THAIRIMS

INSTRUCTIONS FOR APPLICANTS

FDA is adopting a new computer-assisted drug registration system. The system enables applicants to submit applications online as described in the diagram shown in annex 1.

During the first 18 months of operation, applicants will not be required to pay a fee for using the system. After this time a small fee may be required to ensure sustainability of the system.

Reach URL http://thairims.fda.moph.go.th/ and enter username and password to log in.

Two or three options will appear, depending on the scope of access of each user, as selected when requesting username and password. The modern medicines option includes both human and veterinary medicines.

MODERN MEDICINES   VETERINARY TRADITIONAL MEDICINES   UPDATE PROFILE

The Update Profile option will permit to update user's profile and change password. Updating the user profile permits creating/editing alternates to assist a user to perform data entry work. To create/edit an alternate, a user will enter a name and a password for each alternate. The alternate will access the system using the same username as the user but will have a separate password.

The modern medicines option gives access to the main data entry facility where users can: 1. generate an application for a new product registration, a renewal, or a variation (not yet implemented); 2. Edit an existing draft application; 3. Erase an existing draft (i.e. application generated but not yet submitted); 4. Generate a copy of an application (at any processing stage); 5. Print: generates a list of the PDFs uploaded; 6. Submit an application to FDA.

Depending on the context, selecting New will provide specific options, see examples here below. Separate guidance documents will be provided to assist applicants to fill information for the different procedures.

▸ GEN Generic medicine, no BE, ICH NEES

▸ GENA Generic medicine, no BE, ACTD

▸ GENBE Generic medicine, BE required, ICH NEES

BE: bioequivalence; NEES: non-eCTD-electronic submission

1 - Start a new drug registration application or a renewal application.

When generating new applications, a separate application must be generated for each strength, dosage form, and pack size of a product. The system has a "copy" facility to enable users to "replicate" similar applications without typing and uploading the same information again.

A new application is generated by users in draft form. Users can edit, add or remove data, and make any kind of change until they decide to submit the application. After submission, users will no longer be able to make any change to the data submitted, unless requested to do so by FDA. Applications can be kept in draft status for up to **30 calendar days. Past such time, applications will be automatically removed from the system, and data will be lost. The maximum number of draft applications simultaneously open is 50 for each company** (this limit can be increased if necessary).

To start a new application, press the "New" button at the top of the screen shown above. To start a renewal application, press the "Renew" button at the top of the screen shown above. Renewal application start by entering the existing registration number and product name. If information is available in the system, it will be displayed. Applicants will be able to enter data to complement the existing information. Each username/password is related to one company and does not permit access to information on products related to other companies.

The Edit button permits to access draft applications to change/add/remove data as required.

The Erase button fully removes a draft application.

The Copy button generates a new application copying data from an existing application regardless of its status (i.e. it copies data from draft, submitted, under assessment, or approved applications). This facility saves data entry time when preparing applications for different strengths, dosage forms or pack sizes of the same product.

The Print button permits to view/print the list of PDFs.

The Submit button 'locks' application data and 'sends' the application to FDA. After submission, users will not be able to change any data of the submitted application.

Some of the above-mentioned buttons will change label and function depending on the type of applications being shown in the list.

Applications appear in a list at the centre of the screen depending on the following criteria:

Draft: applications in draft form. Can be edited.
Submitted: submitted to FDA. Cannot be edited.
Accepted: accepted by FDA for assessment. Cannot be edited.
Rejected: rejected by FDA. Will not be assessed.
Under assessment: applications have been accepted by FDA and assessment has started.
Finalized: assessment completed and final decision taken.
Trash: draft applications deleted by the user or by the system (uploaded pdfs cannot be restored).
Withdrawn: applicants can withdraw an application any time after it has been submitted

These columns indicate: the date on which the draft application has been created, and whether all the minimum required information has been entered and the application is therefore ready for submission ✓ . Incomplete applications cannot be submitted.

How to enter application data.

Depending on the type of application, the system will require different types of information and documents to be submitted.

