SG-HSA eCTD Industry Briefing Session

9 May 2023

eCTD Team

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Outline

- Introduction to eCTD and HSA's implementation overview
- eCTD industry consultation
- eCTD submission process overview
- SG-HSA eCTD regional specifications – Terminology
- Preparing a SG-HSA eCTD application
- Validating the eCTD sequence
- Submitting the eCTD package
- Providing your comments
- Q&A

INTRODUCTION TO ECTD AND HSA'S IMPLEMENTATION OVERVIEW

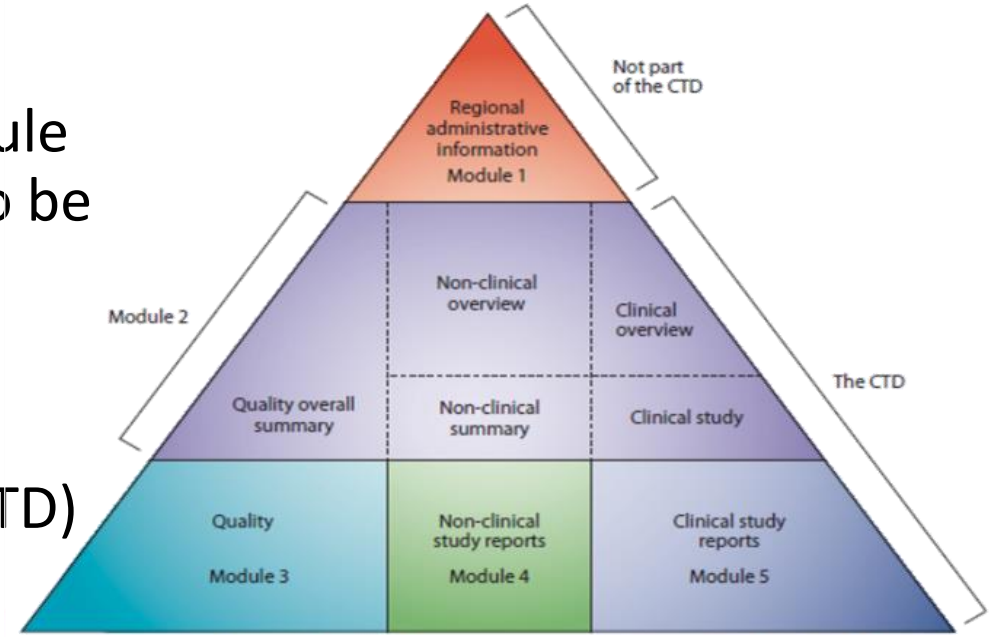
Introduction to eCTD

Electronic Common Technical Document (ICH)

- ICH Common Technical Document (CTD) organises regulatory information into 5 modules, where Module 1 is region-specific and Modules 2-5 are intended to be common for all regions

- eCTD provides a harmonised technical solution to implementing the Common Technical Document (CTD) electronically

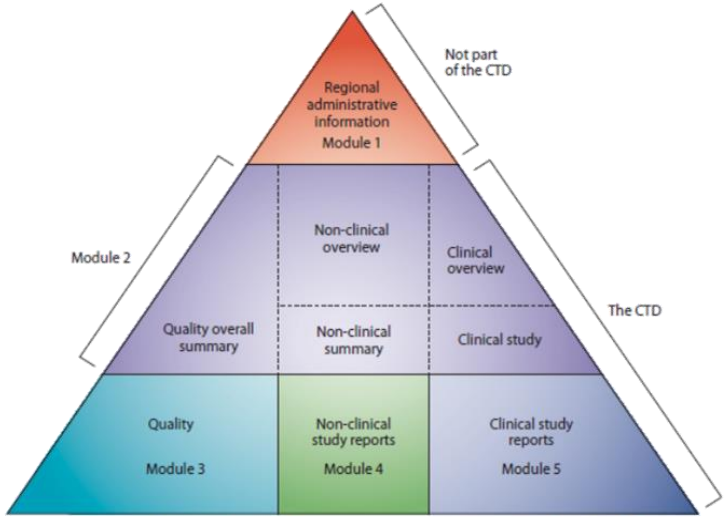
- Standard structured format for the electronic transfer of regulatory information from industry to health authorities



The CTD triangle. The Common Technical Document is organized into five modules. Module 1 is region specific and modules 2, 3, 4 and 5 are intended to be common for all regions.

Benefits of eCTD

- Reduces duplicative effort in dossier preparation during global submissions
- Enables better product life cycle management for industry and HSA
- Faster transfer of data by industry to HSA
- Facilitates HSA's evaluation of dossiers



The CTD triangle. The Common Technical Document is organized into five modules. Module 1 is region specific and modules 2, 3, 4 and 5 are intended to be common for all regions.

HSA eCTD Implementation Overview

At initial launch:

- eCTD submissions will be voluntary
- Based on eCTD version 3.2.2
- Validate according to ICH CTD structure
- After eCTD has commenced for a product, subsequent variations should continue in eCTD
- Modules 1-5 should be in eCTD

<u>Scope:</u>

- New NDA/GDAs and their subsequent post-approval changes
- DMFs if the dossier is submitted in eCTD

Key Dates

17 April 2023	• Notice to Industry issued to Applicant companies
2 May 2023	• Start of Industry Consultation • Release of consultation package on HSA website
9 May 2023	• Industry briefing session (Zoom)
12 May 2023	• Posting of slides from industry briefing session
12 June 2023	• End of Industry Consultation
Q1 2024	• Release of SG-HSA eCTD Specifications v1.0 • Publication of Summary of Changes
Q4 2024	• Test submissions accepted • Target implementation of eCTD in Singapore

ECTD INDUSTRY CONSULTATION

Consultation Package Contents

All information related to HSA's eCTD implementation will be located at https://www.hsa.gov.sg/therapeutic-products/register/ectd-submissions

1. Specification components

- SG-HSA eCTD Regional Specification Document version 0.9
  - SG-HSA eCTD Specifications v0.9 (Word, 499KB)
- Regional SG-HSA Module 1 Schema
  - sg-regional(XSD)
  - MD5 Checksum (TXT) [4EB3787844210F1734B8BA6220914DCC]
- Supporting schemas as required by the Regional Schema xml, xlink (XSD)
- SG-HSA Sample eCTDs(zip file, 670KB)

Download the package as a zip file: SG-HSA Specification Components (806KB)

2. Validation components

- SG-HSA eCTD Validation Criteria including SG-HSA Granularity Annex
  - SG-HSA eCTD Validation Criteria v0.9 (Excel, 95KB)
- Document Matrix
  - document-matrix (XML)
- Submission-Type Matrix
  - submission-type-matrix (XML)
- Defined lists (XML)
  - application-type
  - product-type
  - submission-type
  - sequence-type
  - contact-type

Download the package as a ZIP file: SG-HSA Validation Components (96 KB)

3. Q&A document

- SG-HSA eCTD_Questions and Answers (pdf, 184KB)

ECTD SUBMISSION PROCESS OVERVIEW

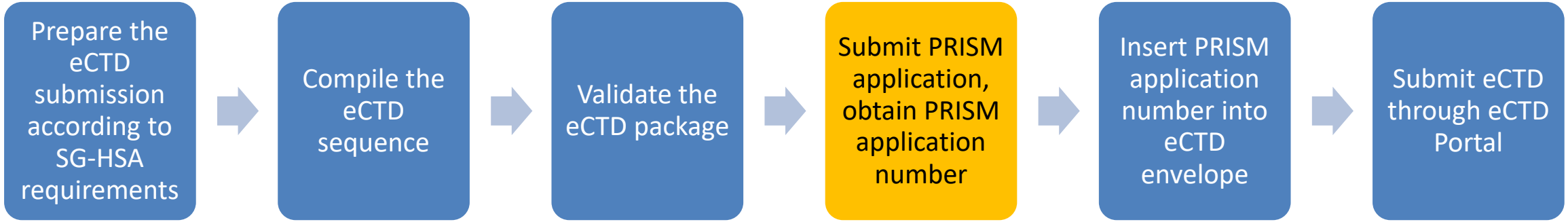
Non-eCTD vs eCTD-based Submissions

	Non-eCTD	eCTD
Submission platform for regulatory application	PRISM	PRISM
Issuance of regulatory approval	PRISM	PRISM
Dossier submission	Applicant couriers CD/DVD to TPB or Applicant uploads into PRISM (one file at a time)	Applicant submits eCTD online via Portal (single zip file upload)
Dossier format	ICH CTD ASEAN CTD	ICH CTD

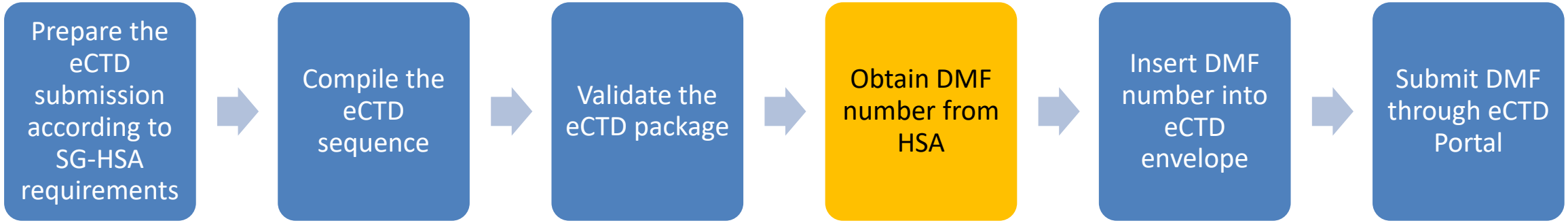
PRISM: Pharmaceutical Regulatory Information System; used by applicants to carry out transactions for health products with HSA

eCTD Pre-Submission Steps

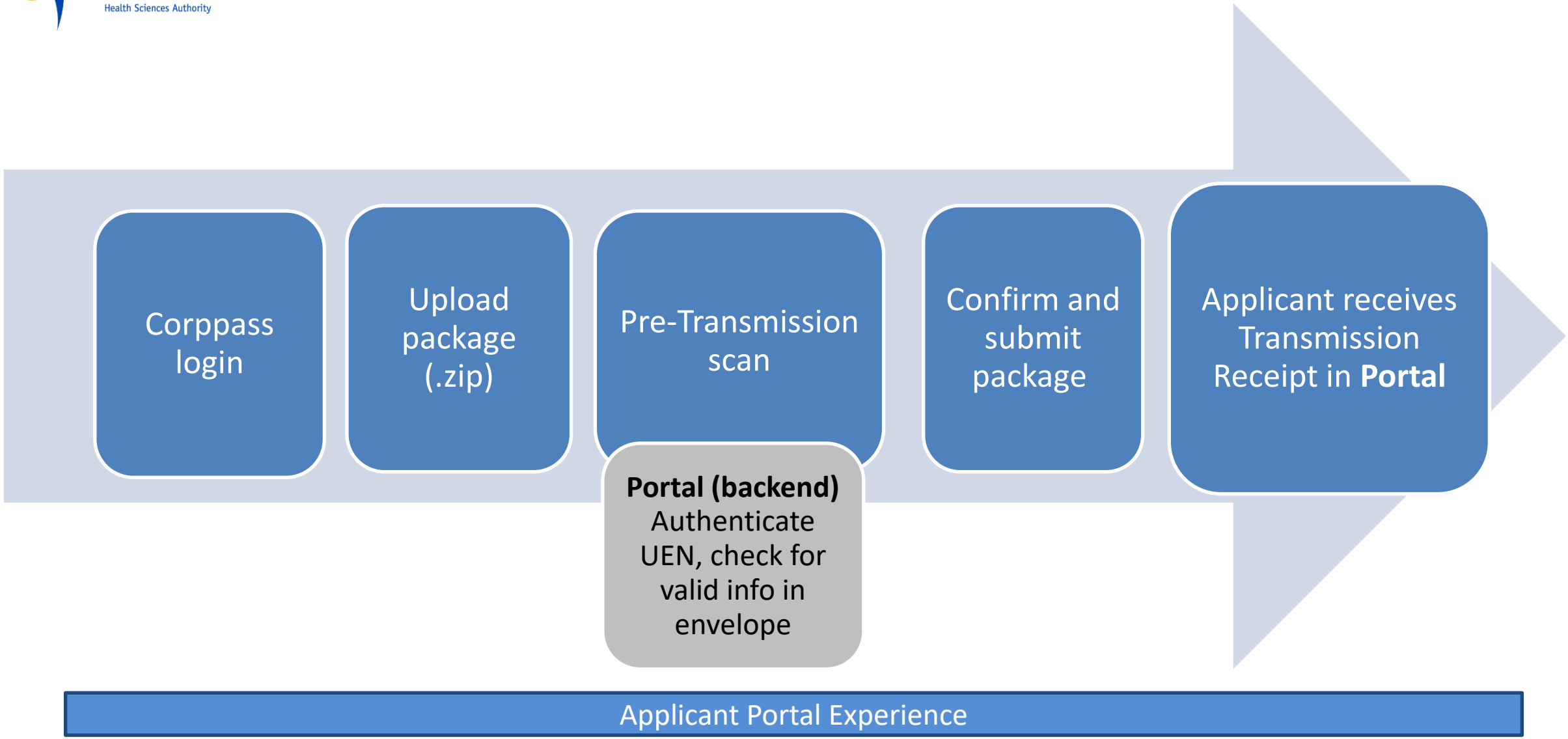
For registration submissions:



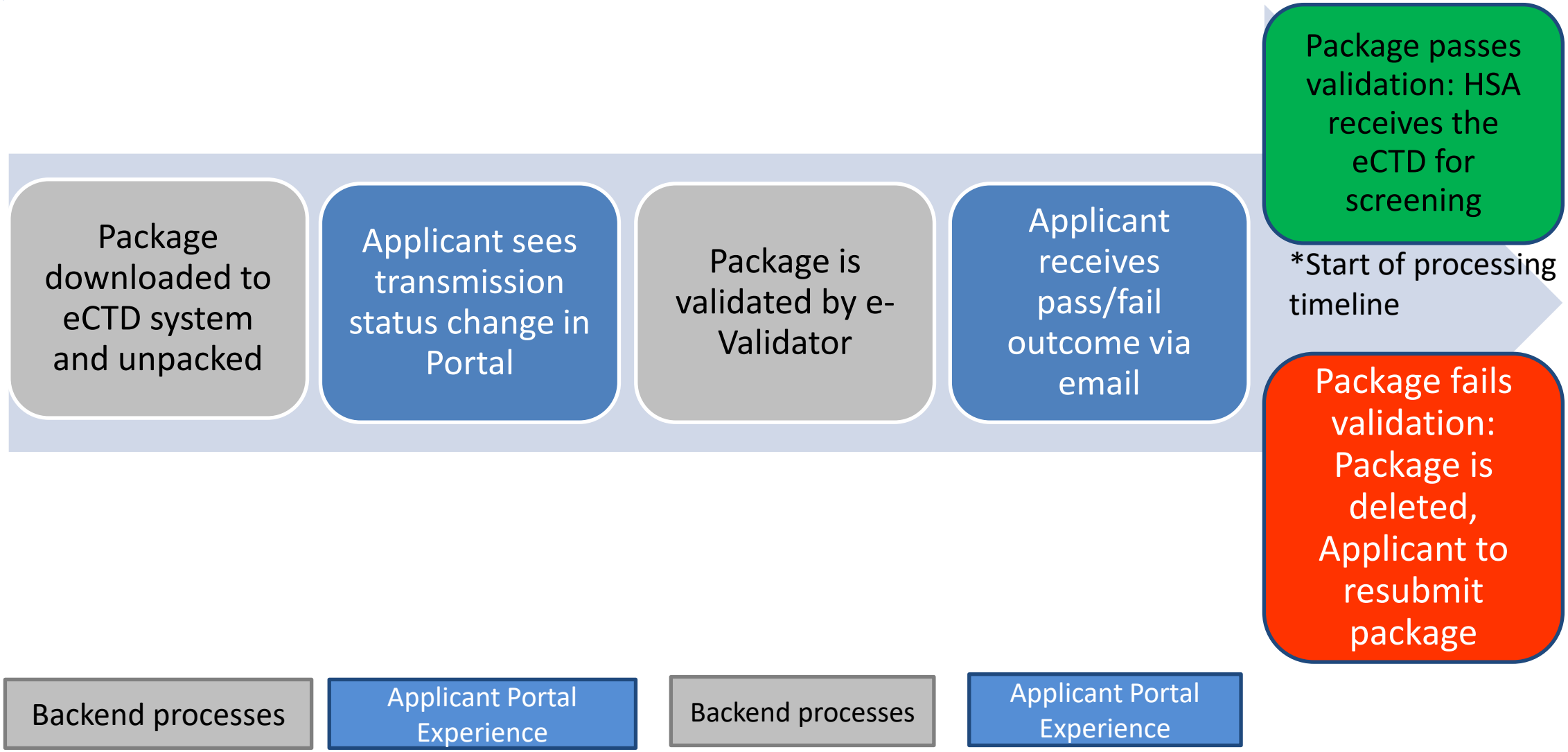
For DMF submissions:



Submitting the eCTD Package via eCTD Portal



Submitting the eCTD Package via eCTD Portal



SG-HSA ECTD REGIONAL SPECIFICATIONS - TERMINOLOGY

eCTD Terminology

Application level

- Highest overall level representing the product
- Can contain multiple strengths of the same product but not multiple pharmaceutical forms
- Made up of multiple Submissions and Sequences over time

Submission level

- Represents a regulatory activity which may be made up of one or more sequences
- Each time a new activity is started, a new Submission will be created
- The Sequences assigned to a Submission may not be sequential as parallel Submissions may be under review, causing some Sequence numbers to be skipped within a Submission

Sequence level

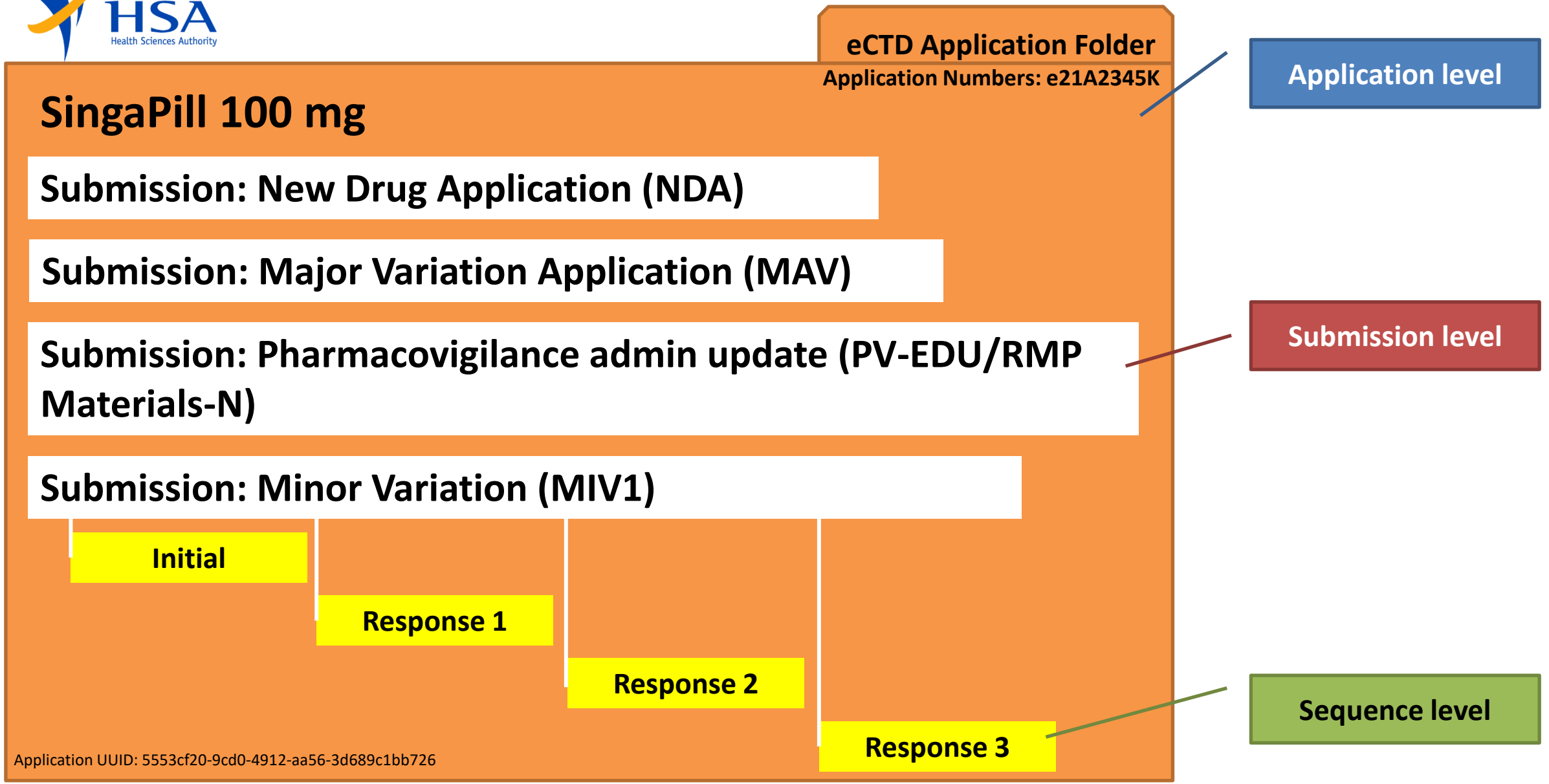
- Lowest level, representing each package of information provided
- Each Sequence must be assigned to a Submission either as the initial sequence or as a follow-up sequence in the form of supplemental information, a response, withdrawal or closing information

eCTD Glossary

Term	Definition
Applicant	The company responsible for the application
Application	A collection of eCTD Submissions and Sequences over time
Application Type	Therapeutic product
Submission	A specific regulatory activity involving a collection of Sequences ≈ PRISM application
Submission Type	• New Drug Application (NDA1, NDA2, NDA3), Full or Abridged route • New Drug Application (NDA1, NDA2, NDA3), Verification route • Generic Drug Application (GDA1, GDA2), Abridged route • DMF • etc
Sequence	A package of information bundled together in an electronic structure
Sequence Type	• Initial • Response • etc

