KASA

KASA
Generics | New Drugs | Biologics

FDA

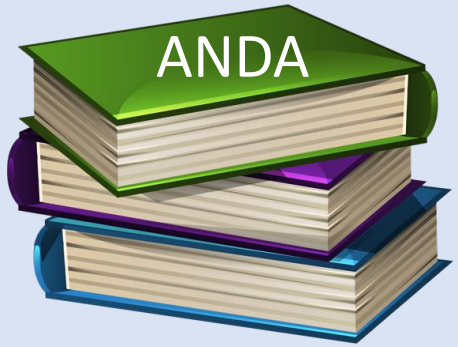
Knowledge-Aided Assessment and Structured Application (KASA) DRUG PRODUCT ASSESSMENT

Presented by: **Peter Capella, PhD**
Division Director,
DIMRPII/OLDP/OPQ/CDER/FDA

Knowledge-Aided Structured Application (KASA)
DRUG PRODUCT ASSESSMENT

Drug Product Quality ANDA Assessment **Before** KASA

+ GUIDANCE



Decision

KASA Drug Product Assessment Focal Points in ANDA Application

Basic ANDA Information and Assessment Discipline Summary

Drug Substance (DS) Critical Quality Attribute Analysis

Drug Product Design (DP)

DS and DP Risk Evaluation Based on Complexity of DS Attributes and DP Design

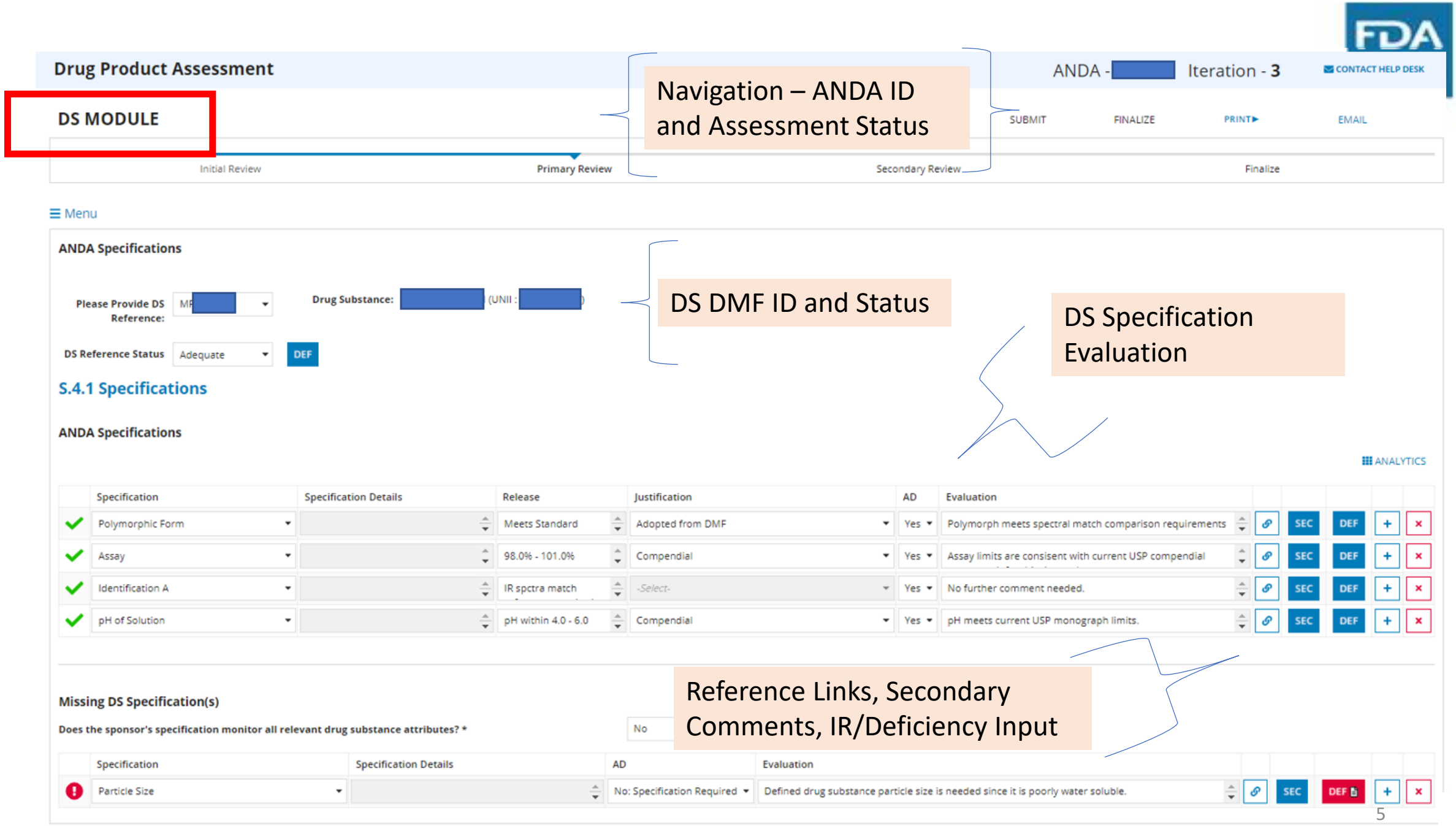
Excipients Critical Quality Attribute Analysis