An application number is automatically generated by the system. Data entry is carried out in three different ways:

1. Some data must be entered directly by the applicant by typing in the available spaces (e.g. product name, packaging description).
2. Some data will be selected from look-up tables (e.g. ATC code). This will ensure consistency of terminology. If a specific term is not found in the look-up tables, applicants should first make sure that a synonym is not already included in the tables. If no synonym is found, users should select the "unassigned" option that has been included in all look-up tables. In addition, applicants can ask FDA to consider adding the new term by writing in the Comments field available in all applications.
3. Some data will have to be uploaded by applicants as PDF files or JPG/PNG images. All files in other formats, such as .DOC or .XLS, will have to be converted by applicants to PDF before uploading. See 'Submitting PDFs to FDA' below. Occasionally, FDA may request applicants to submit specific documents in other formats, but this will be done outside the online application system.

An example of data to be typed directly is the product name

Product name	Type product name here

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An example of data to be selected from a look-up table is the dosage form. Press this icon

This window will appear

Type 3 characters and select from the list.

To be able to save a draft, applicants must enter at least the basic product information appearing on the first screen (product name, generic name, strength, dosage form, etc.). Additional information, such as manufacturers, ingredients and other data (see the buttons below) can be added later.
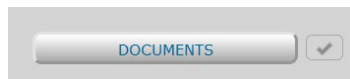
These 'button' opens a new windows to upload dossier documents.

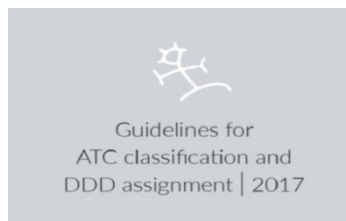**Naming files**: applicants do not need to follow any specific rule for naming files to upload. Operational file names are generated by the system and will include the application number and a string with the document name as it appears in the applicable reference format, ICH eCTD 3.2.2 or ASEAN Common Technical Dossier (ACTD). An additional field is available for applicants who wish to add a file description when several files must be uploaded for the same dossier entry. This is optional and should be used only when it is useful to distinguish different generations of pdf files.

2 - ATC Classification and generic names

The Anatomical Therapeutic Chemical (ATC) classification system is recommended by the WHO and widely used internationally (e.g. European Medicines Agency, Australia's TGA). Follow this link https://www.whocc.no/atc_ddd_index_and_guidelines/guidelines/ for the most recent guidelines. To select the ATC code, click on the magnifying lens and type a few characters as shown here

Some APIs are associated to more than one ATC code. To select the most appropriate code it is necessary to consult the guidelines if one is not already familiar with the ATC classification system. The guidelines explain that the classification is organized as shown in these examples.

To verify that the appropriate code has been selected, the system will display the therapeutic class.

| ATC Code | J01GB03 | 🔍 | gentamicin |
| Therapeutic class | J01 | 🔍 | ANTIBACTERIALS FOR SYSTEMIC USE |

| ATC Code | S01AA11 | 🔍 | gentamicin |
| Therapeutic class | S01 | 🔍 | OPHTHALMOLOGICALS |

The ATC classification has entries for multiple-ingredient products (e.g. multivitamins) and an entry "Unassigned" for cases where no matching term has been found.

Search: multivi

Code	Description
B03AE03	iron and multivitamins
B03AE02	iron, multivitamins and folic acid
B03AE04	iron, multivitamins and minerals
A11AA02	multivitamins and calcium
A11AA01	multivitamins and iron
A11AA03	multivitamins and other minerals, incl. combinations
A11AA04	multivitamins and trace elements

Search: unas

Code	Description
X01XX99	unassigned

3 - Use of the ATC classification in special cases

3.1 FOR PRODUCTS WITH MORE THAN ONE ACTIVE INGREDIENT

In the search, type the name of one of the ingredients and then select the appropriate option. It may be necessary to conduct more than one search to find the appropriate entry (see examples below).

Data List ✖

Search: omepra

Code	Description
A02BC05	esomeprazole (oral)
A02BC05	esomeprazole (parenteral)
A02BD06	esomeprazole, amoxicillin and clarithromycin
M01AE52	naproxen and esomeprazole (oral)
A02BC01	omeprazole (oral)
A02BC01	omeprazole (parenteral)
A02BD05	omeprazole, amoxicillin and clarithromycin
A02BD01	omeprazole, amoxicillin and metronidazole

Data List ✖

Search: proto

Code	Description
B01AC56	acetylsalicylic acid, combinations with proton pump inhibitors

3.2 INGREDIENT NAMES THAT CANNOT BE FOUND IN THE ATC CLASSIFICATION

If, in spite of the above searches, the desired name cannot be found, then the term UNASSIGNED should be selected. FDA will provide feedback to the applicant as appropriate.