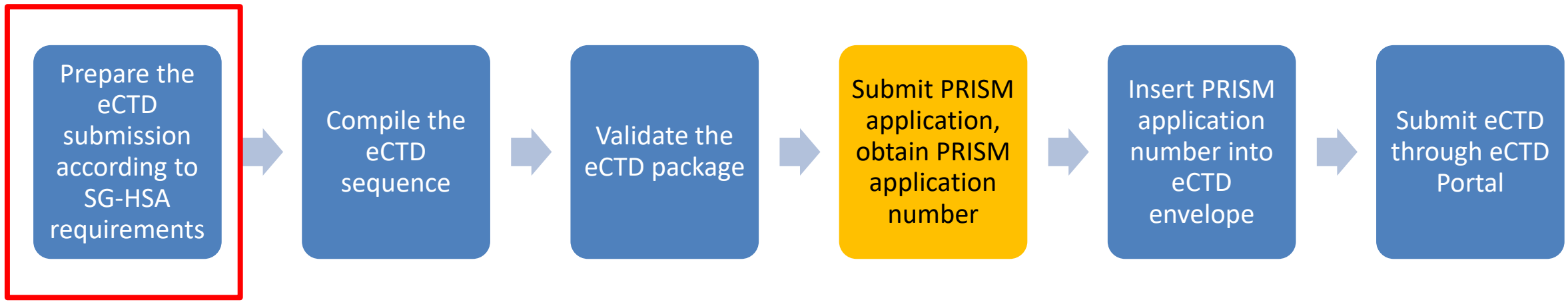
For other submissions currently performed outside PRISM, please refer to the *SG-HSA eCTD Specifications*.

eCTD Structure (Example)



Specific eCTD Glossary

- Please refer to the *SG-HSA eCTD Specifications* for detailed definitions and examples of other terms relevant to eCTD



PREPARING A SG-HSA ECTD APPLICATION

Preparing Your eCTD Application

- Application Number
- Submission Number
- Sequence Number
- Application Folder Naming
- Module 1 Heading Elements
- eCTD Cover Letter
- Note to Evaluator
- Envelope Elements
- Grouping Submissions in a Single Sequence

eCTD Application Number

- Product Registration:
  - Each product should have a unique eCTD Application Number
  - The NDA/GDA Application Number in PRISM will be used for the eCTD Application Number
  - A prefix of ‘e’ should be added to the PRISM application number to form the eCTD Application Number
  - The eCTD Application Number remains unchanged throughout a product’s lifecycle

Mandatory

- DMF submission:
  - The DMF number for a new DMF needs to be requested from HSA
  - A prefix of ‘e’ should be added to the DMF number to form the eCTD Application Number

Mandatory

eCTD Application Number (Example)

Examples:

- New product registration (NDA-1): SingaPill 100 mg

1. Submit NDA-1 Application in PRISM
2. Obtain PRISM Application Number: 21A2345K
3. Submit eCTD using Application Number e21A2345K

- New DMF: Ezetimibe

1. Obtain DMF number from HSA: 015-688
2. Submit eCTD using Application Number e015-688

eCTD Submission Number

Different submission types may have different submission numbers:

Type of eCTD Submission	eCTD Submission Number
NDA GDA MAV MIV Transfer of eCTD application	PRISM application number(s)
Pharmacovigilance submissions	“PV”
DMF submission	“DMF”
Submission to fulfil registration condition Application withdrawal Baseline submission	“Other”

eCTD Submission Number (Example)

Product: SingaPill 100 mg

New product registration (NDA-1):

1. Submit NDA-1 Application in PRISM
2. Obtain PRISM Application Number: 21A2345K
3. Submit eCTD under
    1. Application Number: e21A2345K
    2. Submission Number: 21A2345K

Post-approval Variation (MAV-1)

1. Submit MAV-1 Application in PRISM
2. Obtain PRISM Application Number: 23A0121H
3. Submit eCTD under
    1. Application Number: e21A2345K
    2. Submission Number: 23A0121H

eCTD Sequence Number

- 4-digit number matching Sequence folder submitted
- New Applications of NDA or GDA submissions should start with Sequence 0001

Example:
Within an NDA-1 eCTD Submission:
- Initial sequence: 0001
- 1st Response to query letter: 0002
- 2nd Response to query letter: 0003

eCTD Application Folder

- When submitting Sequences, the Sequence Folder must be provided in an Application Folder
- It is important to use the same Application Folder for all future Sequences of the Application
- The Application Folder Name does not change over time
- Name the eCTD Application Folder after the Application Number omitting the last letter if applicable

Example: If eCTD Application Number = e22A2345A,

Application Folder name = e22a2345

Application Folder (Example)

eCTD Application Folder e21a2345

Application Numbers: e21A2345K

SingaPill 100 mg

Submission: New Drug Application (NDA)

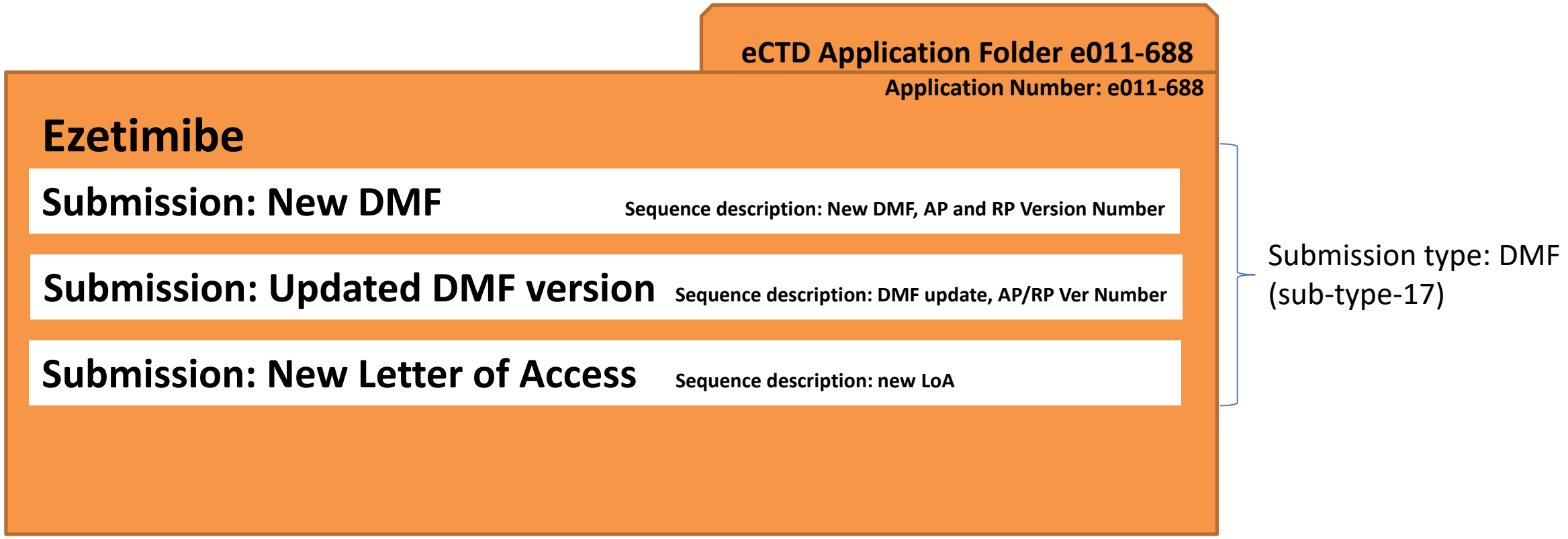
Submission: Major Variation Application (MAV1)

Submission: Pharmacovigilance admin update (PV-EDU/RMP Materials-N)

Same Application Folder used for all Submissions in this eCTD Application

Application UUID: 5553cf20-9cd0-4912-aa56-3d689c1bb726

Application Folder (DMF Example)



Multiple Strengths in One eCTD Application Folder

- If a new Application Folder is created for a product with multiple strengths, i.e. sharing a common dossier and same eCTD Application:
  - Include the multiple eCTD Application Numbers in the envelope
  - The Application Folder name reflects the multiple Application Numbers as a range

Example: If the Application Numbers are sequential,

Product	Strength	Form	eCTD Application Number
SingaPill	100 mg	Film Coated Tablet	e21A2345K
SingaPill	200 mg	Film Coated Tablet	e21A2346P
SingaPill	400 mg	Film Coated Tablet	e21A2347B

The appropriate Application Folder Name for this Application would be e21a2345-7.

Multiple Strengths in One eCTD Application Folder

- If a new Application Folder is created for a product with multiple strengths, i.e. sharing a common dossier and same eCTD Application:
  - Include the multiple eCTD Application Numbers in the envelope
  - The Application Folder name reflects the multiple Application Numbers as a range

Example: If the Application Numbers are not sequential, a range should still be used:

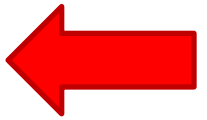
Product	Strength	Form	eCTD Application Number
IncrediPill	20 mg	Injection	e22A2499A
IncrediPill	40 mg	Injection	e22A2502B

The appropriate Application Folder Name for this Application would be e22a2499-502

New Application Folder (Example – 3 strengths)

In this example, a new Application Folder is created for a product with 3 strengths and the Application Folder Name reflects the range of Application Numbers.

eCTD Application Folder e21a2345-7



Application Numbers: e21A2345K, e21A2346P, e21A2347B

SingaPill 100 mg, 200 mg, 400 mg

Submission: New Drug Application (NDA)

Application UUID: 5553cf20-9cd0-4912-aa56-3d689c1bb726

New Application Folder (Example – add 1 strength)

In this example, there is an existing Application Folder for a product with 1 strength.

eCTD Application Folder e22a1234

Application Numbers: e22A1234A

SingaInjection 100 mg

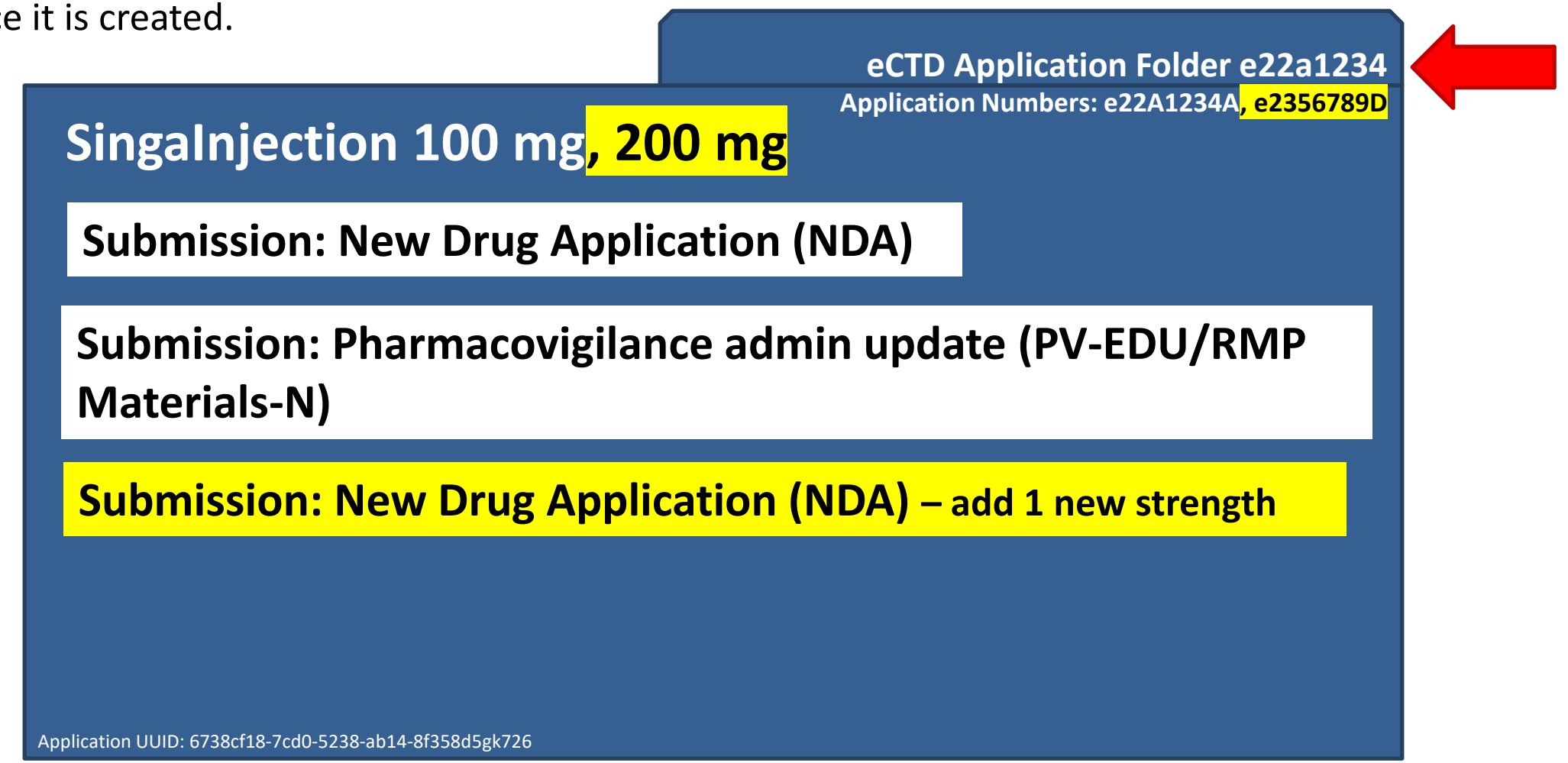
Submission: New Drug Application (NDA)

Submission: Pharmacovigilance admin update (PV-EDU/RMP Materials-N)

Application UUID: 6738cf18-7cd0-5238-ab14-8f358d5gk726

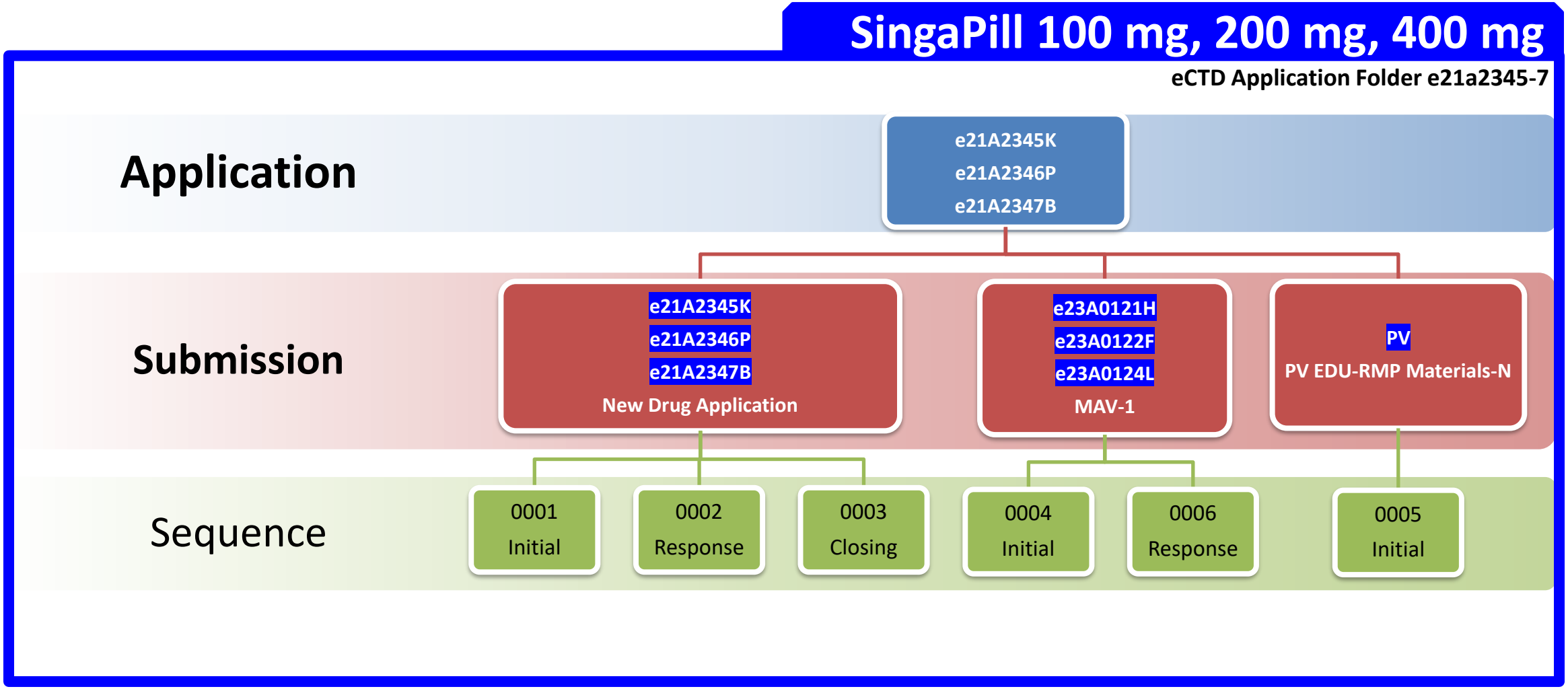
New Application Folder (Example – add 1 strength)

In this example, there is an existing Application Folder for a product with 1 strength. Adding a new strength 1 year later does not change the Application Folder Name because an Application Folder name is fixed once it is created.