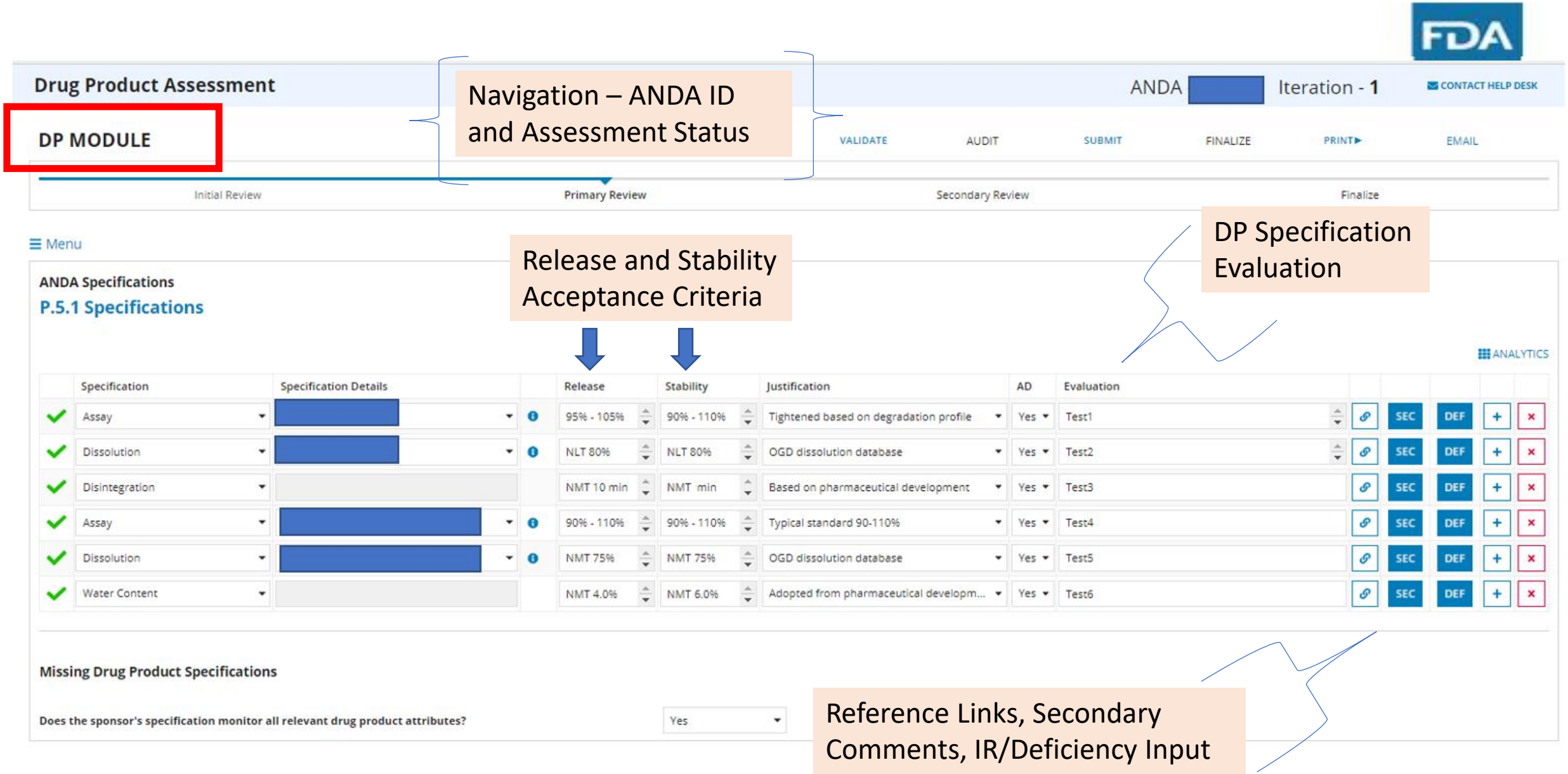
Drug Product (DP) Critical Quality Attribute Analysis