4 - Entering ingredients

Ingredients data are entered in the screen shown below.

Substance names must be selected from a look-up table. For active substances, INNs must be used if available. The look-up table includes all INNs and the US-FDA UNII (Unique Ingredient Identifier - https://precision.fda.gov/uniisearch/archive). If an **active** substance name is not found, applicants should first make sure that a synonym is not already included in the look-up table and, if no synonym is found, choose UNASSIGNED from the look-up table and type the proposed name in the 'Complementary information' field. If an **inactive** ingredient is not found, just type its name in the substance name field and the system will accept it, pending verification by FDA during the assessment process.

When a salt or other specification is not included in the table, applicants will be able to enter additional information about the substance in the 'Complementary information' field.

Quantities and related measurement unit are then entered. A blank field is available to enter units that are not the milligram, the microgram or the international unit.

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Entered ingredients appear in a table like the one shown here below.

		Substance name	Type	Quantity	Unit
✏	🗑	AMOXICILLIN	Active	500.000	Milligram
✏	🗑	LACTOSE MONOHYDRATE - CELLULOSE, MICROCRYSTALLINE	Inactive		.

The two icons on the left permit to edit or delete entered data. There is no limit to the number of ingredients that can be entered.

The tags that appear at the top of the ingredient data entry screen (Second form, Third form, etc.) are meant to enable applicants to enter data referred to complex products (such as certain oral contraceptives) where the same blister pack includes different dosage forms with different compositions (e.g. yellow tablets contain AAA 3mg; red tablets contain AAA 2mg and BBB 5mg; white tablets contain only inactives, etc.). Another example is a product consisting of two primary containers: a vial with powder for injection and an ampoule with water for injection.

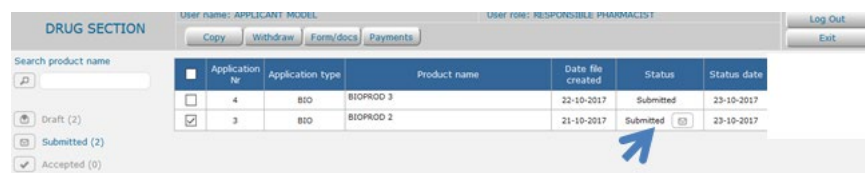**How to manage submitted applications.**

Completed applications can be submitted to FDA. The system will not allow submitting incomplete applications and will mark with different signs those ready for submission ☑ and those still incomplete.

Submission is done simply by pressing the submit button that appears on the bar over the grid showing draft applications.

 After submission, applicants will receive a confirmation email message. FDA will screen the application. Screening has two possible outcomes: a) the content of submitted application is readable and meets all the required formal aspects (this does not mean the documentation has been assessed and found approvable), or b) there is a problem with one or more elements of the information submitted. In the first case, applicants will receive an email confirming that the application has been accepted for assessment.

If there is a problem with some aspects of the application, applicants will receive an email mentioning the problem(s) and inviting to make the necessary amendments. The graphic below shows two types of submitted applications.

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The applications that appear in the grid and have no icon are those submitted and still under FDA review. Those with an envelope icon are applications that require applicant's attention. Clicking on the icon, applicants can see the content of FDA's email mentioning application shortcomings.

Clicking elsewhere on the row of that application will enable applicant to access selected content of the application and make the necessary amendments. In the example shown in the image, observations have been raised on the 'clinical overview' part and these should be addressed by the applicant by uploading a new document.

An extra field is available to upload unspecified documents when applicants are requested to provide information but this cannot be related to any specific dossier item.

After editing part of an application, applicants will be asked if other changes are needed at a later stage or the amended application is ready for re-submission.
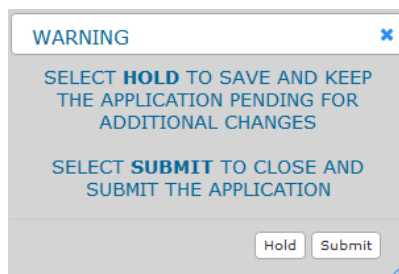
5 - Submitting PDFs to FDA