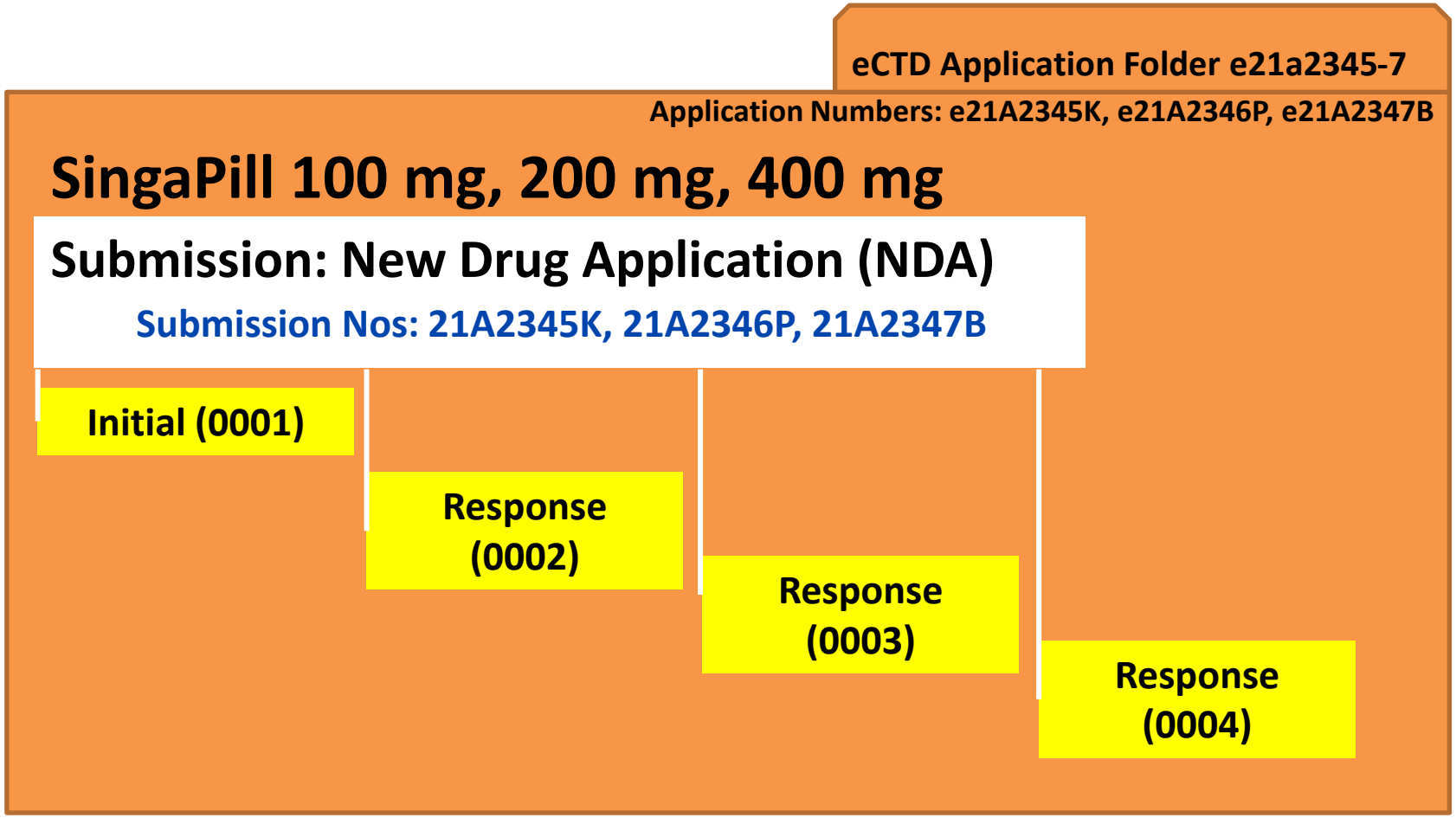
Multiple Submission Numbers (Example)

If multiple strengths share a common dossier and the same eCTD Application, multiple Submission Numbers may be applicable:



Brief recap

- Application number
- Submission number
- Sequence number
- Application folder naming
- Multiple strengths



Module 1 Heading Elements

Section 4.4 of SG-HSA eCTD Specifications

- The SG-HSA Module 1 Heading Elements are organised into 10 tables which mirror current requirements:
  - 1.0 Correspondence
  - 1.2 Administrative Information
  - 1.3 Product Information
  - 1.4 Information about the Experts
  - 1.5 Master Files and Certificates of Suitability
  - 1.7 Good Manufacturing Practice
  - 1.8 Information Relating to Pharmacovigilance
  - 1.9 Foreign Regulatory Information
  - 1.A Additional Data

- Please refer to the *SG-HSA eCTD Document Matrix* for the content required per submission type
- Please refer to the *Guidance on Therapeutic Products Registration in Singapore* for the content required for each title

eCTD Cover Letter

Section 2.5 of SG-HSA eCTD Specifications

- The eCTD Cover Letter replaces the “Introduction” document currently submitted under Module 1 and is a mandatory document

- In addition to what is defined in the *Guidance on Therapeutic Products Registration in Singapore,* the Cover Letter should include:
  - From the eCTD Envelope: Application Number, Submission Number, Sequence Number, Related Sequence
  - Description of anti-virus software
  - Validation information
  - Any warnings or possible missing documents

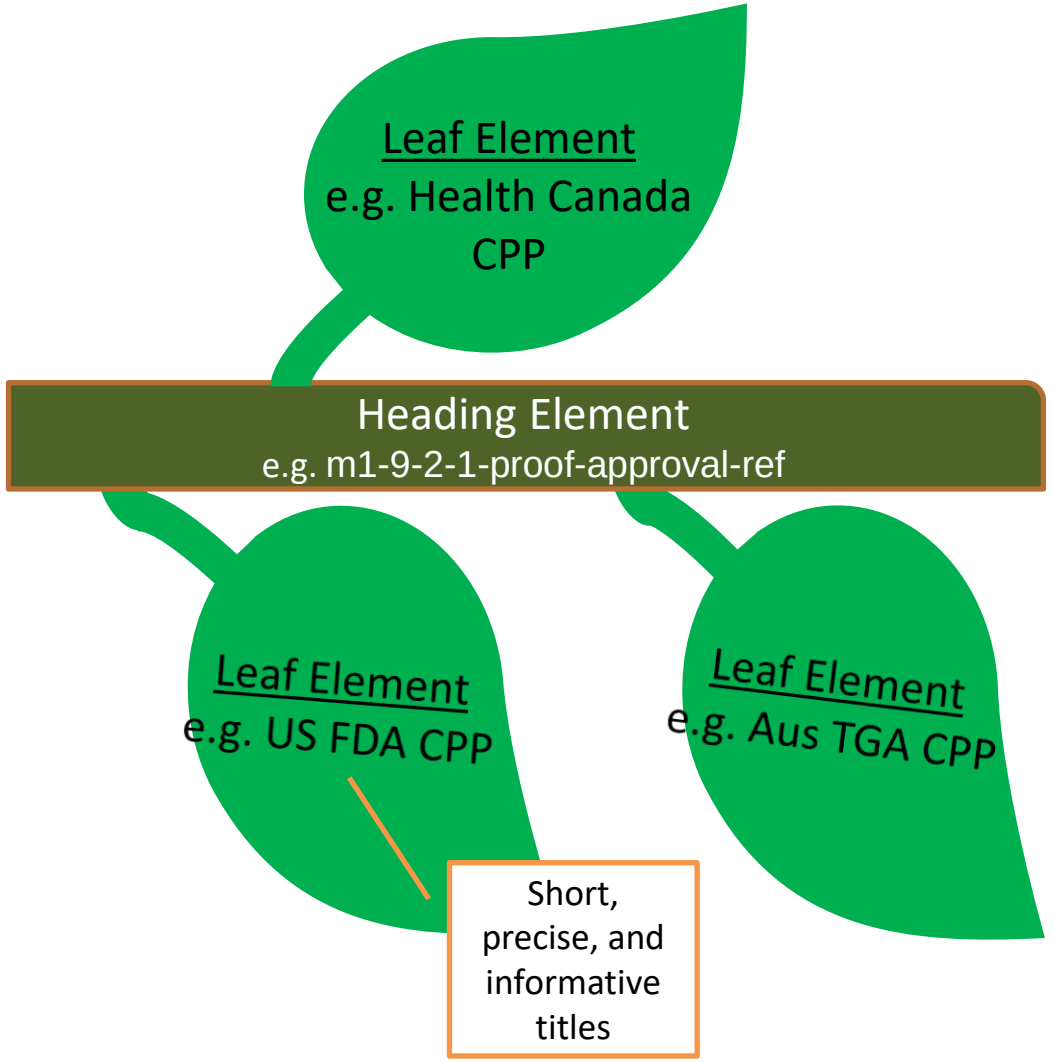
- Refer to the SG-HSA eCTD Specifications for more details

Note to Evaluator

- The Note to Evaluator allows Applicants to inform the HSA evaluator about specific points concerning the eCTD Submission/Sequence to facilitate an efficient review by the evaluator
- It may include, but is not limited to, the following:
  - Files referenced at multiple locations
  - Documents with relevance to more than one module
  - Hyperlink appearance and strategy
  - Particulars of module organisation
  - List of documents available on request

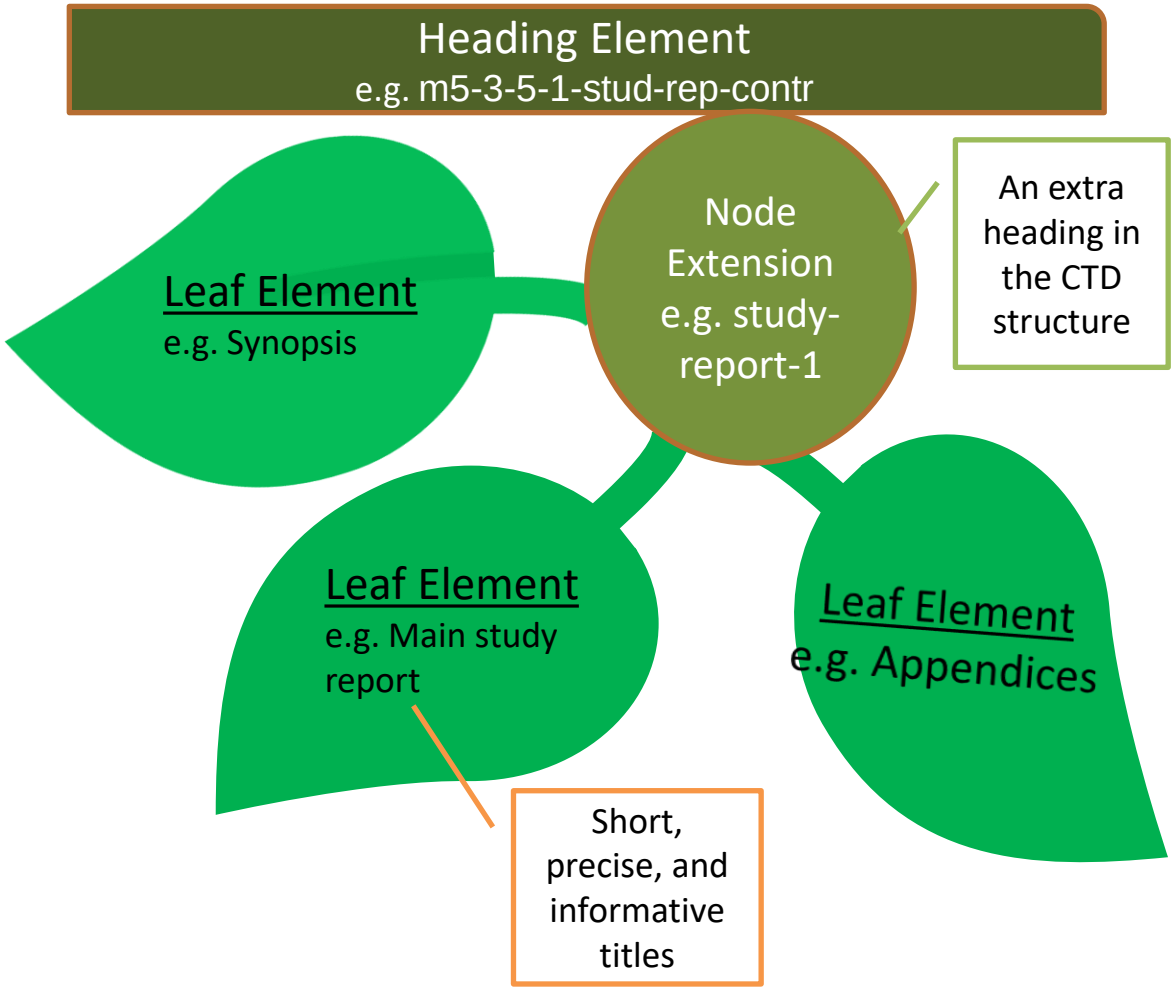
Heading Elements, Node Extensions and Leaf Titles

- Provide documents in the respective heading sections according to the granularity defined in the *Granularity Annex* for Module 1 and ICH M4 for the Modules 2-5



Heading Elements, Node Extensions and Leaf Titles

- Node extensions are additional heading structures beyond those defined by the specifications and are a way of providing additional information in the Sequence.
- Node extensions are required for all clinical studies and content provided in Module 5.3.



Envelope Elements

Section 4.3 of SG-HSA eCTD Specifications

- The Envelope comprises a list of key administrative information required by the receiving Authority to process the eCTD Application over time.

- **Sections:**
  - Application
  - Submission
  - Sequence
  - Contact details

- **Defined lists:**
  - Application Type
  - Product Type
  - Submission Type
  - Sequence Type
  - Contact Type

Envelope Elements

Element	Description	Constraint	Occurrence	Defined List*
sg-envelope	Root element for envelope meta-data			
application	Parent element for Application meta-data indicating Type	Mandatory	Single	X
application-uuid	Application Identifier	Mandatory	Single	
application-number	Application Number(s)	Mandatory	Unique	
uen	CorpPass UEN (Unique Entity Number)	Mandatory	Single	
inn	International Non-proprietary Names	Mandatory	Unique	
product-type	Product Type	Mandatory	Single	X
dmf-number	DMF Number	Optional	Unique	
pmf-number	PMF Number	Optional	Unique	
proprietary-name	Proprietary Name(s)	Mandatory	Unique	
sin-number	Singapore Registration Number	Optional	Unique	
submission	Parent element for Submission meta-data indicating Type	Mandatory	Unique	X
submission-number	Submission Number	Mandatory	Unique	
sequence	Parent element for Sequence meta-data indicating Type	Mandatory	Single	X
sequence-description	Sequence Description	Mandatory	Single	
sequence-date	Sequence Date of Submission	Mandatory	Single	
sequence-number	Sequence Number	Mandatory	Single	
related-sequence-number	Related Sequence Number	Mandatory	Single	
contact	Parent element for Contact meta-data indicating Type	Mandatory	Multiple	X
contact-name	Contact Name	Mandatory	Single	
contact-email	Contact Email	Mandatory	Single	
contact-phone	Contact Phone	Optional	Single	

Envelope Elements – Submission type

- NDA, GDA, MAV-1 and MIV-1 have separate types for the full/abridged and verification evaluation routes
- MIV-1s are also separated by the type of change (Clinical PI changes, CMC changes)
- Pharmacovigilance (PV) documents and documents to fulfil registration conditions can also be submitted in eCTD

List Code	List Value	Description
sub-type- 1	NDA	New Drug Application (NDA1, NDA2, NDA3), Full or Abridged route
sub-type-2	NDA-V	New Drug Application (NDA1, NDA2, NDA3), Verification route
sub-type-3	GDA	Generic Drug Application (GDA1, GDA2), Abridged route
sub-type-4	GDA-V/CECA	Generic Drug Application (GDA1, GDA2), Verification route
sub-type-5	MAV1	Major Variation-1, Full or Abridged route
sub-type-6	MAV1-V	Major Variation-1, Verification route
sub-type-7	MAV2	Major Variation-2, Abridged route
sub-type-8	MIV1-PI	Minor Variation-1, Clinical PI Changes
sub-type-9	MIV1-PI-V	Minor Variation-1, Clinical PI Changes, Verification route
sub-type-10	MIV1-CMC	Minor Variation-1, CMC Changes
sub-type-11	MIV1-CMC-V	Minor Variation-1, CMC Changes, Verification route
sub-type-12	MIV2-N	Minor Variation-2, Notification
sub-type-13	MIV2-DnT	Minor Variation-2, Do-and-Tell
sub-type-14	PV-EDU/RMP Materials-N	Pharmacovigilance - Admin updates to Educational/Risk Management Plan Materials (Notification)
sub-type-15	PV - PBRER/RMP Reports	Pharmacovigilance - Periodic Benefit-Risk Evaluation Report/Risk Management Plan Reports
sub-type-16	Reg Cond (non-PV)	Submissions to Fulfil Registration Conditions (Non-PV Related)
sub-type-17	DMF	Submission of new, updated Drug Master File, Letter of Access
sub-type-18	Baseline	Baseline Submission (not for initial launch)
sub-type-19	Application Withdrawal	Submission to Withdraw eCTD Application
sub-type-20	Transfer of Application	Submission to Update Change of Registrant (Transfer) in eCTD
sub-type-21	Other Regulatory Activity	Other Regulatory Activities

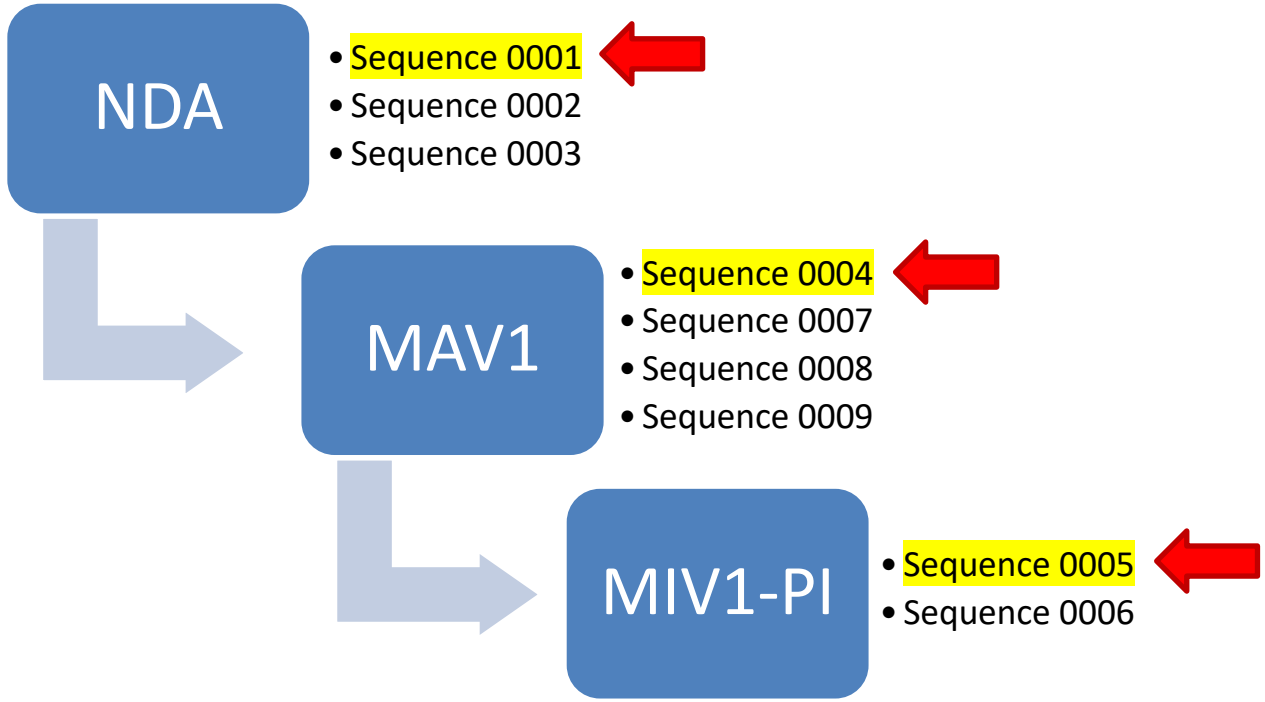
Envelope Elements – Sequence type

- Sequence type:
  - There are 5 sequence types:

List Code	List Value	Remarks
seq-type-1	Initial	The first sequence for a new eCTD Submission
seq-type-2	Supplementary Information	For providing additional information not under other sequence types
seq-type-3	Response	Responses to query letters issued by HSA
seq-type-4	Closing Information	Only for providing Module 1 information under “Approval Pending” or “Approved” situations. Following this sequence, other sequence types cannot be submitted within the same Submission, i.e. only Closing Information (seq-type-4) can be submitted
seq-type-5	Submission Withdrawal	For withdrawing the current Submission. For withdrawal of an eCTD Application, use Submission type: **sub-type-19** instead

Envelope Elements – Related Sequence Number

- Use the Related Sequence Number to group Sequences belonging to the same Submission
- Each Initial Sequence of a Submission will reference itself.
- Each follow-up Sequence of a Submission will reference the initial Sequence of that Submission.



