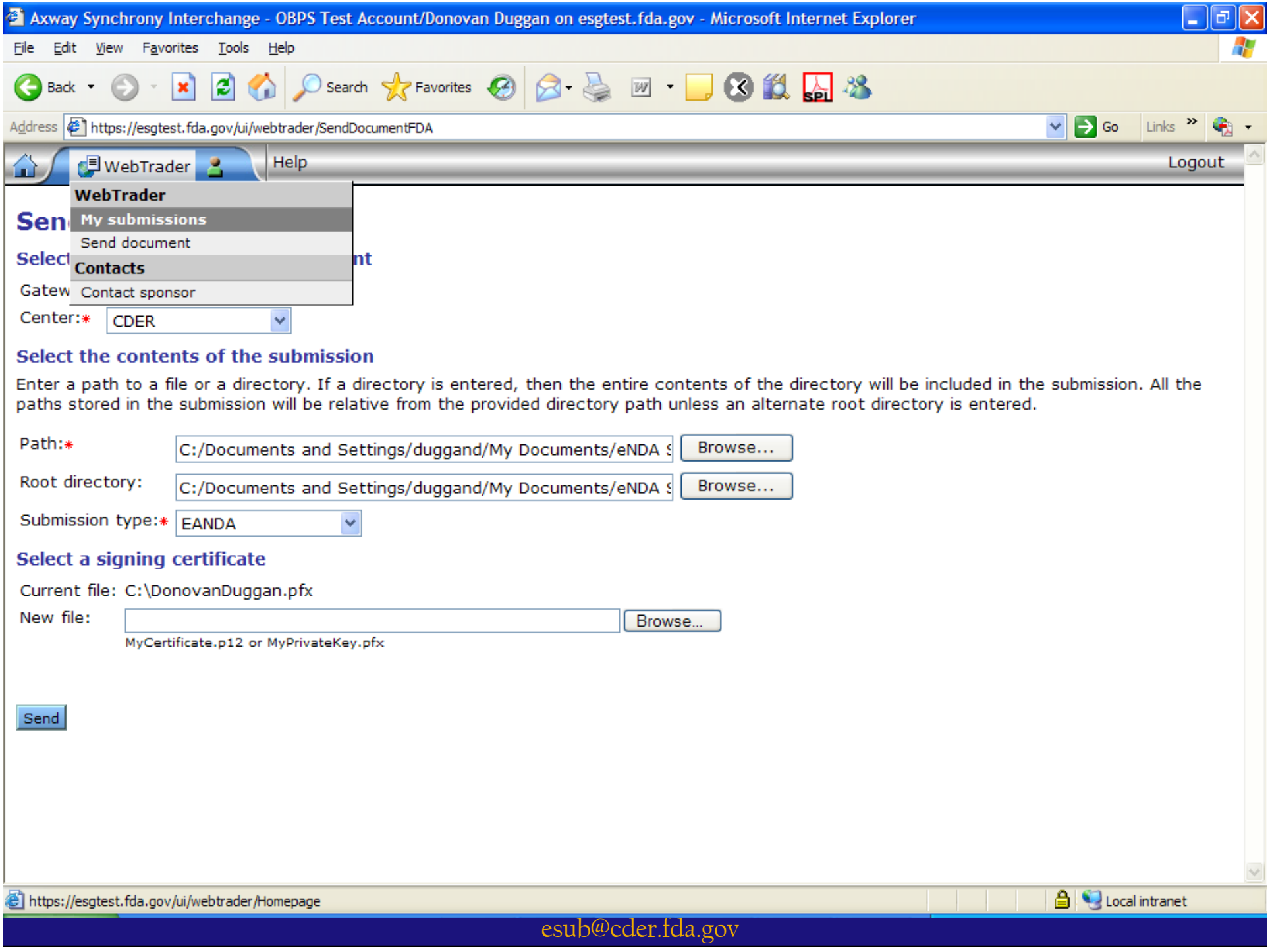
Path:* C:/Documents and Settings/duggand/My D
Root directory: C:/Documents and Settings/duggand/My D
Submission type:* EANDA
Select a signing certificate
Current file: C:\DonovanDuggan.pfx
New file:
MyCertificate.p12 or MyPrivateKey.pfx
Send
Upload Progress
Done.
Pause
Close
> Uploading C:\Documents and Settings\duggand\.cyclone\upload\N123456.tar.gz1225332203637
>
WARNING:
Do not close your browser until you receive a response from the server. This may take many minutes for large submissions. If you get a red bar and processor error, do not resubmit until you are sure the receipts were not sent.
> Done.
> Click the Close button to continue.
Java Applet Window
Applet FDA Document Signing Applet started
Local intranet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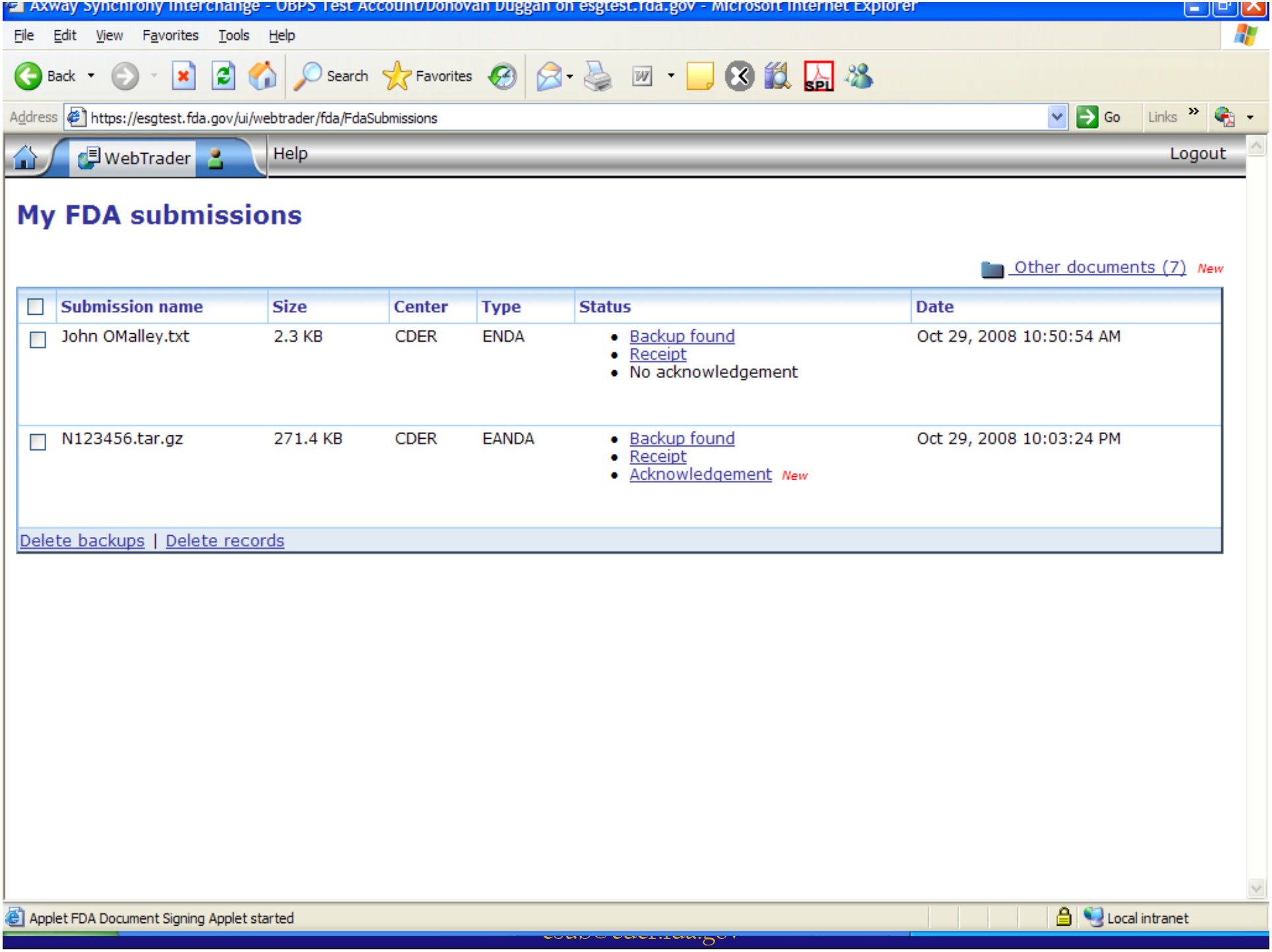
Select the contents of the submission