All PDF files submitted to FDA must conform to the following criteria:
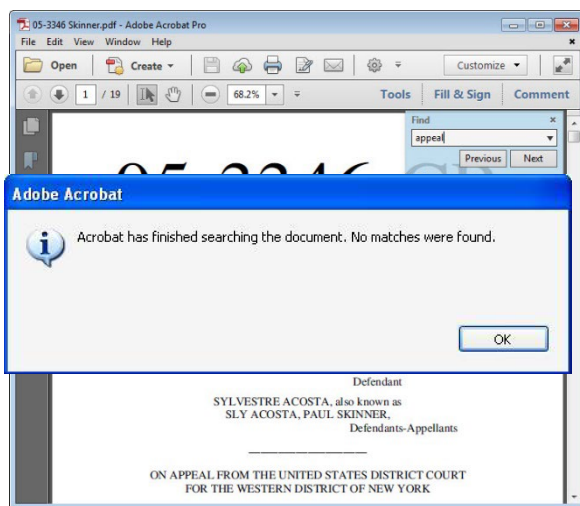
1. **must be text-searchable**
2. **must not be password-protected**
3. **page size must be A4, i.e. 210 x 297mm (8.3 x 11.7inches).**

PDF files with non-A4 page size may result truncated or otherwise unreadable.

1 - How to determine whether a PDF is text-searchable

After opening the PDF, try searching for a word known to be in the document by clicking CTRL-F and entering the word in the Find box.

If you are sure that the word is present but the message below appears, the document is not text-searchable.

An alternative way to determine if the text is searchable is using the mouse to highlight one word in the text. If a single word cannot be highlighted and the entire page turns blue, the text is not searchable. See point 3.

2 - How to check if a PDF is password-protected

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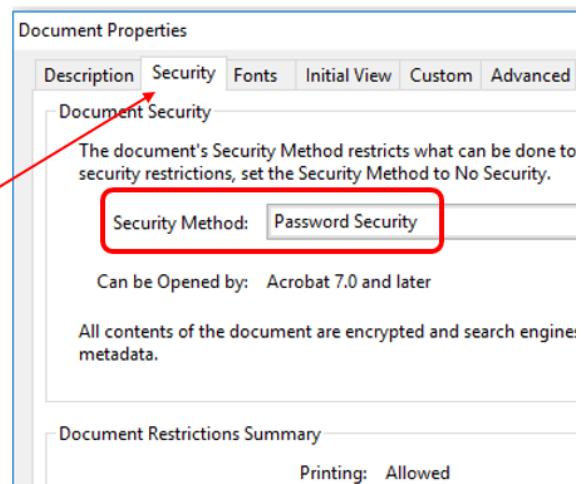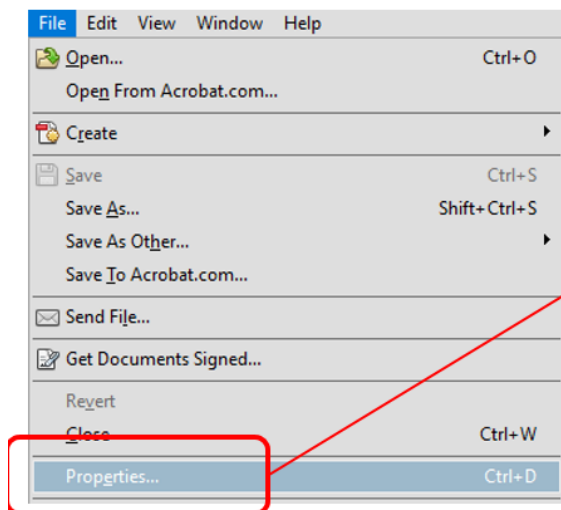
If a PDF is password-protected, applicants can remove protection by one of these three ways: a. by the document owner (assuming s/he remembers the password); b. using commercially available software[1]; c. by following the procedure described here below for making a PDF text-searchable (only works if printing is allowed).