Envelope Elements – Contact type

- Contact type:
  - There are 3 contact types for:
    - Regulatory personnel
    - eCTD technical personnel, and
    - Singapore local contact (mandatory)

List Code	List Value
contact-type-1	Regulatory
contact-type-2	Technical
contact-type-3	Agent Singapore

- The contacts listed in the envelope will be notified of the eCTD validation outcome
- The Singapore local contact stated in the envelope should preferably be the same as the PRISM applicant

Grouping Submissions in a Single Sequence

- The Singapore Envelope is designed to allow Applicants to designate multiple Submission Types in a single Submission, i.e. Work Grouping
  - e.g., MIV1-CMC + MIV2-N

- Refer to the *Submission Type Matrix* to see which Submission Types can be combined in a single Submission

Submission Type Matrix

Submission Type-Long	Submission Type-Short	NDA	NDA-V	GDA	GDA-V/CECA	MAV1	MAV1-V	MAV2	MIV1-PI	MIV1-PI-V	MIV1-CMC	MIV1-CMC-V	MIV2-N	MIV2-DnT	PV-EDU/RMP Materials-N	PV-PBRER/RMP Reports	Reg Cond (non-PV)	DMF	Baseline	Application Withdrawal	Transfer of Application	Other Regulatory Activity
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
New Drug Application (NDA1, NDA2, NDA3), Full or Abridged route	1																					
New Drug Application (NDA1, NDA2, NDA3), Verification route	2																					
Generic Drug Application (GDA1, GDA2), Abridged route	3																					
Generic Drug Application (GDA1, GDA2), Verification route	4																					
Major Variation-1, Full or Abridged route	5																					
Major Variation-1, Verification route	6																					
Major Variation-2, Abridged route	7																					
Minor Variation-1, Clinical PI Changes	8												12	13								
Minor Variation-1, Clinical PI Changes, Verification route	9												12	13								
Minor Variation-1, CMC Changes	10												12	13								
Minor Variation-1, CMC Changes, Verification route	11												12	13								
Minor Variation-2, Notification	12								8	9	10	11		13								
Minor Variation-2, Do-and-Tell	13								8	9	10	11	12									
Pharmacovigilance - Admin updates to Educational/Risk Management Plan Materials (Notification)	14																					
Pharmacovigilance - Periodic Benefit-Risk Evaluation Report/Risk Management Plan Reports	15																					
Submissions to Fulfil Registration Conditions (Non-PV Related)	16																					
Submission of new, updated Drug Master File, Letter of Access	17																					
Baseline Submission	18																					
Submission to Withdraw eCTD Application	19																					
Submission to Update Change of Registrant (Transfer) in eCTD	20																					
Other Regulatory Activities	21																					

Grouping Submissions in a Single Sequence

- Work Grouping also means that the results of each Submission evaluation must be the same
  - i.e., all Submissions are approved or all Submissions are Withdrawn/Rejected
- Work Grouping can lead to issues when one of the Submissions combined in the Work Grouping is Withdrawn or Rejected

- Refer to the *SG-HSA Specifications* for information on the steps when different outcomes are reached during Work Grouping.

Grouping Submissions in a Single Sequence

Example:

Applicant submits an MIV-1 application in PRISM (PRISM application number: 2212378K) which includes 2 changes normally categorised as MIV-1 and MIV-2 changes.

Applicant should indicate both Submission Types in the envelope:

Submission Type	**sub-type-10** (MIV1-CMC for Addition of drug substance manufacturer without CEP – MIV checklist B1) **sub-type-12** (MIV2-N for Change of specification of non-compendial drug substance– MIV checklist C6)
Submission Number	2212378K
Sequence Description	Chemical, MIV checklist B1, C6

Grouping Submissions in a Single Sequence

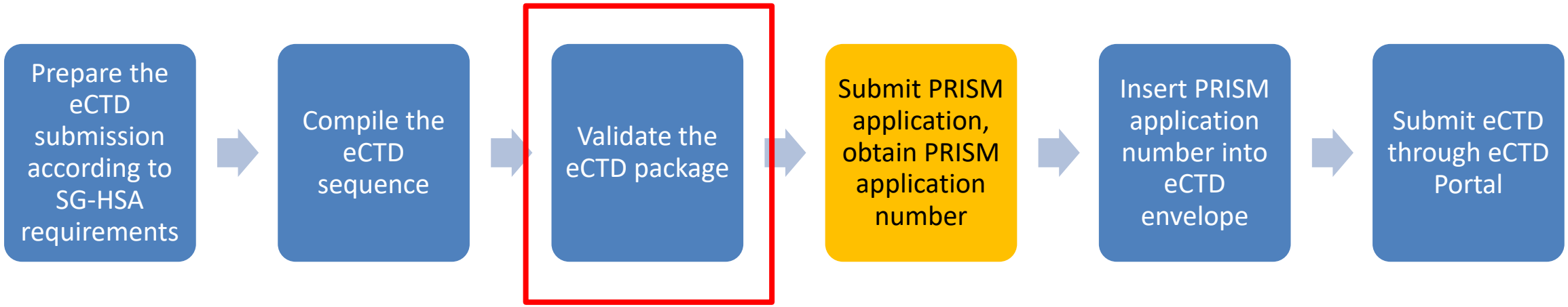
- For multiple submissions of the same Submission Type, do not replicate the Submission Type.

Example:

Applicant submits a single MIV-2 application in PRISM (PRISM application number: 2223792R) containing 2 MIV-2 changes.

Applicant should indicate 1 Submission Type in the envelope:

Submission Type	**sub-type-13** (MIV2-DnT for PI administrative update and change of outer carton pack sizes – MIV checklist D13, D15)
Submission Number	2223792R
Sequence Description	Biologic, MIV checklist D13, D15



VALIDATING THE ECTD SEQUENCE

Validating Your eCTD Sequence

- The Sequence must be validated in order to pass the e-Validation step
- The validation software that is used should be able to validate using the *SG-HSA eCTD Validation Criteria* and *SG-HSA eCTD Regional Criteria (Document Matrix, Submission Type Matrix, Granularity Annex)*.
- eCTD validation findings
  - **ERROR** – Critical Pass/Fail finding ⟹ Rejection
  - **WARNING** – Best Practice violations ⟹ Address Warnings in the Cover Letter
  - **INFO** – Information collected about the data being submitted
- Sequences with errors will need to be corrected and resubmitted under the same Sequence Number.

*HSA does not endorse, recommend or mandate any specific eCTD validation tool

SG-HSA eCTD Validation Criteria

- Structure:
  1. eCTD XML Identification
  2. Files/Folders
  3. ICH Backbone
     - 3.1 The index.xml
     - 3.2 MD5 Checksum
     - 3.3 References
     - 3.4 Heading Elements, Leaves and Node Extensions
     - 3.5 Life Cycle Management
     - 3.6 File Existence
  4. Singapore Regional
     - 4.1 The regional.xml
     - 4.2 MD5 Checksum
     - 4.3 References
     - 4.4 Headings, Elements, Leaves and Node Extensions
     - 4.5 Life Cycle Management
     - 4.6 File Existence
     - 4.7 Envelope
     - 4.8 Content
  5. STF
  6. PDF Analysis
     - 6.1 PDF Readability
     - 6.2 Bookmarks
     - 6.3 Hyperlinks
     - 6.4 PDF Properties

: Singapore-specific content, please note

Document Matrix

- Refer to the *Document Matrix* for the submission rules for documents submitted under each Submission Type

Section	Section Title	NDA	NDA-V	GDA	GDA-V/CECA	MAV1	MAV1-V	MAV2	MIV1-PI	MIV1-PI-V	MIV1-CMC	MIV1-CMC-V	MIV2-N	MIV2-DnT	PV-EDU/RMP Materials-N	PV-PBRER/RMP Reports	Reg Cond (non-PV)	DMF	Baseline	Application Withdrawal	Transfer of Application	Other Regulatory Activity
1	Module 1 Administrative and Prescribing Information																					
1.0	Correspondence																					
1.0.1	Cover Letter	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E
1.0.2	Note to Evaluator	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
1.0.3	Correspondence with HSA	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
1.0.4	Response to Input Request	NV	NV	NV	NV	NV	NV	NV	NV	NV	NV	NV	NV	NV	NV	NV	NV	NV	XE	NV	XE	NV
1.0.5	Meeting Information	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P

Empty or Missing eCTD Sections

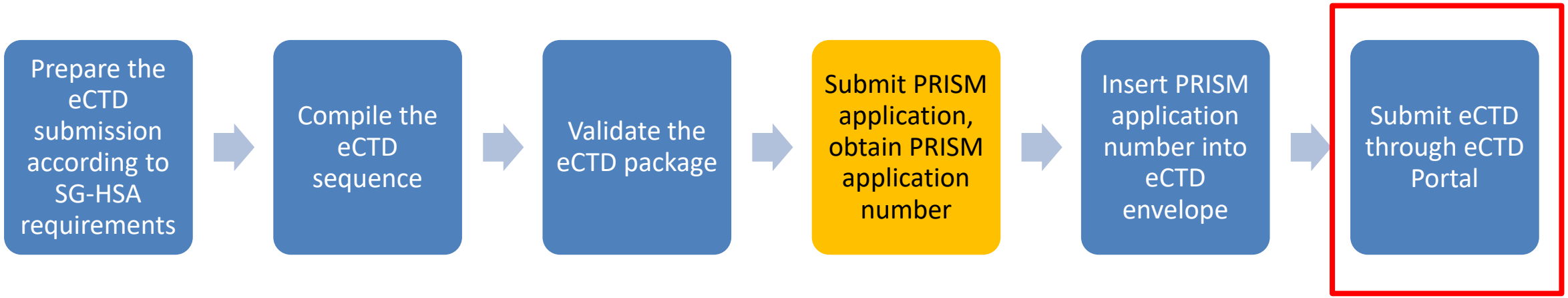
- For content marked W (warning) or P (Possible) provide detailed statements in the Cover Letter justifying the absence of expected data or specific CTD sections

- Do not submit information for content marked XE

- Placeholder documents with no substantive content should not be provided

Preparing an eCTD Submission

- HSA does not endorse, recommend or mandate any software to prepare an eCTD Submission
- We recommend Applicants to:
  - Prepare the eCTD using an authenticated commercial eCTD preparation tool
  - Find a solution which supports current and ongoing SG-HSA eCTD requirements and meets your overall business needs
  - Validate the prepared Sequences using an authenticated commercial eCTD validation tool

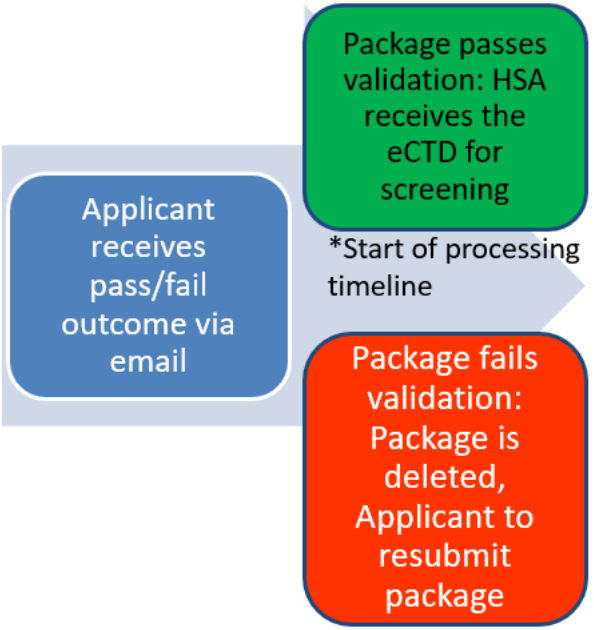


SUBMITTING THE ECTD PACKAGE

Submitting Your eCTD Sequence

- Sequences are to be submitted via the Portal and validated by the e-Validator

- If there are any errors during the validation of the eCTD Sequence, the Applicant will be notified using the contact details provided in the envelope



- If a sequence passes validation with no errors, it will be received and reviewed as part of HSA's screening and/or evaluation process (start of processing timeline)

- Any content deficiencies discovered during the screening and evaluation process will need to be addressed in a follow-up Sequence as part of the Application life cycle

Authentication and Authorization (Log in with Corppass)

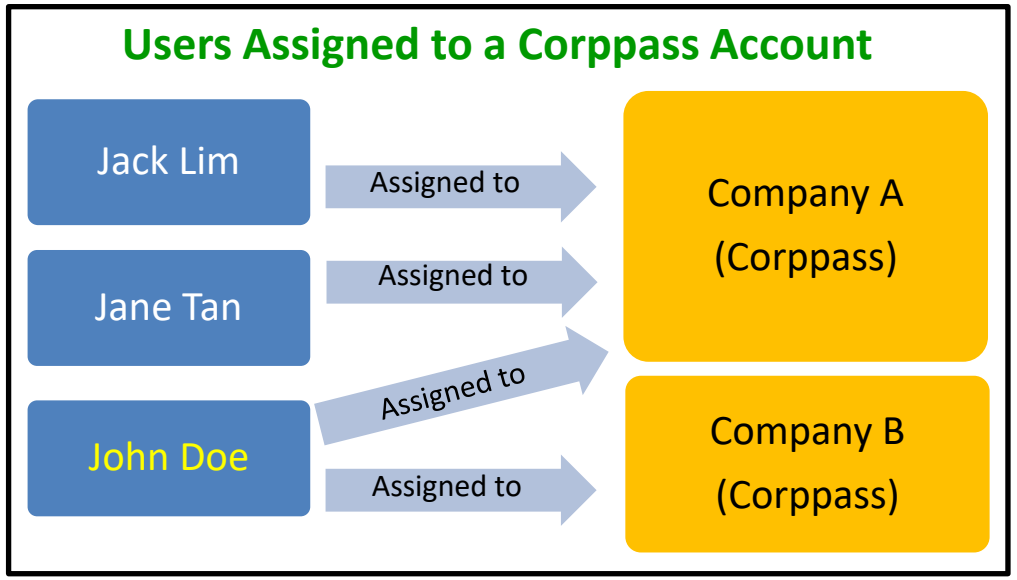
- Company must have Corppass account.
- Company must register for the Portal eService.

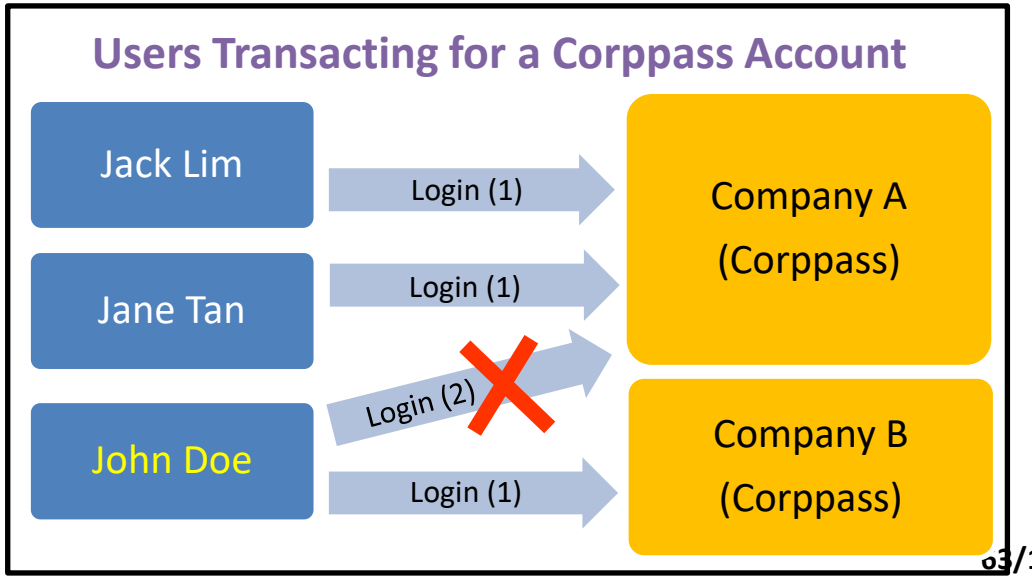
Foreign companies (e.g., DMF holders) submitting eCTD to HSA will require a Corppass account to access the eCTD Portal

1. Submit the request via www.corppass.gov.sg (Services > Register for Corppass > Foreign Entity)
2. Once Approved, a Singpass account for the Corppass Admin of the foreign entity will be created:
   a) Email with onboarding instructions will be sent to the foreign user
   b) Foreign user will onboard by registering with userid/password and SP App.
   c) Once onboarded, the CP Admin will need to activate the CP Admin account in CP Portal
   d) CP Admin can then create and authorise more CP users from the foreign company
3. Once authorised, Foreign CP Admin or CP users can then access the respective CP eservices.

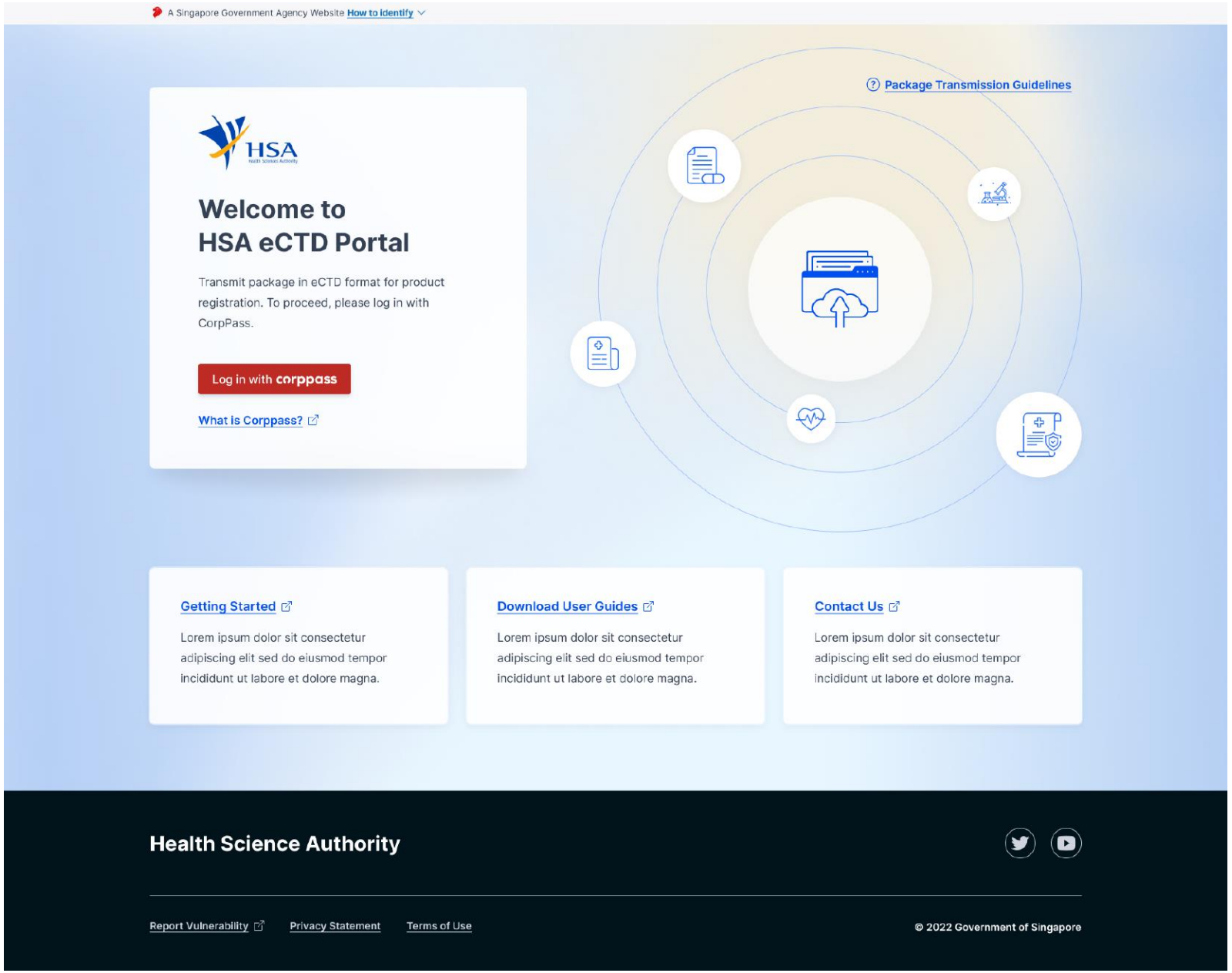
Portal View

- **Company** can assign multiple users to their Corppass account.
- Multiple users for the **Company** can transmit concurrently.
- A **User** can submit more than one transmission. However, each transmission can only be initiated once the previous transmission has completed.
- A **User** can be assigned to multiple Corppass accounts (different companies). However, during any session, the activity is limited to a specific Corppass account.