Enter a path to a file or a directory. If a directory is entered, then the entire contents of the directory will be included in the submission. All the paths stored in the submission will be relative from the provided directory path unless an alternate root directory is entered.
Path:*
C:/Documents and Settings/duggand/My Documents/eNDA
Browse...
Root directory:
C:/Documents and Settings/duggand/My Documents/eNDA
Browse...
Submission type:*
EANDA
Select a signing certificate
Current file: C:\DonovanDuggan.pfx
New file:
Browse...
MyCertificate.p12 or MyPrivateKey.pfx
Send
https://esgtest.fda.gov/ui/webtrader/Homepage
Local intranet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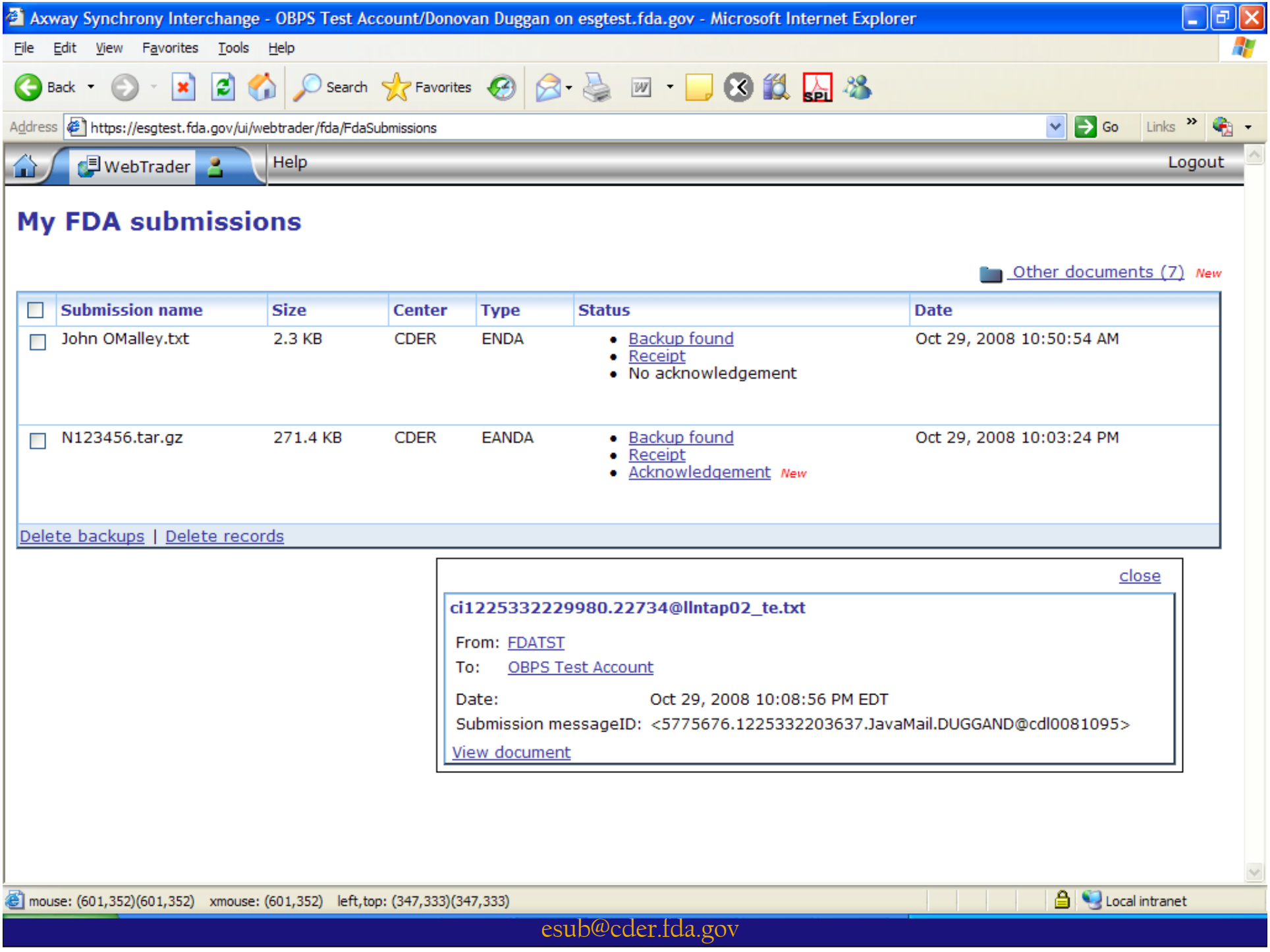
Back Search Favorites
Address https://esgtest.fda.gov/ui/webtrader/fda/FdaSubmissions
Go Links
WebTrader
Help
Logout
My FDA submissions
Other documents (7) New
Submission name
Size
Center
Type
Status
Date
John OMalley.txt
2.3 KB
CDER
ENDA
Backup found
Receipt
No acknowledgement
Oct 29, 2008 10:50:54 AM
N123456.tar.gz
271.4 KB
CDER
EANDA
Backup found
Receipt
Acknowledgement New
Oct 29, 2008 10:03:24 PM
Delete backups | Delete records
Applet FDA Document Signing Applet started
Local intranet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Address https://esgtest.fda.gov/ui/webtrader/fda/FdaSubmissions
Go Links
WebTrader
Help
Logout
My FDA submissions
Other documents (7) New
Submission name
Size
Center
Type
Status
Date
John OMalley.txt
2.3 KB
CDER
ENDA
Backup found
Receipt
No acknowledgement
Oct 29, 2008 10:50:54 AM
N123456.tar.gz
271.4 KB
CDER
EANDA
Backup found
Receipt
Acknowledgement New
Oct 29, 2008 10:03:24 PM
Delete backups | Delete records
close
ci1225332229980.22734@llntap02_te.txt
From: FDATST
To: OBPS Test Account
Date: Oct 29, 2008 10:08:56 PM EDT
Submission messageID: <5775676.1225332203637.JavaMail.DUGGAND@cdl0081095>
View document
mouse: (601,352)(601,352) xmouse: (601,352) left,top: (347,333)(347,333)
Local intranet
esub@cder.fda.gov