3 - How to check and change page size of PDF
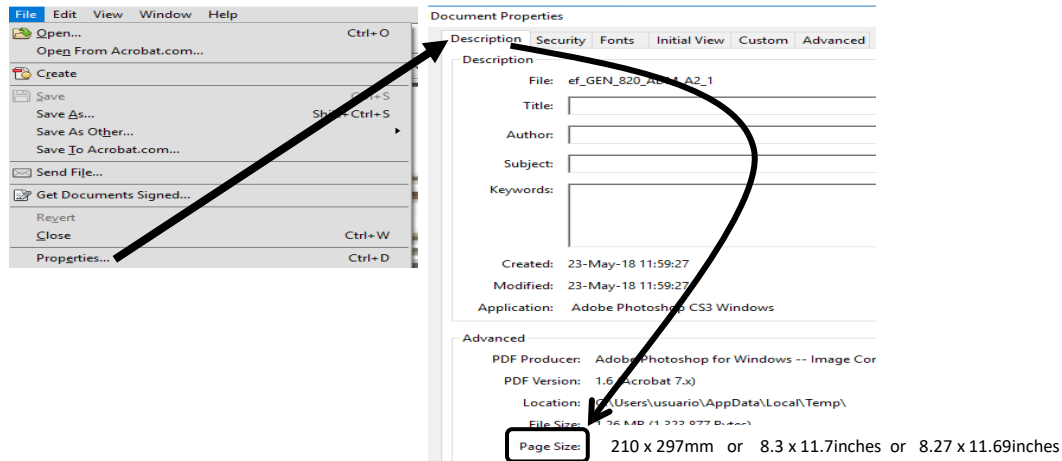
If the page size is different than A4 convert it to A4 as follows:

- select Print and then select Adobe or Microsoft to PDF as printer
- click on Page Setup
- Select A4 and click OK
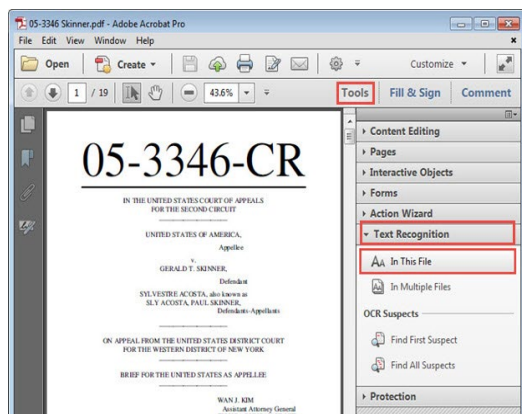- Click OK to print, choose destination directory and file name as appropriate.

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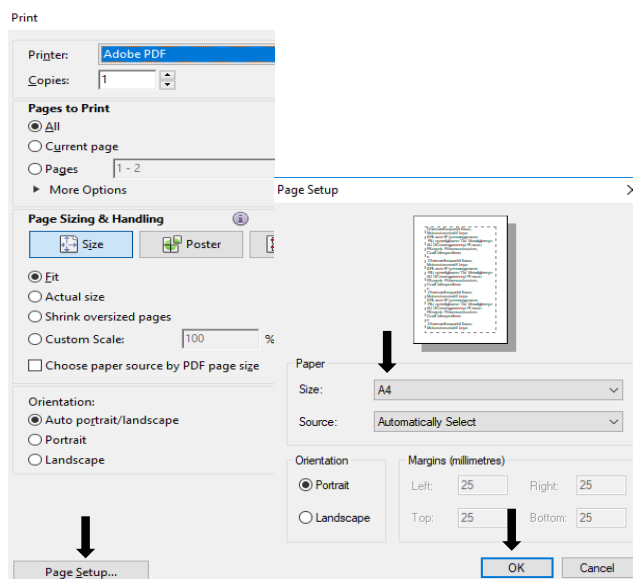
[1] Google "pdf password remover" to pick the method of your choice.
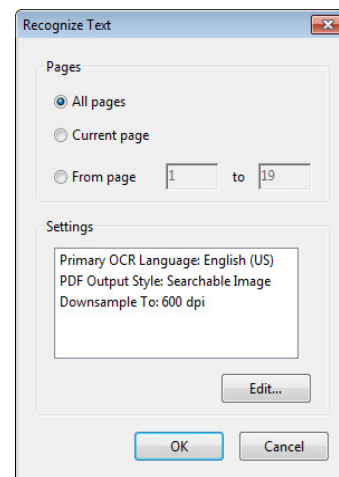
4 - How to make a PDF text-searchable

The following instructions apply to **Adobe Acrobat** Professional or Standard[2]:

Click on **Tools > Text Recognition > In This File.**

 The **Recognize Text** popup box opens. Select **All pages**, then click **OK**.

When all the pages in all documents are processed, try the same search (point 1 above) to verify that each document now is text-searchable.

If the error message "...renderable text…" appears.