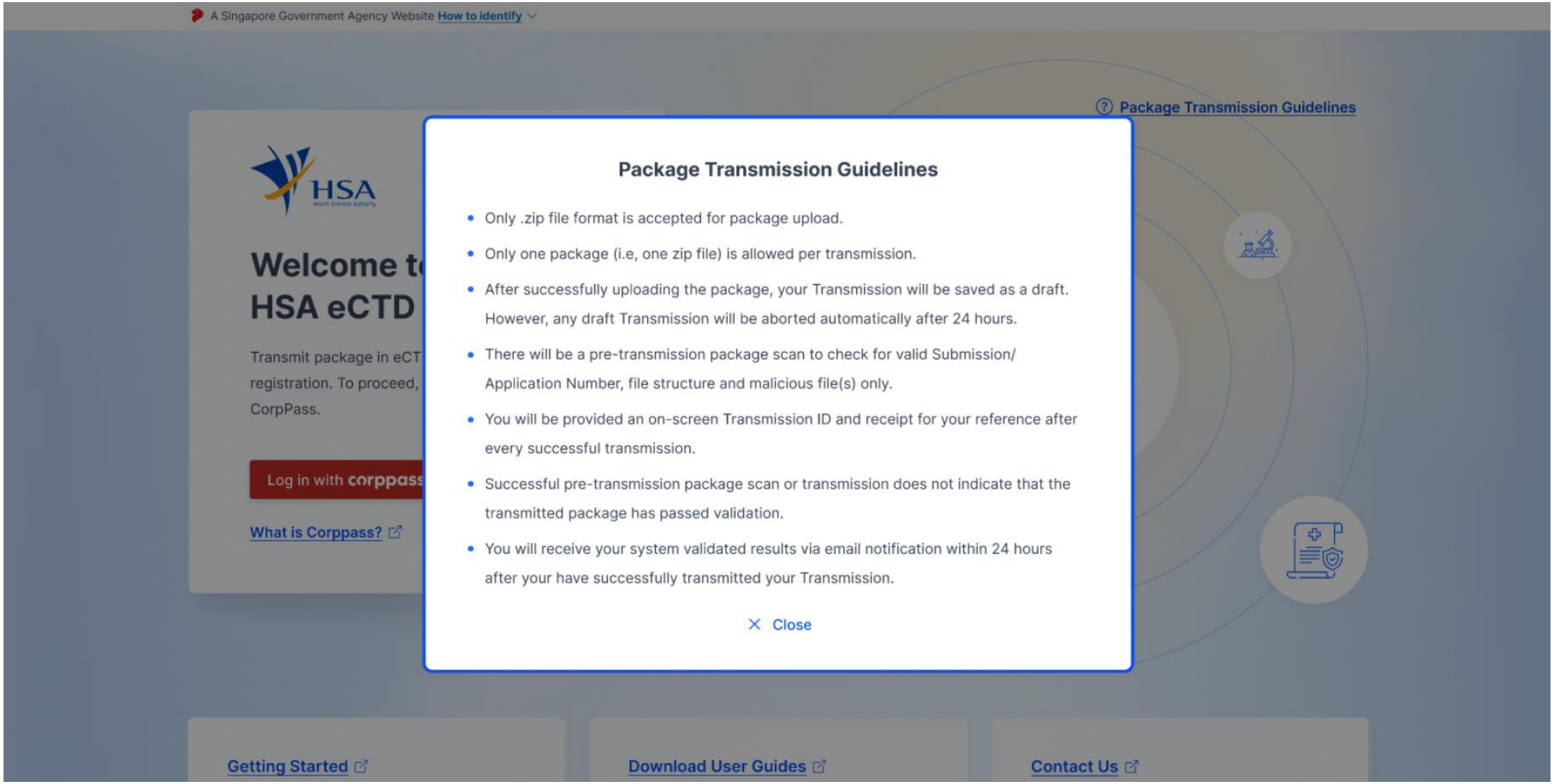


Portal View - Homepage



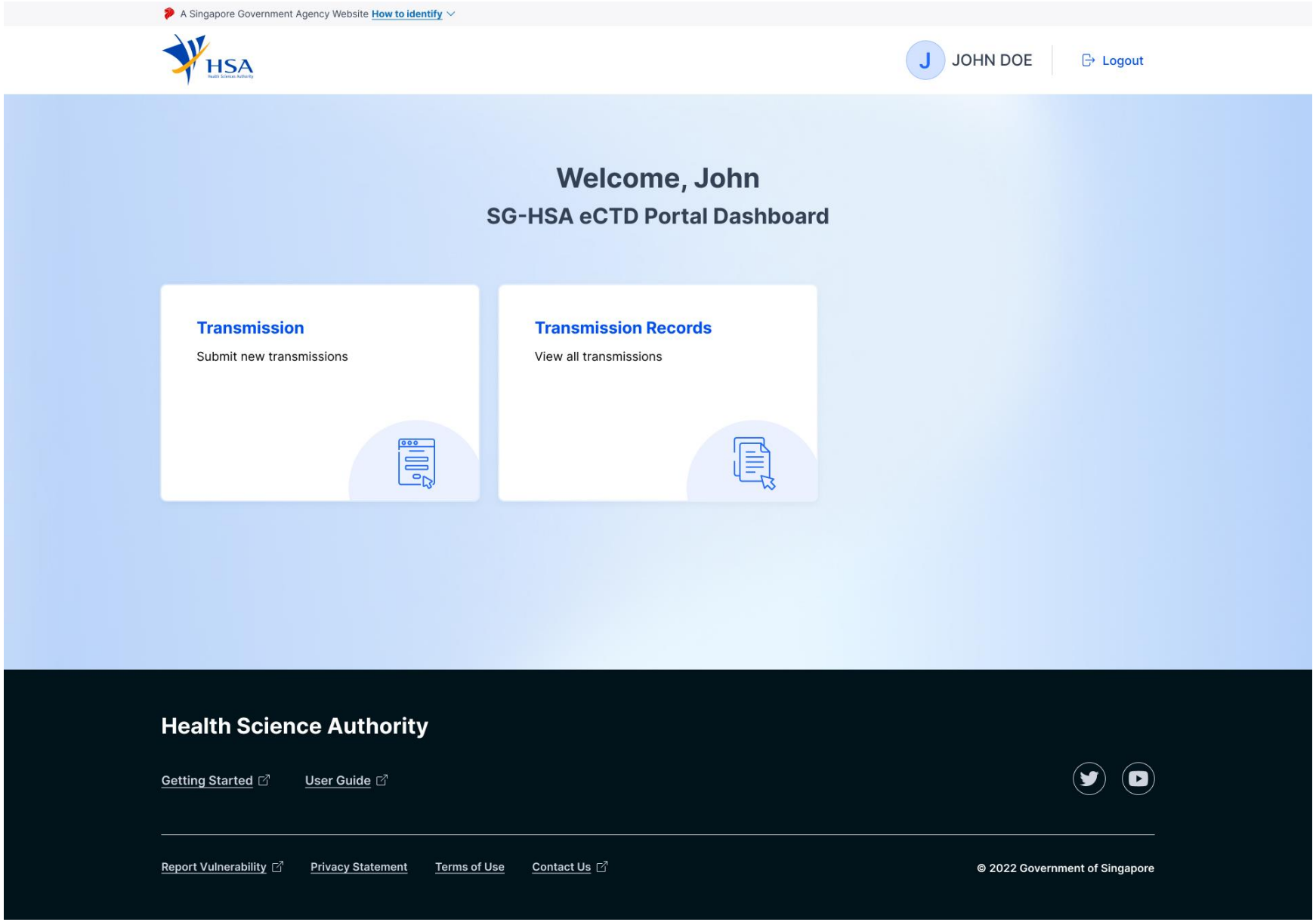
Please note that the portal mockups shown are currently work in progress and may be subject to changes.

Portal View - Homepage



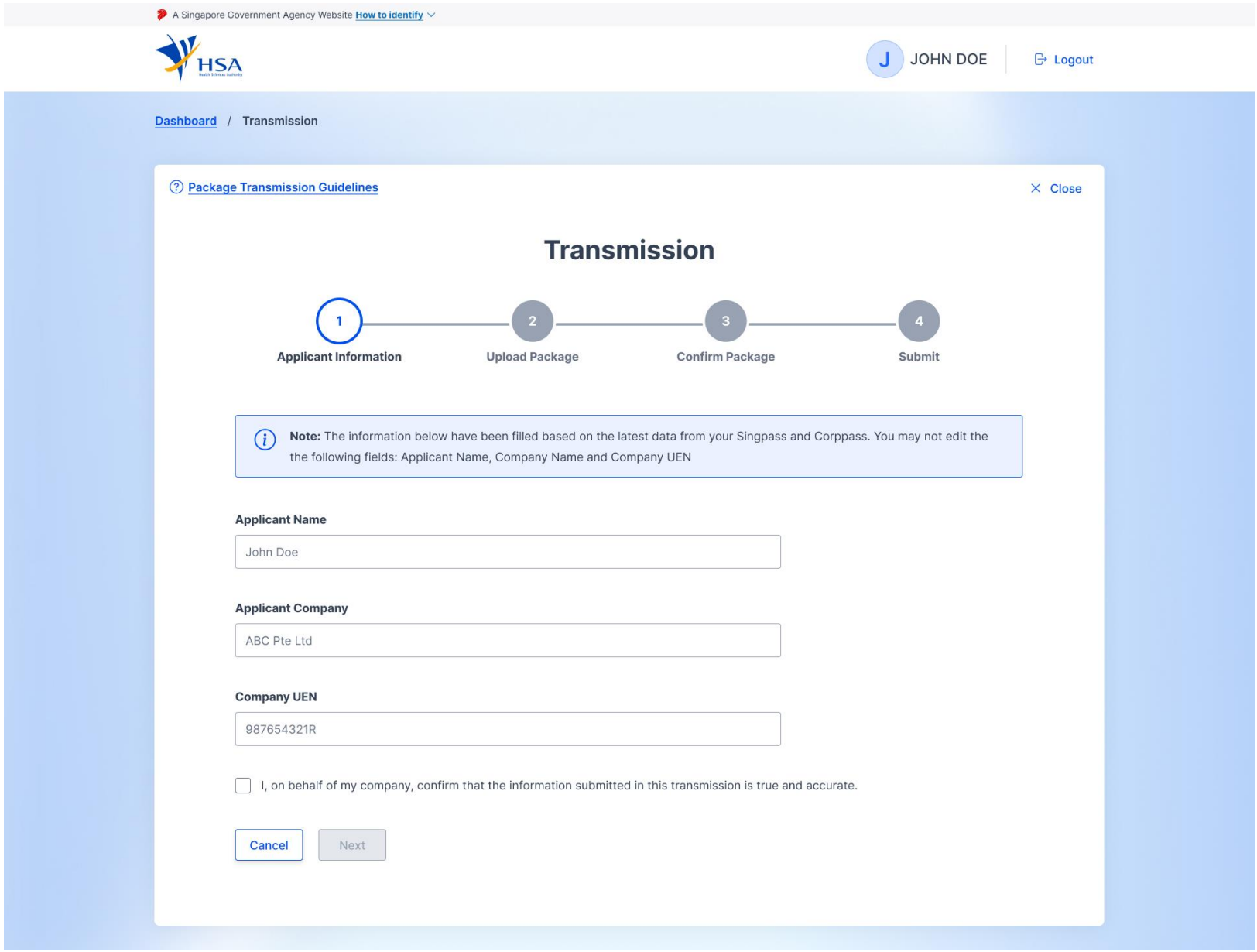
Please note that the portal mockups shown are currently work in progress and may be subject to changes.

Portal View – Dashboard



Please note that the portal mockups shown are currently work in progress and may be subject to changes.

Portal View – Transmission Step 1



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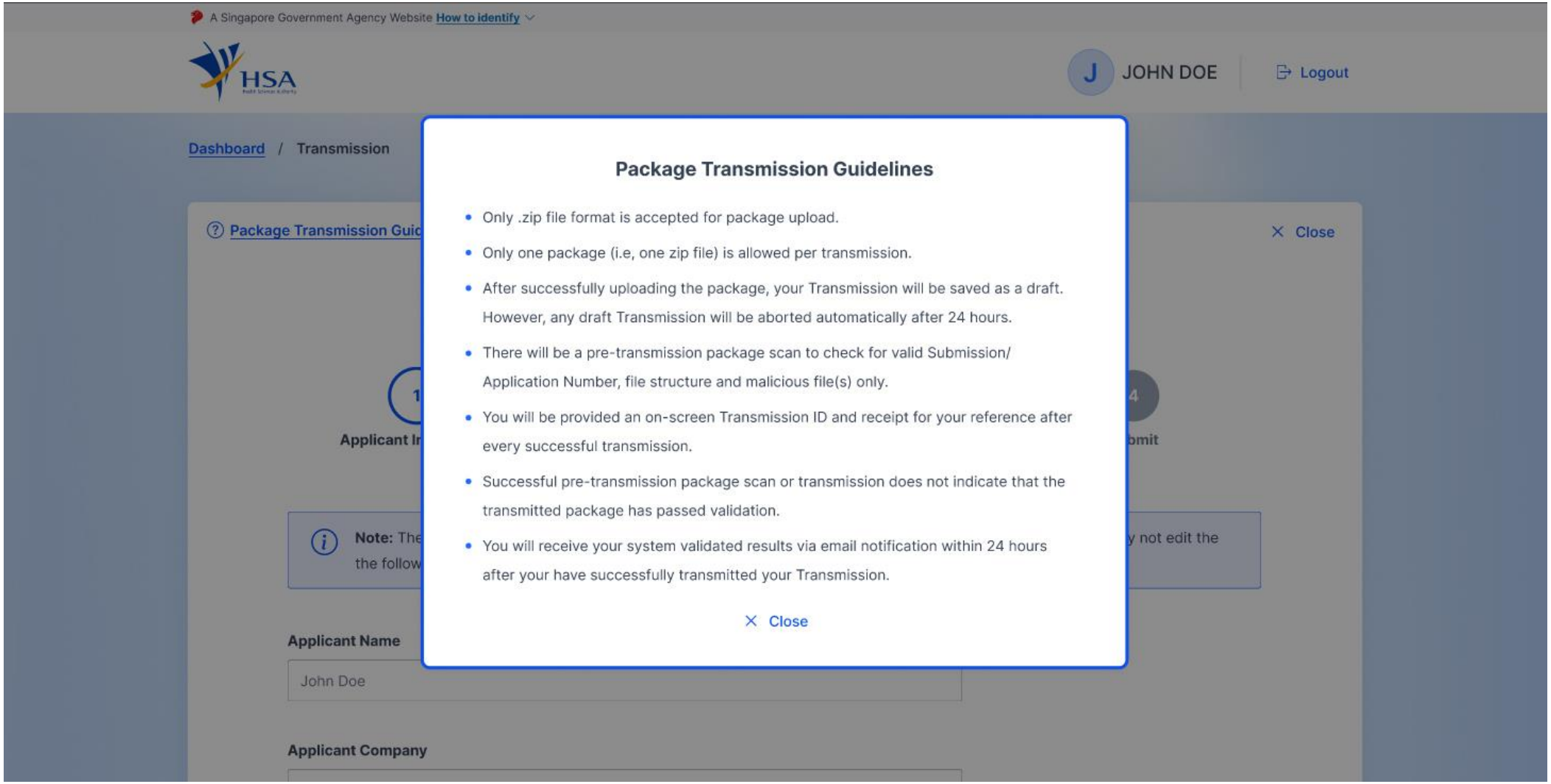
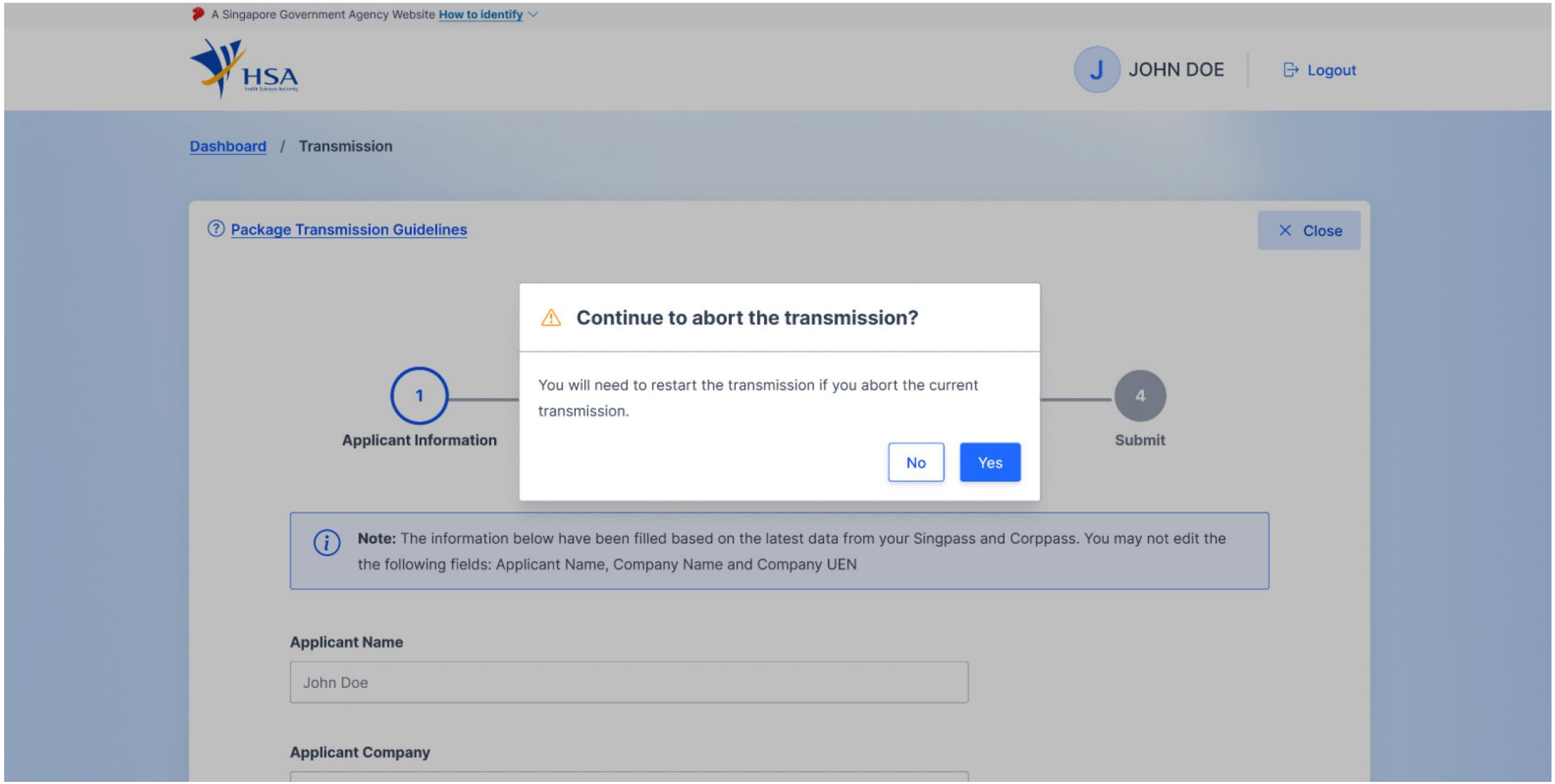
Portal View – Transmission Step 1