eCTD Validation

- Gateway Validation
- ASR Validation
- eCTD Tool Validation
- Qualitative Validation

Gateway Validation

- Once you have established an account this is almost never an issue
- The Gateway Validation is concerned with file integrity

Automated Submission Receipt (ASR)

- ASR
  - Processes your submission
  - Loads the submission into CDER's tracking system
  - Notifies the Regulatory Project Manager
- **To operate efficiently we need**
  - eCTD
  - Fillable Form 356h
  - Accurate Information, e.g., application number

eCTD Tool Validation

- Identifies and rates the severity of the errors encountered
  - High Errors vs. Medium Errors vs. Low errors
- The criteria for these are available here:
  - http://www.fda.gov/cder/regulatory/ersr/validation_specs.htm

Division Quality Checks

- OGD Checklist is followed - http://www.fda.gov/cder/ogd/anda_checklist.pdf
- Hyperlinks should be functional
- PDF document legibility
- Table of Contents Issues
- Missing Files

Validation Issues

- Lack of 356h
- Fillable Form not used
- More than one form in a submission
- Mismatched application number between the US-Regional.xml and the form
- Incorrect, missing or no application number - either on the form or in the us-regional.xml
- Bad Characters in file or folder names

Validation Issues contd.

- More than one sequence included in one gateway submission
- One submission applied to more than one application
- Single PDF file submission
- Mismatch between application type and form - an ANDA with a 1571.PDF

Why should you care?