In some cases, this error message may appear: "Acrobat could not perform recognition (OCR) on this page because: This page contains renderable text." If you cannot obtain another version of the pdf file that does not contain renderable text, this must be addressed as follows:

Short description:

a. Print the .PDF file that gave the error message to the "Microsoft XPS Document Writer" printer driver (it should appear among the printers or you will need to install it, see below).
b. Convert the resulting .XPS file to a new .PDF file.
c. Perform OCR.

Please note:

- You need the full (or "Pro") version of Adobe® Acrobat® or a suitable alternative to complete this procedure.
- This can only be done on Windows® computers.
- This process generates some large files. Your final files will be larger than the original file.

If you need to install the XPS printer driver:

a. Download the XPS printer driver here: https://learn.microsoft.com/en-us/windows-hardware/drivers/print/xpsdrv-printer-driver

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[2] Many alternative options exist: https://pdf.wondershare.com/pdf-software-comparison/adobe-acrobat-alternative.html

b.   Save the file and double-click it to start the install. Follow the prompts to complete the installation. This will create a new printer in your printer list. To print to it, you simply choose that printer instead of your usual printer when you print a document.

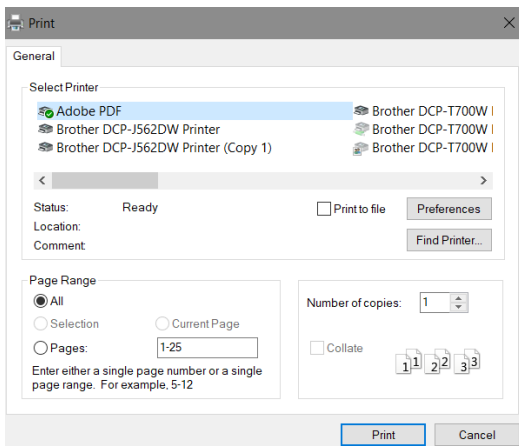**Print the .PDF file to the .XPS "printer.":**
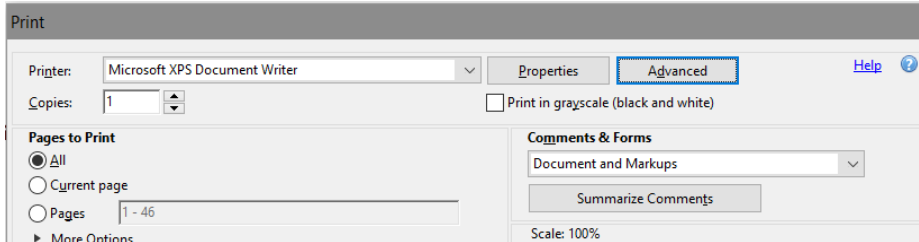
Convert the .XPS file back into a .PDF file.