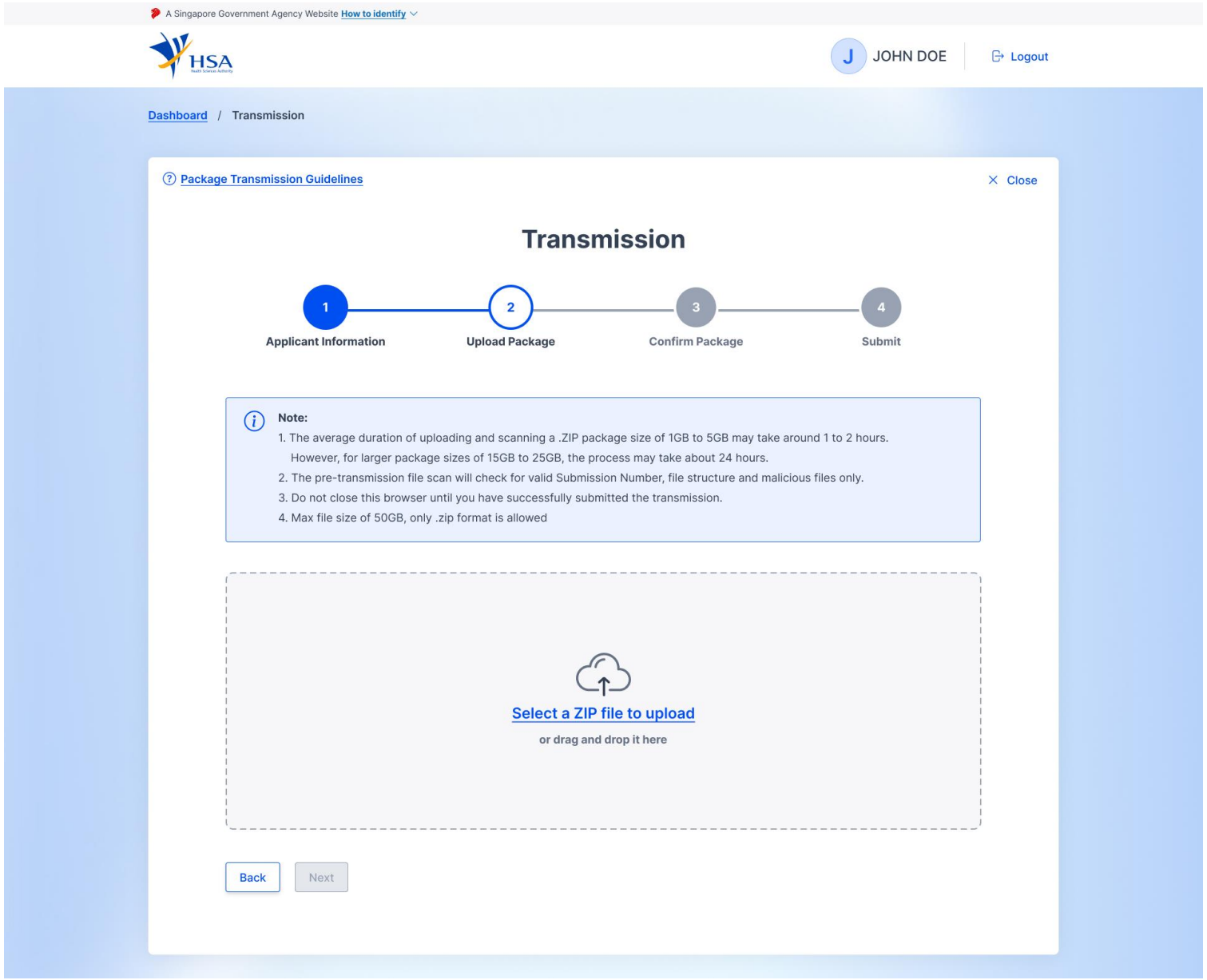
Please note that the portal mockups shown are currently work in progress and may be subject to changes.

Portal View – Transmission Step 1



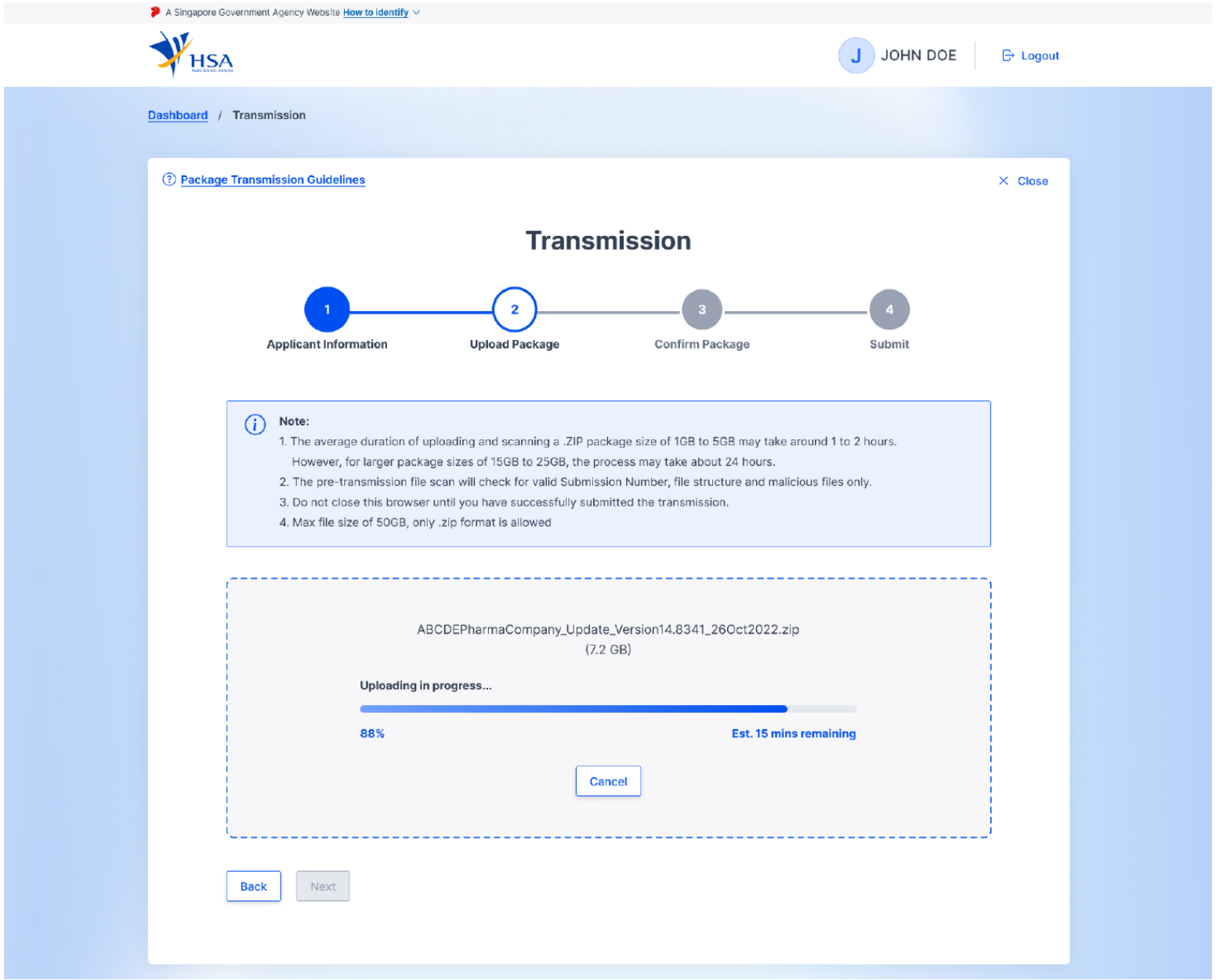
Please note that the portal mockups shown are currently work in progress and may be subject to changes.

Portal View – Transmission Step 2 (Select Package)



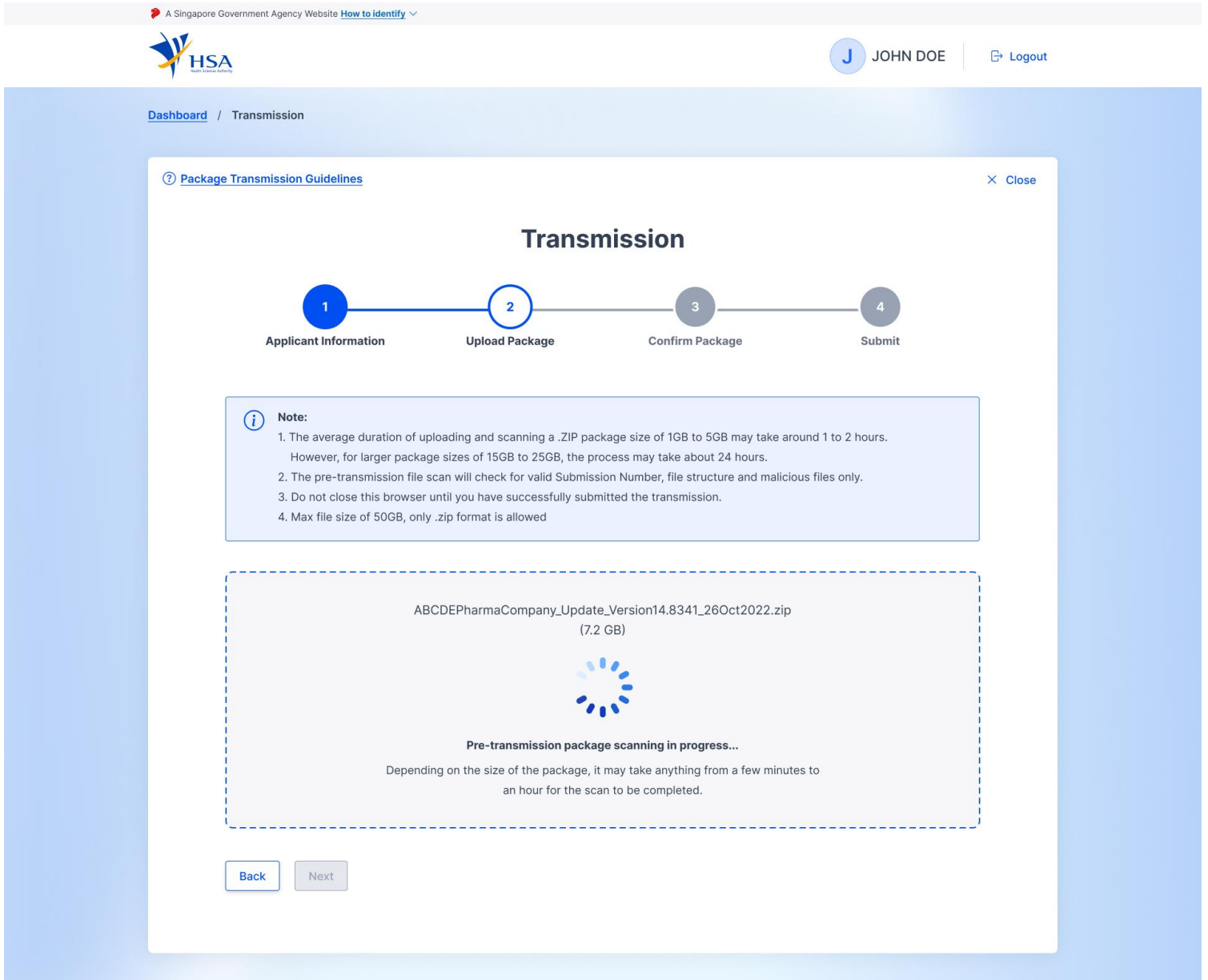
Please note that the portal mockups shown are currently work in progress and may be subject to changes.

Portal View – Transmission Step 2 (Upload Package)



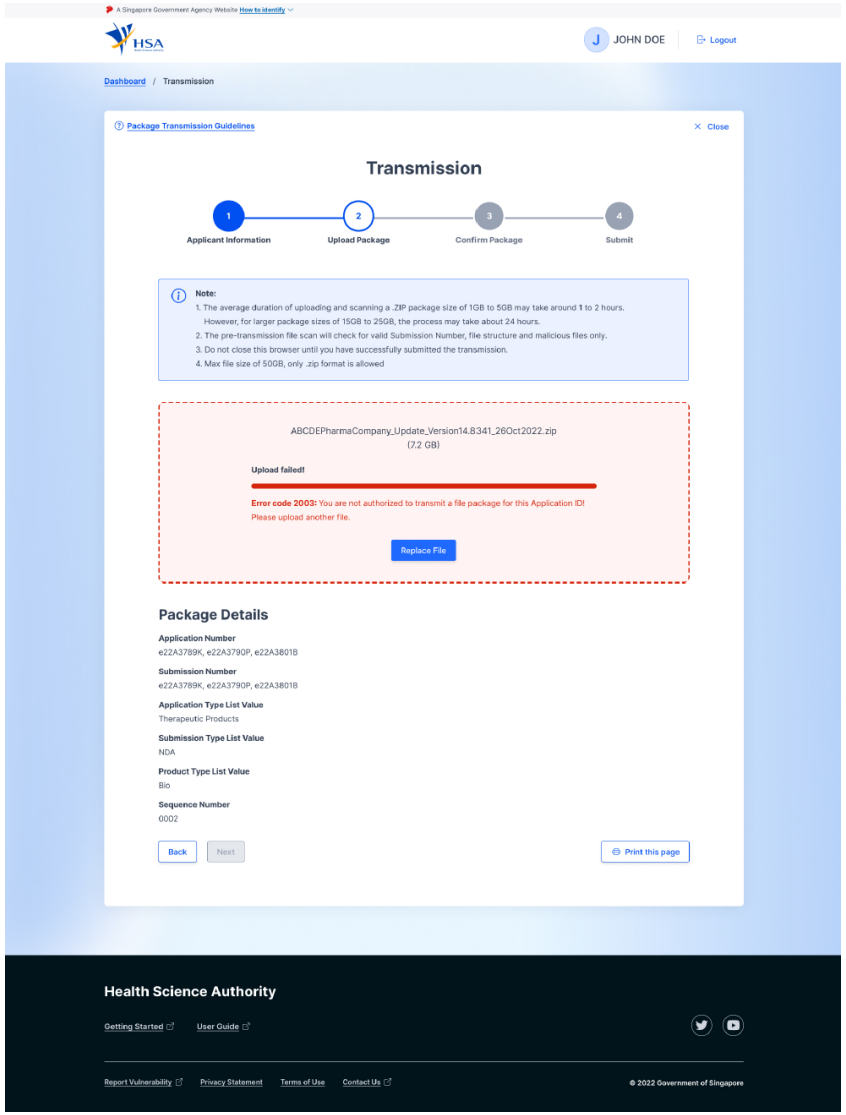
Please note that the portal mockups shown are currently work in progress and may be subject to changes.

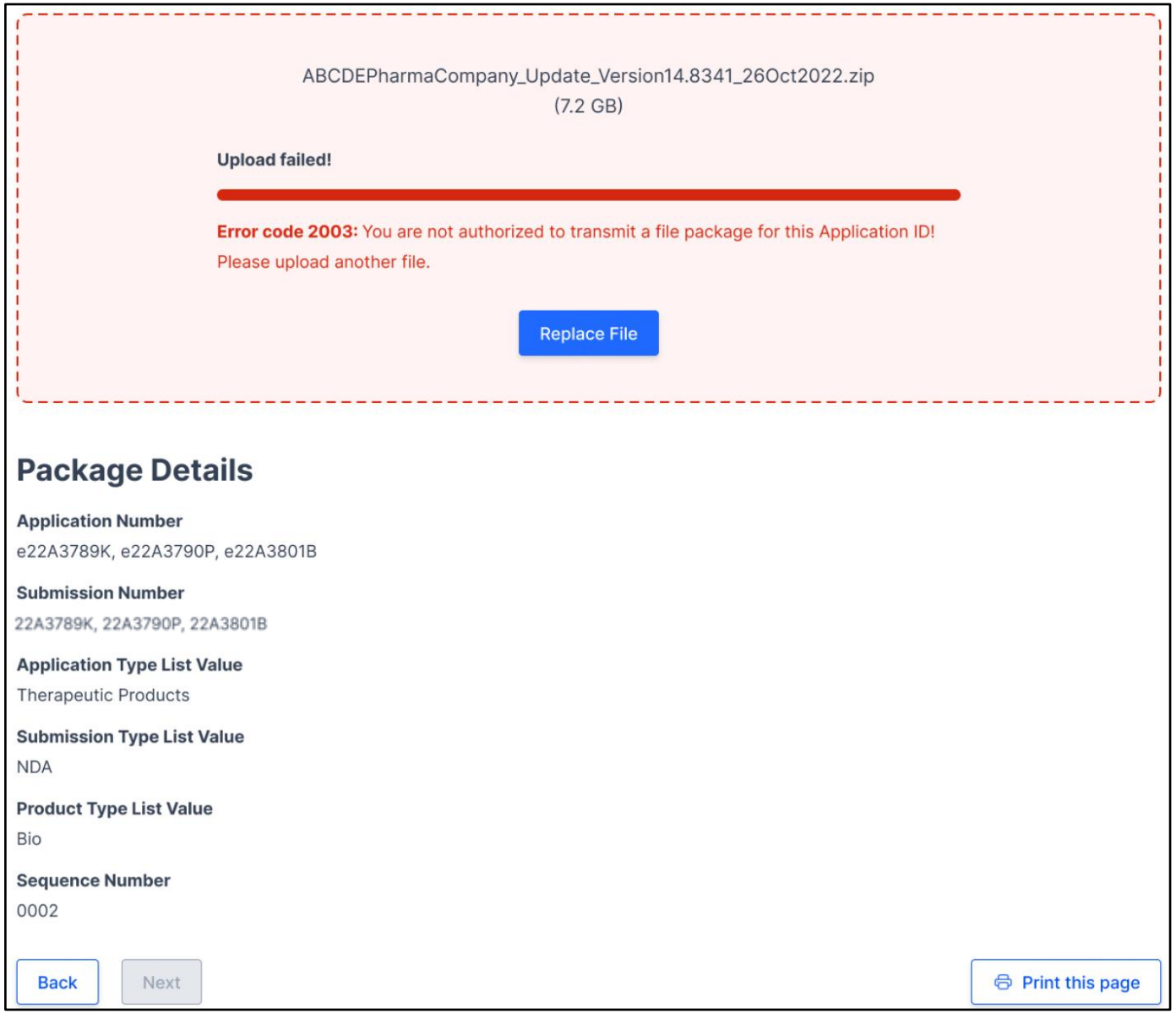
Portal View – Transmission Step 2 (Scan Package)



Please note that the portal mockups shown are currently work in progress and may be subject to changes.