- These errors require us to manually process your gateway submission
- Manually processed submissions delay access to your material
- More hands in the pot increases chances for error
- Sometimes these issues result in us rejecting your submission

Reasons for Rejection

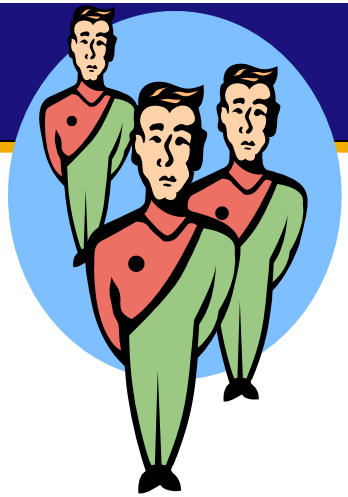
- Duplicate Submission
- us-regional.xml / form mismatch
- us-regional.xml cannot be read / non-standard eCTD
- Sent to the wrong Center
- Portions sent outside the eCTD
- Empty folder

Reasons for Rejection contd.

- Corrupted files
- Multiple Sequences sent via the Gateway
- No us-regional.xml

How to avoid problems

Duplicate Submissions
Duplicate Submissions



- Once is enough
- We only process the first submission not the duplicate
- If the first submission was in error contact CDER ESUB
  - esub@fda.hhs.gov

PDF Form and US-Regional.XML Mismatch

- The form has your application number
- The US-Regional.XML has your application number
- They need to be the same number
- It's great to reuse XML – just clean it up first

Include a 356h form

- The information assists us in processing your submission
- If you are using the Gateway it is extremely helpful to have a form

Use a Fillable PDF form

- Fillable forms allow us to extract the data necessary to automatically process your submission
- Using a scanned form will delay processing
- http://www.fda.gov/opacom/morechoices/fdaforms/cder.htm

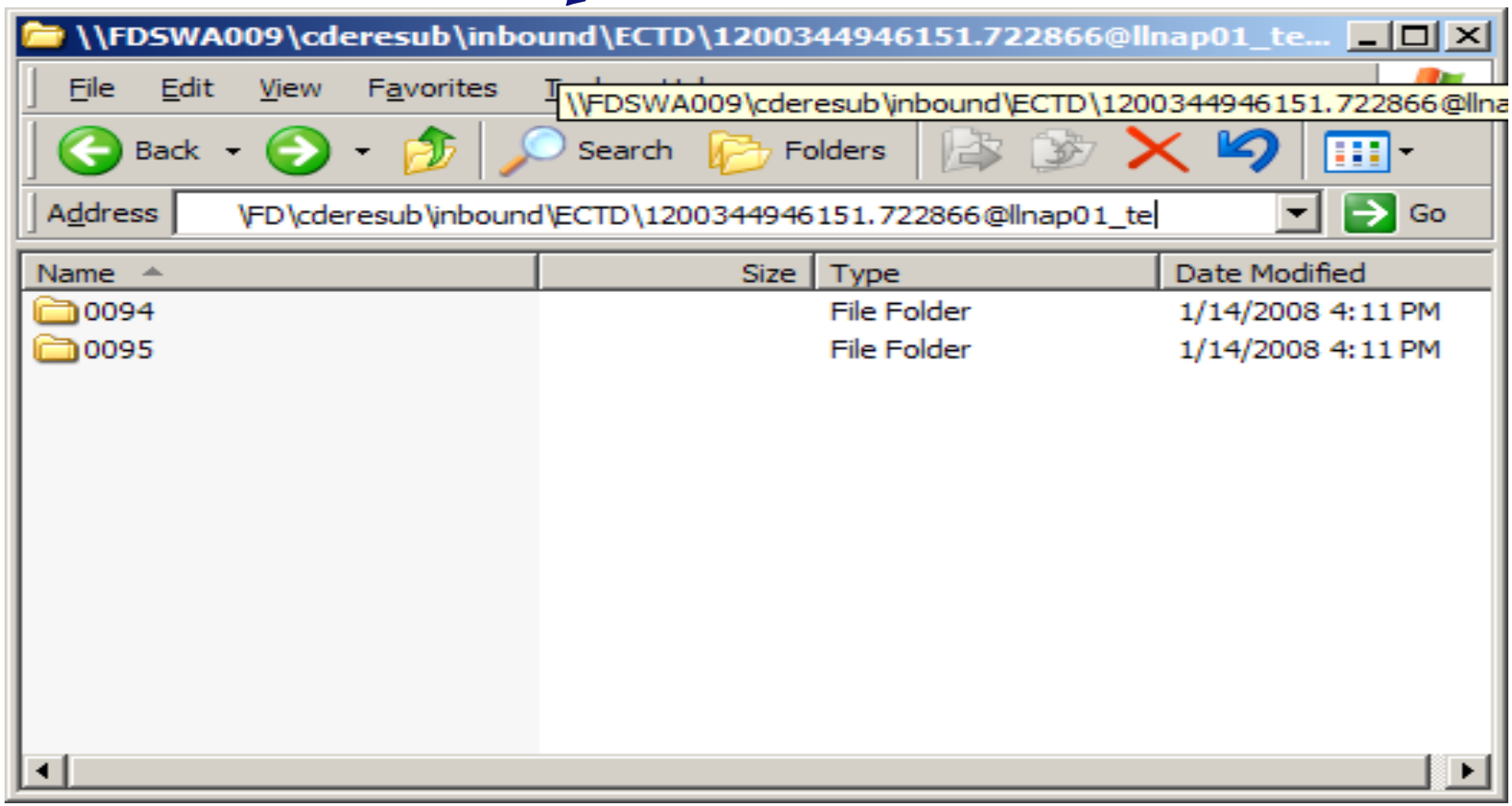
Don't send in more than one 356h form in a submission