This step may take a long time if you have a large document with lots of "rendered text," and it will look as if your computer isn't doing anything.
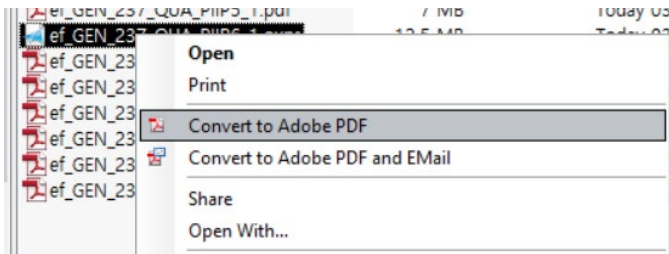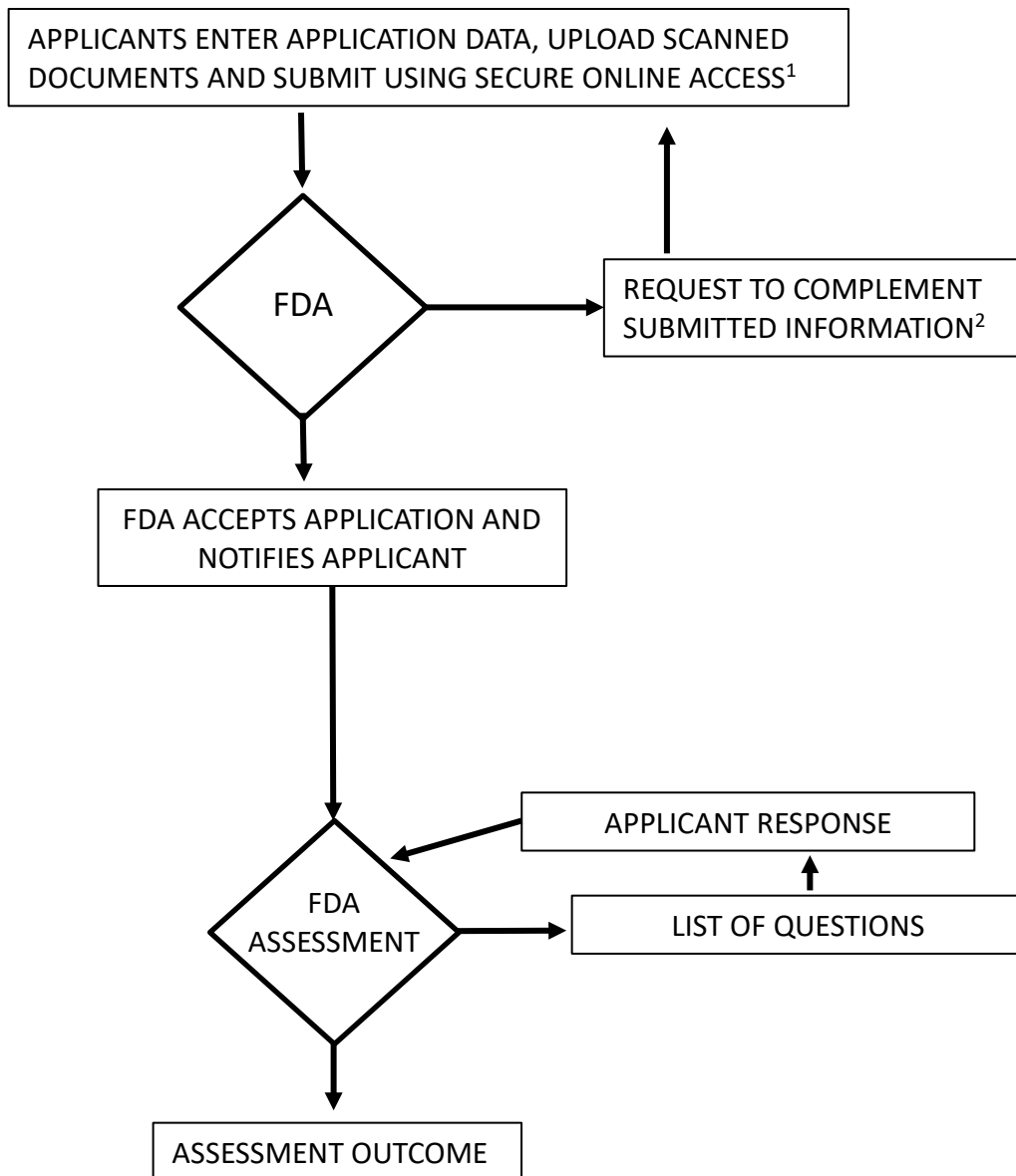

a.   Right click on the .XPS file and choose either "Combine supported files in Acrobat..." or 'Convert to Adobe PDF.'

b.   Choose Adobe PDF as printer and an appropriate file name to save the converted file, and **DO NOT overwrite** your original file.

A new, searchable, PDF will be created. It will be larger than the source file. After performing the OCR on the new file, the size will be reduced. Note, however, that pages with the most text produced the greatest increase in size when printing to the .XPS file. After processing a 350-page, 10MB .pdf document that contains mostly text, the XPS file can be 175MB, and the resulting document would be 15MB if OCRed using the ClearScan OCR method (i.e. about 1.5 times bigger than the original, non-searchable file).

APPLICANTS ENTER APPLICATION DATA, UPLOAD SCANNED DOCUMENTS AND SUBMIT USING SECURE ONLINE ACCESS[1]

FDA

REQUEST TO COMPLEMENT SUBMITTED INFORMATION[2]

FDA ACCEPTS APPLICATION AND NOTIFIES APPLICANT

FDA ASSESSMENT

APPLICANT RESPONSE

LIST OF QUESTIONS

ASSESSMENT OUTCOME

NOTES:

1 - For each application, the system will allow data entry and document upload for up to 30 days from the date on which data entry is started. During this time data can be modified as needed. However, after submitting an application, applicants will no longer be able to modify anything.

2 - If FDA requests additional data to be uploaded, applicants will only have access to the specific part of the application where data is required. The rest of the application will not be editable.