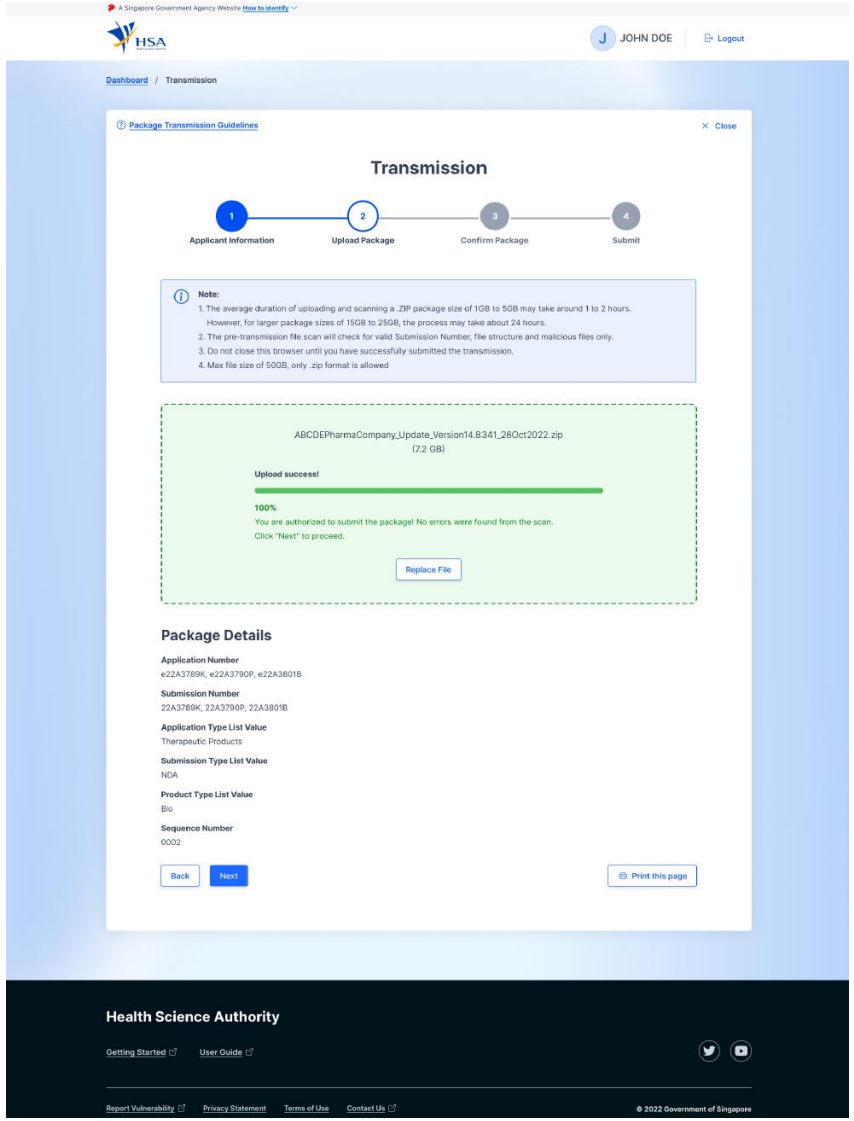
Portal View – Transmission Step 2 (Upload Package Failed)

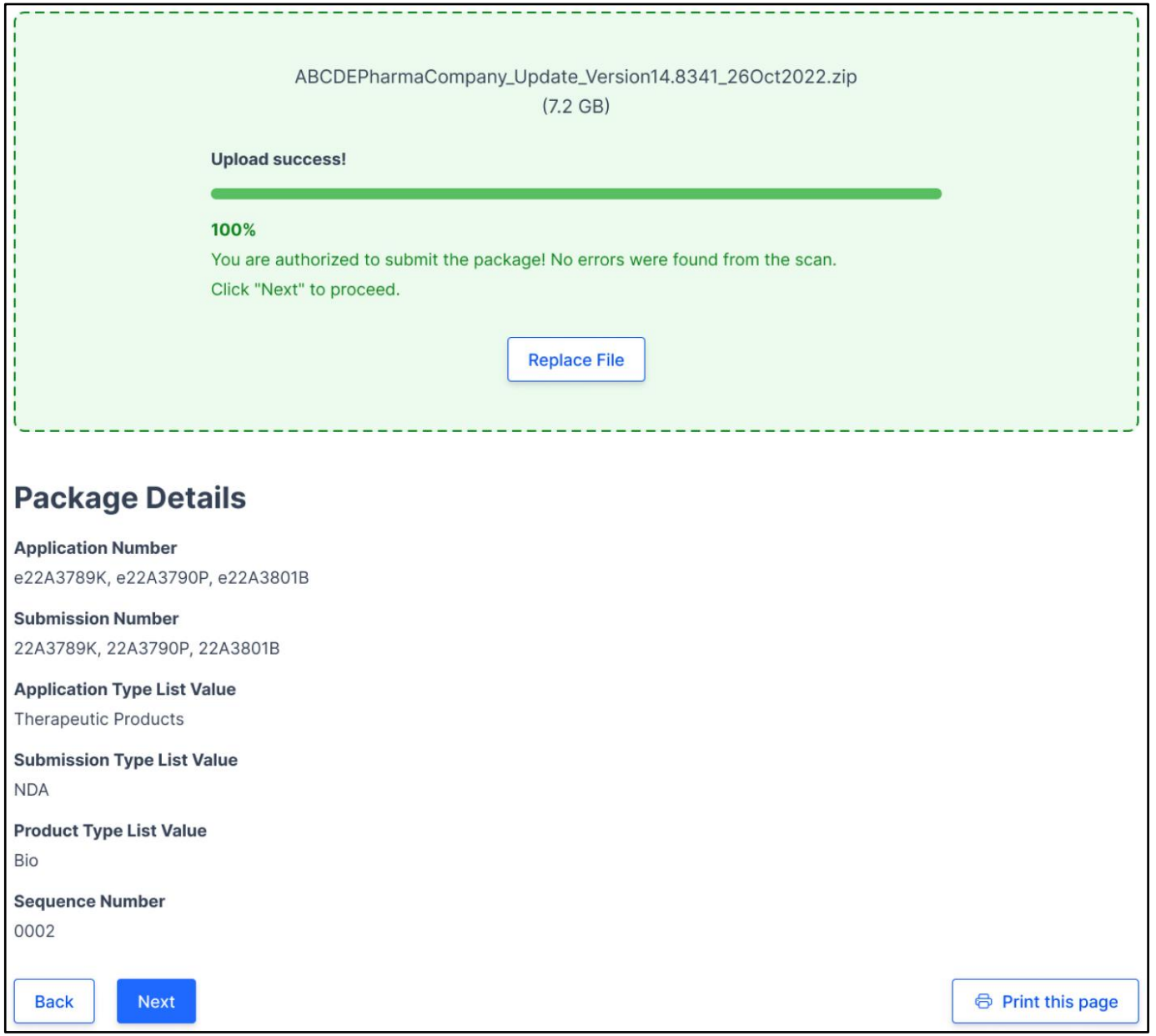




Please note that the portal mockups shown are currently work in progress and may be subject to changes.

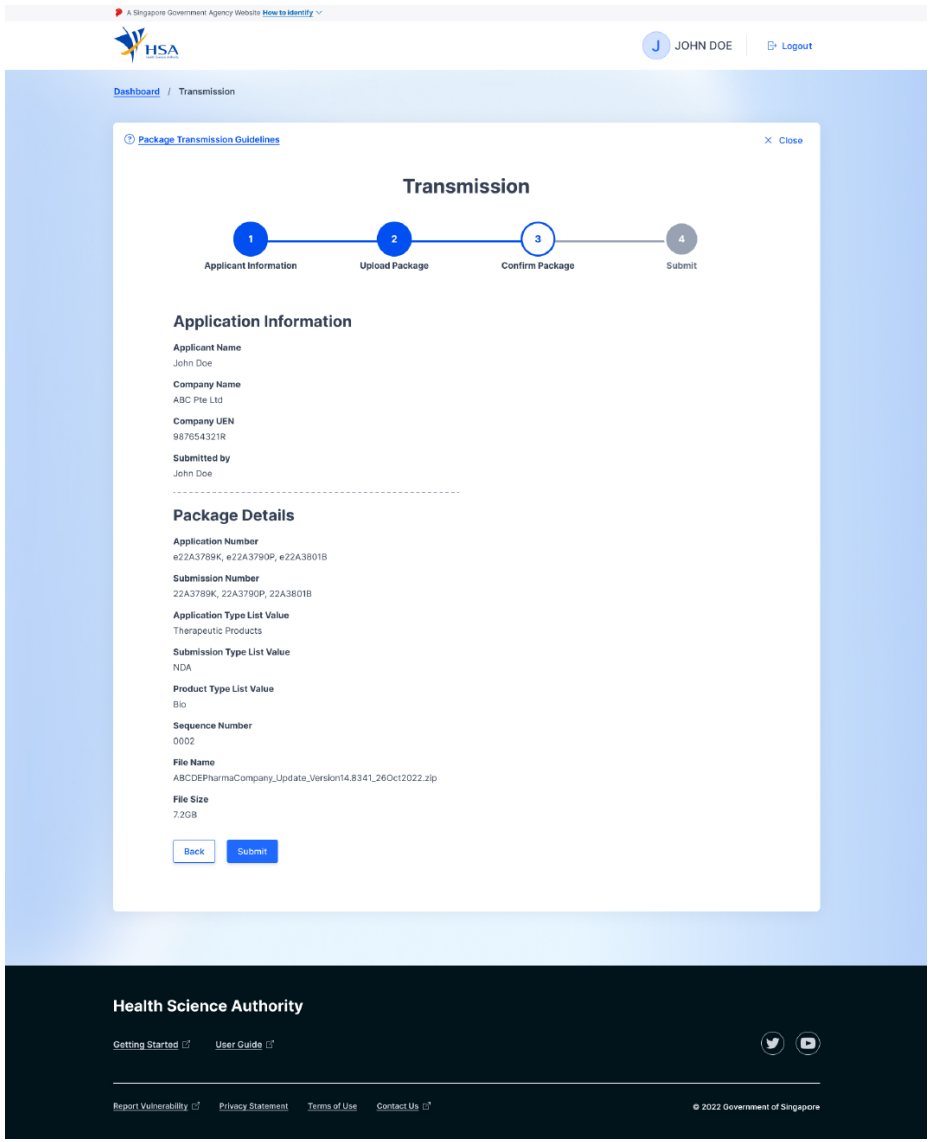
Portal View – Transmission Step 2 (Upload Package Success)

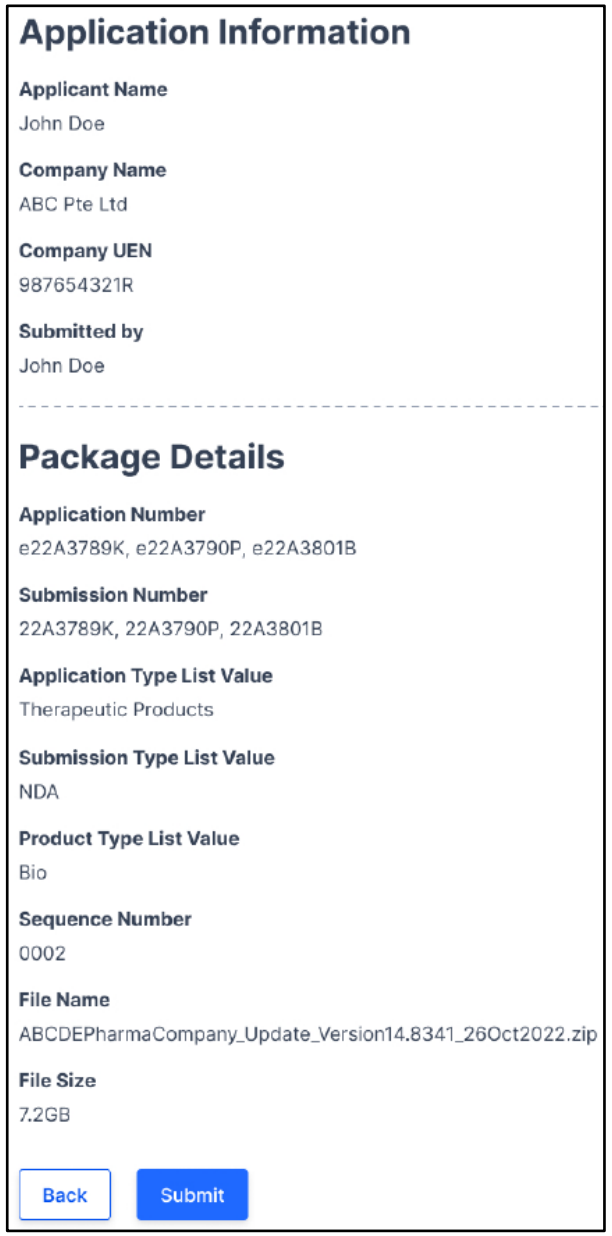




Please note that the portal mockups shown are currently work in progress and may be subject to changes.

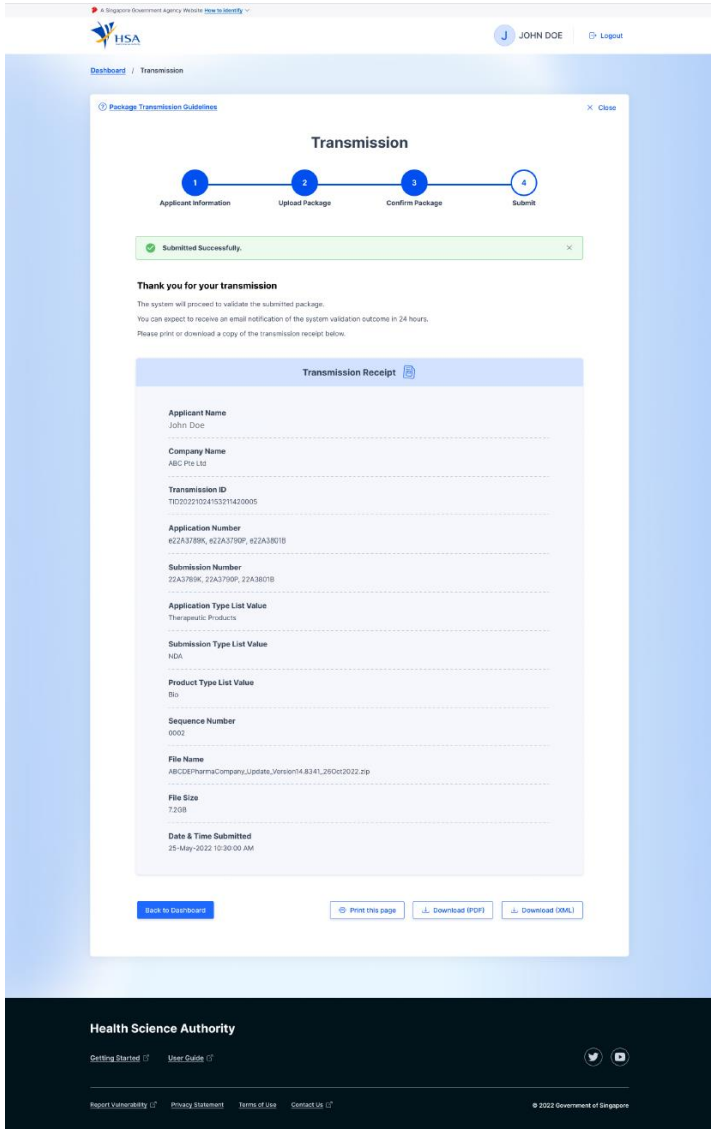
Portal View – Transmission Step 3 (Confirm Package)





Please note that the portal mockups shown are currently work in progress and may be subject to changes.

Portal View – Transmission Step 4 (Submit)



Thank you for your transmission

The system will proceed to validate the submitted package.

You can expect to receive an email notification of the system validation outcome in 24 hours.

Please print or download a copy of the transmission receipt below.

Transmission Receipt

Applicant Name
John Doe

Company Name
ABC Pte Ltd

Transmission ID
TID20221024153211420005

Application Number
e22A3789K, e22A3790P, e22A3801B

Submission Number
22A3789K, 22A3790P, 22A3801B

Application Type List Value
Therapeutic Products

Submission Type List Value
NDA

Product Type List Value
Bio

Sequence Number
0002

File Name
ABCDEPharmaCompany_Update_Version14.8341_26Oct2022.zip

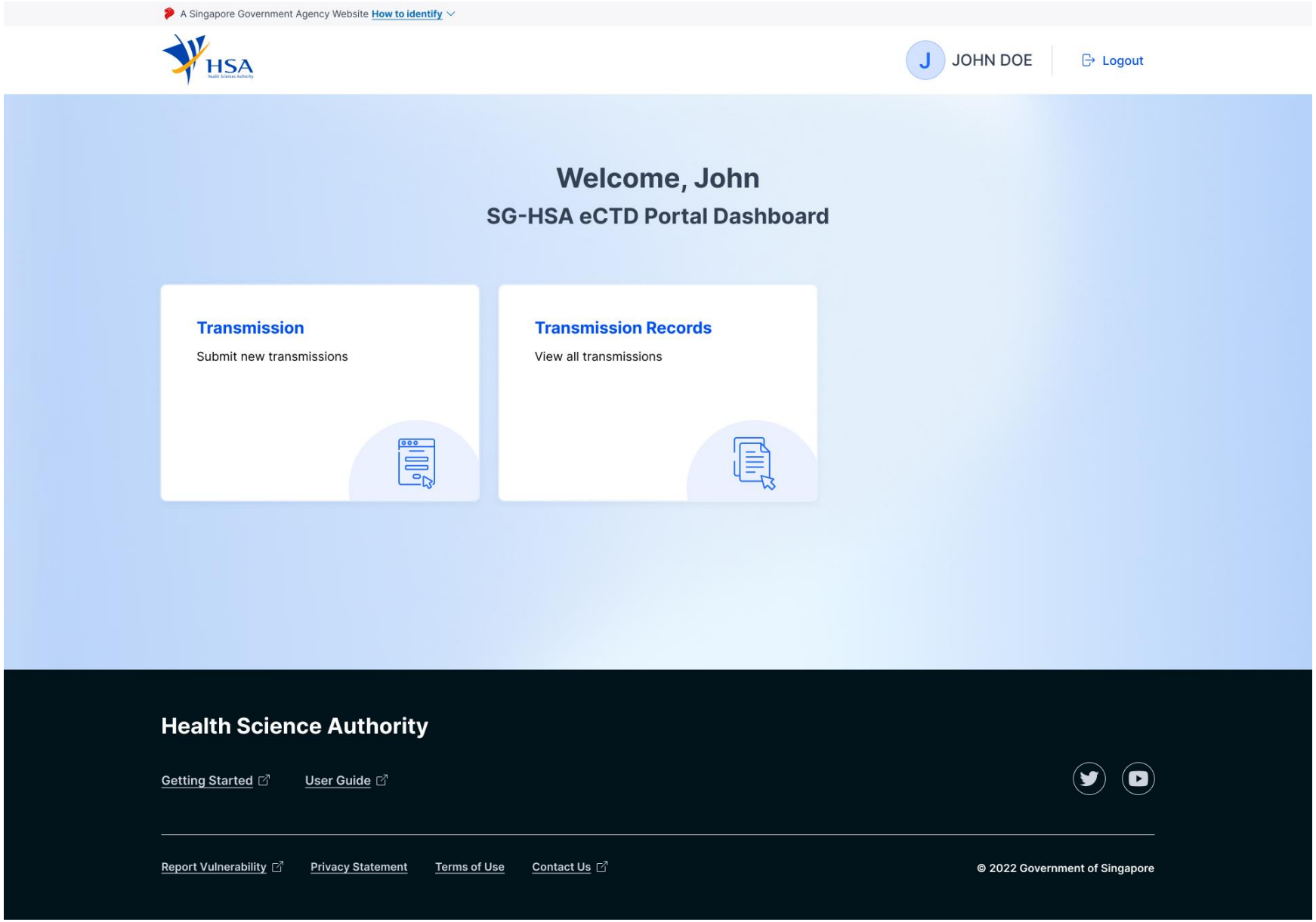
File Size
7.2GB

Date & Time Submitted
25-May-2022 10:30:00 AM

Back to Dashboard | Print this page | Download (PDF) | Download (XML)

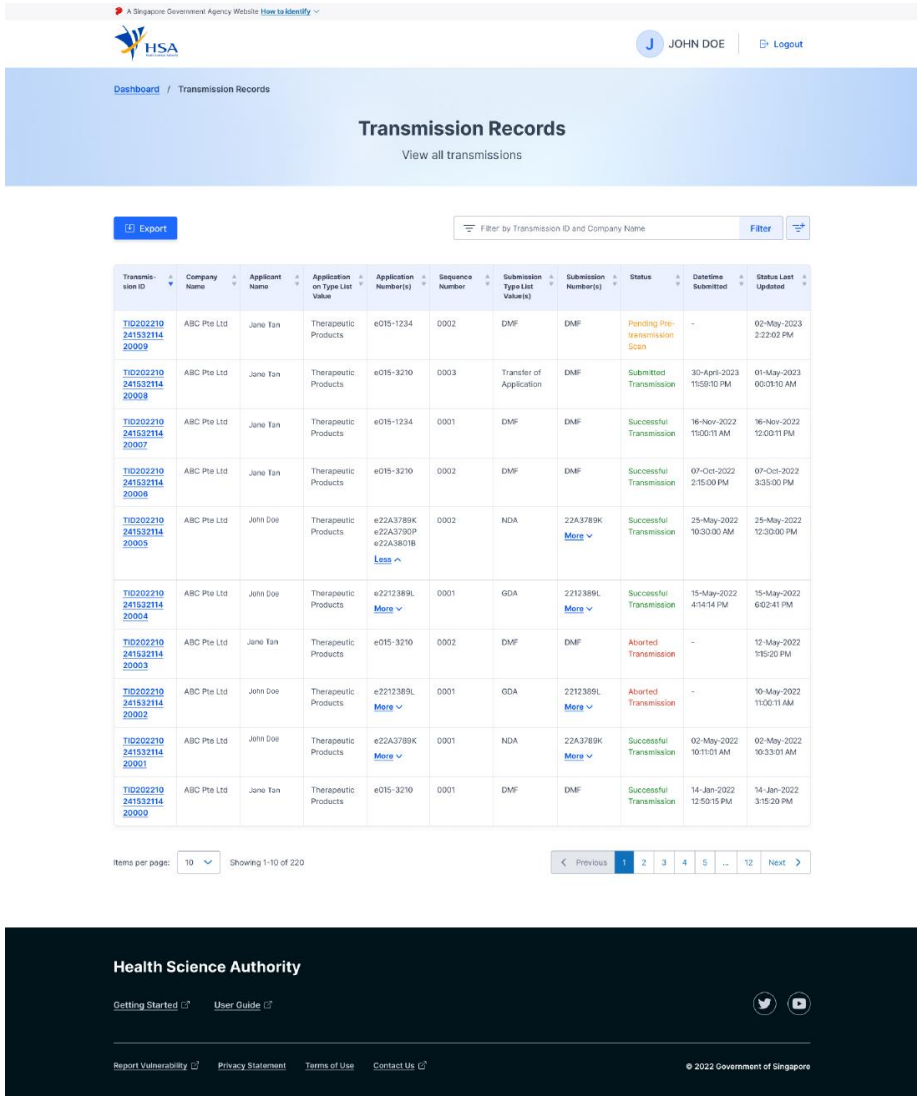
**Please note that the portal mockups shown are currently work in progress and may be subject to changes.*

Portal View – Dashboard



Please note that the portal mockups shown are currently work in progress and may be subject to changes.