- Our ASR program looks for the "356h" in 356h.PDF
- 356h_append.PDF looks like another 356h.pdf to our program.
- If you need a continuation sheet consider name such as application_form_addendum that don't include the form number.

Bad Characters in the file or folder names

- Using ***spaces*** in folder or file names is not recommended – use a hyphen or underscore
- Other illegal characters:
- / - forward slash
- \ - backslash
- : - colon
- ? - question mark
- " - quotation marks
- < - less than sign
- > - greater than sign
- | - vertical bar,

Please send in one Sequence per transaction – please be sure that one sequence is correct



Do not send in a Single PDF File Submission

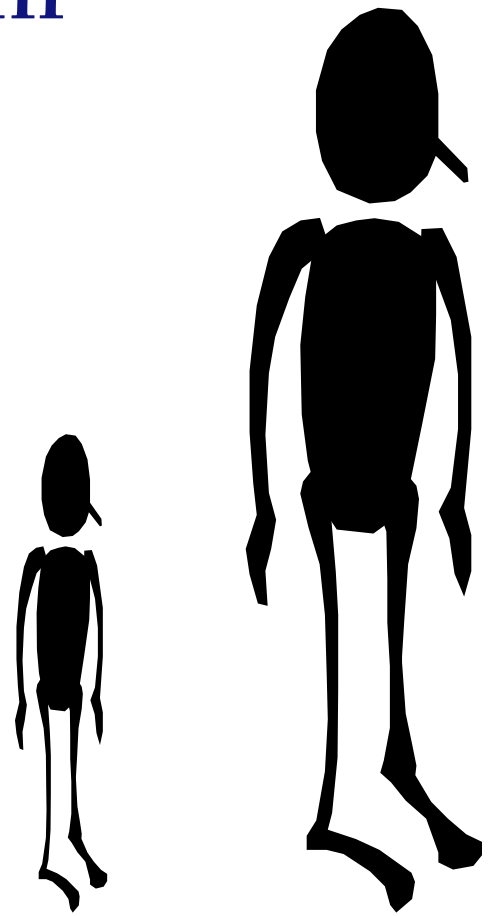
- Granularity aids in processing and review
- Gateway submissions to be processed automatically must have the proper fillable forms

Incorrect or Missing Application Number on the form or US-Regional

- If the number is missing or nonexistent or incorrect – we can't automatically process it
- Before you use the Gateway – get a number first
- http://www.fda.gov/cder/regulatory/ersr/preassigned_application.htm

Mismatch between application type and form

- ANDA with a 1571.PDF
- IND with a 356h.PDF



Please do not send in one submission to be applied to multiple applications

- When working with the eCTD this will not work
- One submission should contain one sequence for one application
- The eCTD is designed to be self contained
- You can cross reference your submission information

Still have questions?
Send us an email:
esub@fda.hhs.gov

Thank You