Portal View – Transmission Records



Export

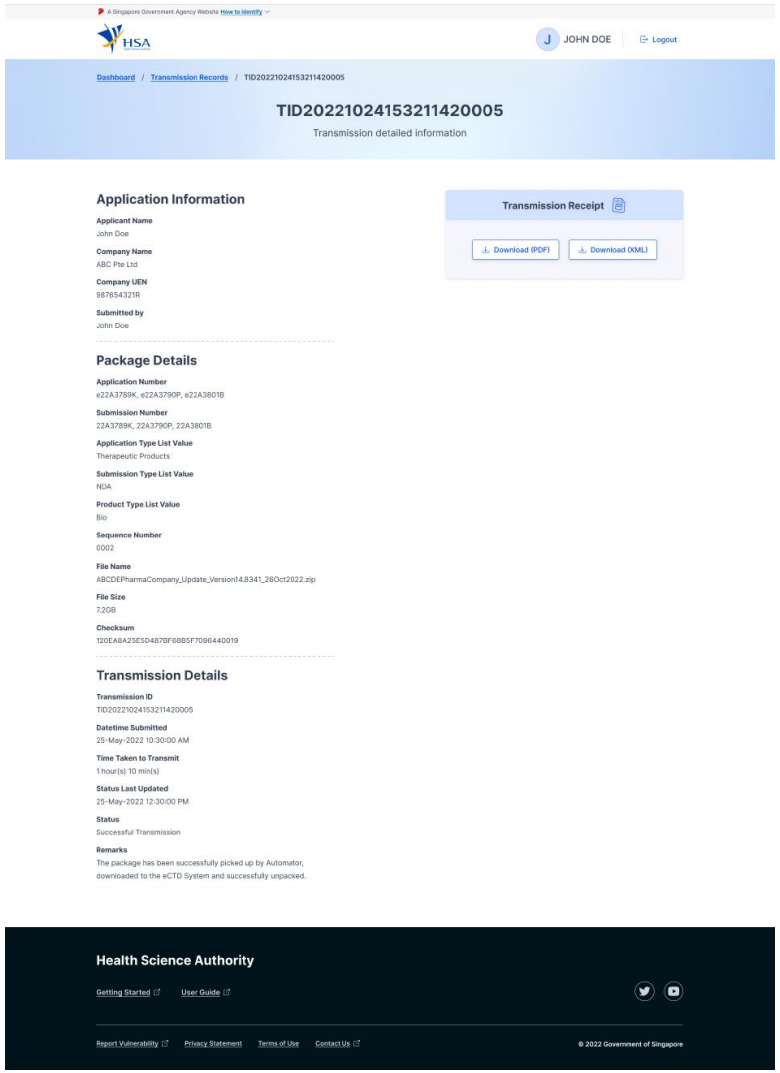
Filter by Transmission ID and Company Name

Filter

Transmission ID	Company Name	Applicant Name	Application Type List Value	Application Number(s)	Sequence Number	Submission Type List Value(s)	Submission Number(s)	Status	Datetime Submitted	Status Last Updated
TID20221024153211420009	ABC Pte Ltd	Jane Tan	Therapeutic Products	e015-1234	0002	DMF	DMF	Pending Pre-transmission Scan	-	02-May-2023 2:22:02 PM
TID20221024153211420008	ABC Pte Ltd	Jane Tan	Therapeutic Products	e015-3210	0003	Transfer of Application	DMF	Submitted Transmission	30-Apr-2023 11:59:10 PM	01-May-2023 00:01:10 AM
TID20221024153211420007	ABC Pte Ltd	Jane Tan	Therapeutic Products	e015-1234	0001	DMF	DMF	Successful Transmission	16-Nov-2022 11:00:11 AM	16-Nov-2022 12:00:11 PM
TID20221024153211420006	ABC Pte Ltd	Jane Tan	Therapeutic Products	e015-3210	0002	DMF	DMF	Successful Transmission	07-Oct-2022 2:15:00 PM	07-Oct-2022 3:35:00 PM
TID20221024153211420005	ABC Pte Ltd	John Doe	Therapeutic Products	e22A3789K e22A3790P e22A3801B Less	0002	NDA	22A3789K More	Successful Transmission	25-May-2022 10:30:00 AM	25-May-2022 12:30:00 PM
TID20221024153211420004	ABC Pte Ltd	John Doe	Therapeutic Products	e2212389L More	0001	GDA	2212389L More	Successful Transmission	15-May-2022 4:14:14 PM	15-May-2022 6:02:41 PM
TID20221024153211420003	ABC Pte Ltd	Jane Tan	Therapeutic Products	e015-3210	0002	DMF	DMF	Aborted Transmission	-	12-May-2022 1:15:20 PM
TID20221024153211420002	ABC Pte Ltd	John Doe	Therapeutic Products	e2212389L More	0001	GDA	e2212389L More	Aborted Transmission	-	10-May-2022 11:00:11 AM
TID20221024153211420001	ABC Pte Ltd	John Doe	Therapeutic Products	e22A3789K More	0001	NDA	22A3789K More	Successful Transmission	02-May-2022 10:11:01 AM	02-May-2022 10:33:01 AM
TID20221024153211420000	ABC Pte Ltd	Jane Tan	Therapeutic Products	e015-3210	0001	DMF	DMF	Successful Transmission	14-Jan-2022 12:50:15 PM	14-Jan-2022 3:15:20 PM

Please note that the portal mockups shown are currently work in progress and may be subject to changes.

Portal View - Transmission Record Details



Application Information

Applicant Name
John Doe

Company Name
ABC Pte Ltd

Company UEN
987654321R

Submitted by
John Doe

Package Details

Application Number
e22A3789K, e22A3790P, e22A3801B

Submission Number
22A3789K, 22A3790P, 22A3801B

Application Type List Value
Therapeutic Products

Submission Type List Value
NDA

Product Type List Value
Bio

Sequence Number
0002

File Name
ABCDEPharmaCompany_Update_Version14.8341_26Oct2022.zip

File Size
7.2GB

Checksum
120EA8A25E5D487BF68B5F7096440019

Transmission Details

Transmission ID
TID20221024153211420005

Datetime Submitted
25-May-2022 10:30:00 AM

Time Taken to Transmit
1 hour(s) 10 min(s)

Status Last Updated
25-May-2022 12:30:00 PM

Status
Successful Transmission

Remarks
The package has been successfully picked up by Automator, downloaded to the eCTD System and successfully unpacked.

Transmission Receipt

Download (PDF) Download (XML)

**Please note that the portal mockups shown are currently work in progress and may be subject to changes.*

PROVIDING YOUR COMMENTS

Invitation to Comment

- Industry stakeholders and interested parties are invited to comment and submit feedback on the eCTD regulatory package for Singapore

- Your feedback is important for us to:
  - To understand the potential impact on industry stakeholders, and
  - To ensure a smooth implementation of eCTD in Singapore

- Your feedback will help us ensure that the final package for eCTD implementation will be fit-for-purpose

Consultation Package Contents

All information related to HSA's eCTD implementation will be located at https://www.hsa.gov.sg/therapeutic-products/register/ectd-submissions

1. Specification components

- SG-HSA eCTD Regional Specification Document version 0.9
  - SG-HSA eCTD Specifications v0.9 (Word, 499KB)
- Regional SG-HSA Module 1 Schema
  - sg-regional(XSD)
  - MD5 Checksum (TXT) [4EB3787844210F1734B8BA6220914DCC]
- Supporting schemas as required by the Regional Schema xml, xlink (XSD)
- SG-HSA Sample eCTDs(zip file, 670KB)

Download the package as a zip file: SG-HSA Specification Components (806KB)

2. Validation components

- SG-HSA eCTD Validation Criteria including SG-HSA Granularity Annex
  - SG-HSA eCTD Validation Criteria v0.9 (Excel, 95KB)
- Document Matrix
  - document-matrix (XML)
- Submission-Type Matrix
  - submission-type-matrix (XML)
- Defined lists (XML)
  - application-type
  - product-type
  - submission-type
  - sequence-type
  - contact-type

Download the package as a ZIP file: SG-HSA Validation Components (96 KB)

3. Q&A document

- SG-HSA eCTD_Questions and Answers (pdf, 184KB)

Industry Consultation Comments & Queries

- Please provide your comments by:
  1. Filling in the Excel template
  2. Submit it using the online Consultation Feedback Form before 12 June 2023

Excel Template

https://www.hsa.gov.sg/docs/default-source/hprg-tpb/ectd/excel-template-for-ectd-feedback.xlsx

Industry Consultation on eCTD Submission for Therapeutic Products (2 May 2023 to 12 Jun 2023)

Consultation Feedback Excel Template - Please submit this excel via the FormSG Consultation Feedback Form

Category	Document Name	Section Header	Line/Row Number (if applicable)	Remarks/Comment

To fill in the table:

- Select the category from the drop-down list:
  - Specification component
  - Validation component
  - Portal
  - Regulatory or Others
- State the document name and section header you are referring to
- State the line number or row number you are commenting on, if applicable
- Provide your remarks/comments, including any suggestions

Consultation Feedback Form

https://form.gov.sg/643518949cfda30012cd25b9

- Q1-8: Fill in your particulars
- Q11: Attach Excel file containing your feedback
- Please respond before 12 June 2023

Recap: Industry Consultation Key Points

- Early feedback is welcome!

- The Q&A document will be updated further based on feedback received during the consultation period

- For information related to HSA's eCTD implementation:
  - Visit the eCTD webpage (www.hsa.gov.sg/therapeutic-products/register/ectd-submissions)
  - Subscribe to HSA Announcements (www.hsa.gov.sg/subscribe)

Q&A

Questions

PRISM application is still required with eCTD submission - will PRISM be retired once eCTD is fully implemented?

HSA's response:

- The eCTD does not replace PRISM. PRISM remains the submission platform for the regulatory application regardless of whether the dossier is submitted via eCTD or not. PRISM is the regulatory system for issuance of registration approvals, and eCTD is a mode for submission of dossiers. The current modes of submissions include CD/DVD submissions or uploading of dossier in PRISM, and eCTD will provide an alternative to the existing modes.

Questions

Would applicants be able to retrieve submissions done via eCTD from PRISM after approval?

HSA's response:

- PRISM is the registration system and does not store any dossier submitted via eCTD Portal, hence the eCTD package will not be retrievable from PRISM. This is similar to CD/DVD submissions where the dossiers are not retrievable from PRISM.

Questions

What is the approximate lead time from submission to approval for the different applications submitted via eCTD?

HSA's response:

- There is no change in application turnaround time (TAT) regardless of the mode of submission of the dossiers to HSA. Please refer to HSA | Fees and turnaround time for therapeutic products for information on TAT.

Questions

Since eCTD follows ICH format, what about ACTD?

HSA's response:

- Currently, eCTD applies to ICH CTD specifications. Submissions using the ACTD dossier format should be submitted through PRISM or CD/DVD as per the current process.

Questions

Is this eCTD session first of many or the one and only?
When will training for the eCTD system for the industry be conducted?

HSA's response:

- This briefing session was conducted to introduce industry to the draft package and to guide the industry on the review of the package for the purposes of the consultation. HSA is open to explore further industry engagement depending on the feedback received on eCTD implementation.
- The training for eCTD Portal submissions will be conducted in 2024.

Questions

During the application process for eCTD application, would there be input request (IR) issued if the eCTD submission was not filed correctly? Or are applicants supposed to restart the whole application process again?

HSA's response:

- Submitted eCTDs will need to go through e-Validation before it reaches HSA for the screening process. During screening, HSA will send an input request (IR) to the applicant if there are deficiencies in the dossier which require clarification, and applicants will need to submit a new eCTD sequence to address those deficiencies.

Questions

It seems that there are many manual steps in terms of file naming additions/deletions that could be system-automated and technology could be better leveraged, such as the addition of "e" and deletions of the last letter in application numbers. Could this be automated by the system?

HSA's response:

- This is related to how the eCTD package is prepared. Applicants do not need to manually prepare the eCTD packages as this can be done by the software vendors, who will encode Singapore HSA profiles which capture HSA specification rules and automate eCTD package preparation. Companies can engage such software vendors to prepare the eCTD package. HSA does not recommend any specific vendors, and applicants can choose the vendor that best meets their needs.

Questions

Will Corppass be needed for accessing the eCTD Portal in PRISM? Or the submitter only requires access rights given in PRISM by the HSA CRIS Administrator?

Does the DMF holder need a HSA PIN to submit the DMF online via the eCTD Portal?

HSA's response:

- PRISM and eCTD Portal are 2 different systems. HSA CRIS account/HSA PIN is only applicable to PRISM and not eCTD Portal. Local and foreign companies that wish to use eCTD Portal should register for a Corppass account, and assign the appropriate Corppass roles to the users within the company to allow users access to the eCTD Portal e-service.

Questions

Is the eCTD pilot phase applicable to NDA-1, NDA-2 and NDA-3? Can companies submit NDA-2 or NDA-3 via eCTD during the pilot phase?

HSA's response:

- All new drug applications can be submitted via eCTD during the initial launch. If the NDA-1 is already registered based on a non-eCTD submission, the NDA-2 and NDA-3 can still be submitted in eCTD format.

Questions

Please share about the situation where you submit multiple MAVs or MIVs at the same time. Or what if it involves bundling, such as MIV-PI and MIV-CMC change? Will there be overlaps of sequences?

HSA's response:

- On the bundling of MIV-1 and MIV-2 applications, applicants should refer to the Submission type matrix which indicates the type of submissions that can be combined together. For this particular example involving MIV-1 PI and MIV-1 CMC changes, such bundling will not be allowed.
- On whether the sequences will overlap, the related sequence numbers included in the envelope will allow the submissions to be grouped together to appear in the correct sequential order to allow for logical and easy access and review of the dossier.

Questions

If I submit 3 sequential NDA applications for 3 different strengths, and subsequently submit another NDA application for a 4th strength, how will it affect the folder name?

HSA's response:

- If an additional strength is added to an existing folder, there will not be any change to the application folder name.

Questions

In your example, the eCTD application number is e22A235B but the application folder name is e22a235, so it is not case specific?

HSA's response:

- The eCTD application number is based on the PRISM application number which may contain an uppercase alphabet as the 3rd character, which in this example, is the "A". However, based on ICH requirements, all the characters in the eCTD application folder name have to appear in lowercase, hence the application folder name would be "e22a235".

Questions

If the company did not use eCTD for initial submission, is it correct that they cannot use eCTD for the MAV?

HSA's response:

- At the initial launch, as the industry and HSA are gaining experience with eCTD submission, we are encouraging submissions with prospective NDA and GDA applications, with their associated Drug Master Files.
- If companies are interested in switching to eCTD format for their current product registrations, please contact us for further discussion.
- We will look into baseline conversion for existing products in a later phase.

Questions

Why is the initial sequence numbered as '0001' instead of '0000' as per global eCTD standards?

HSA's response:

- The sequence '0000' is reserved for baseline submissions to facilitate the conversion of existing products into eCTD format. The sequence '0001' should be used for new applications.
- Sequence '0001' will also be used for new applications in eCTD version 4.0. This will be the new global standard moving forward.

Questions

If the submission is done based on eCTD, we understand that both the registration and DMF must follow the same route. I would like to clarify if the DMF submission refers to the Closed and Open Part DMF submitted by DMF Holder directly to HSA?

HSA's response:

- The DMF Open part should be submitted by the applicant in eCTD format together with the product dossier. We also encourage the submission of the DMF Open and Closed part by the DMF holder in eCTD format. If this is not possible, the DMF holder is able to continue submitting the Open and Closed part of the DMF via CD/DVD to HSA directly.

Questions

What is the eCTD process for submission of a PMF (plasma master file)?

HSA's response:

- Currently, the PMF can be submitted as part of the product dossier. There is no change as the PMF can still be compiled as part of the product dossier under Section 3.2.R.1 in eCTD format and submitted through the eCTD Portal.

Questions

Are the transmission records in eCTD Portal specific to the company entity or specific to the submitter?

HSA's response:

- The current design of the eCTD Portal is such that the submitter is able to see all the transmission records under the same entity. If there are any concerns regarding this design, please do provide your feedback via the Excel template and submit it via the FormSG Consultation Feedback Form.

Questions

As the visibility of transmission record is company (entity)-specific, will submitters be able to see records from previous companies?

HSA's response:

- The submitter would not be able to see records from previous entities, and submitters would only be able to see records based on the current Corppass account which submitters have used to log into the eCTD Portal.

Questions

How long does it take for validation by the e-Validator to be completed from the time of transmission?

HSA's response:

- The time taken for validation may range from a few minutes to more than an hour depending on the size of the package. The time taken from transmission to receipt of the validation outcome by the applicant should not take more than 24 hours.

Questions

Packages which fail validation will be rejected and resubmission will be required. Will there be feedback on which specific sections failed and the reason for validation failure?

HSA's response:

- If there are errors detected during the e-Validation process, the errors will be identified in the validation report which is sent to the applicant.

Questions

What is the timeframe for the voluntary period for eCTD submissions?

HSA's response:

- We understand that the industry would need more time to familiarise themselves with eCTD submissions and explore eCTD adoption, hence the initial launch will be on a voluntary basis. HSA will review the timeframe depending on industry's readiness and the take-up rate. HSA will provide advance notice on any new developments.

Questions

You mentioned that there can be test submissions for about 3 months. What are test submissions?

HSA's response:

- When the system is ready, we will open the system for a 3-month period for test submissions. This is intended to allow industry to provide test submissions and familiarise themselves with the submission process. This will also allow the applicants to see if their eCTD preparation software and validation software are compatible with HSA's eCTD specifications.