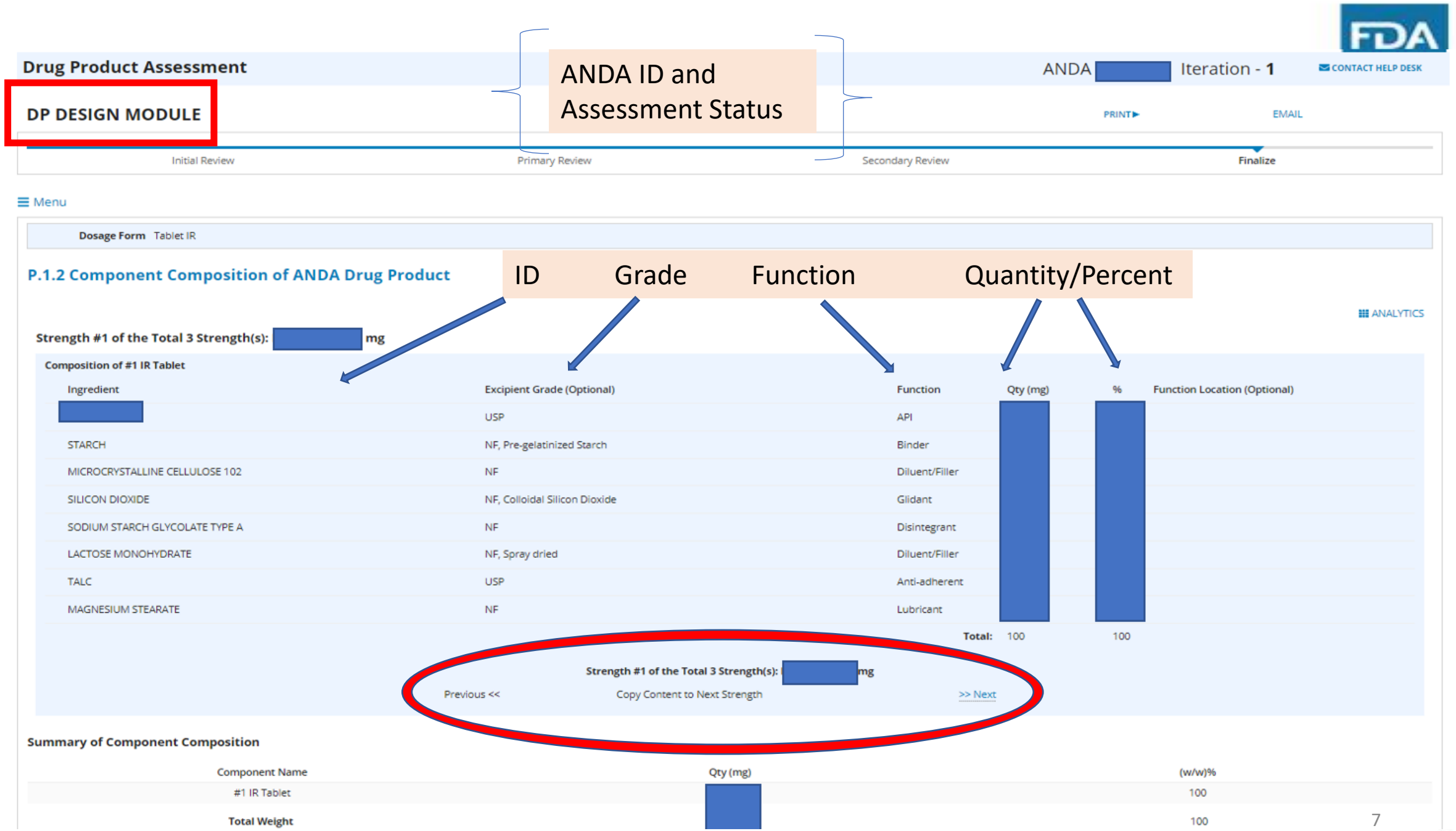
Container Closure Attribute Analysis

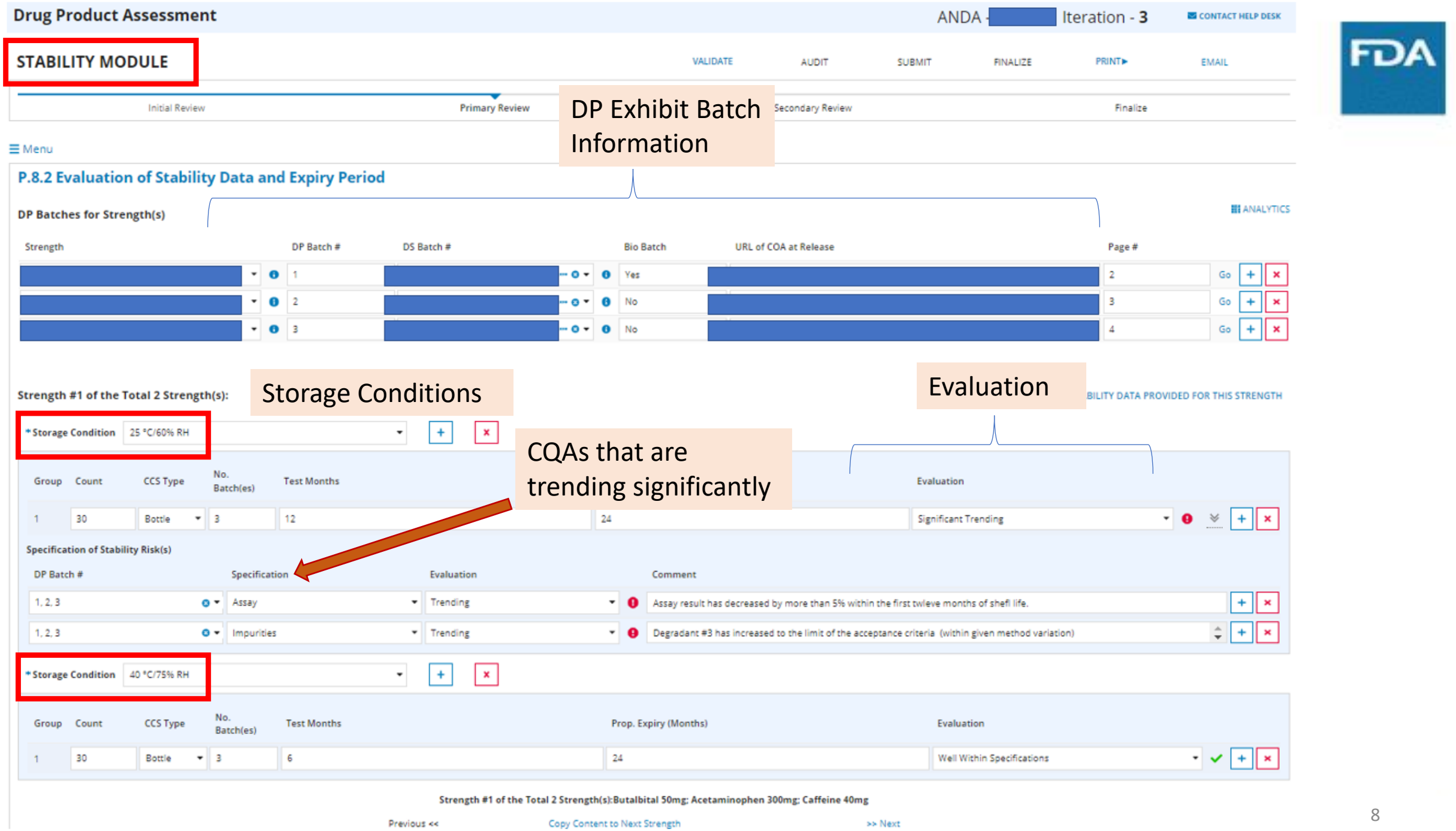
Stability Protocol and Study Data Trending Analysis

Comparability Protocol Analysis


Drug Product Assessment
ANDA - [redacted] Iteration - 3
CONTACT HELP DESK
DS MODULE
SUBMIT
FINALIZE
PRINT
EMAIL
Initial Review
Primary Review
Secondary Review
Finalize
Navigation – ANDA ID and Assessment Status
Menu
ANDA Specifications
Please Provide DS Reference:
Drug Substance:
(UNII :
DS Reference Status
Adequate
DEF
DS DMF ID and Status
DS Specification Evaluation
S.4.1 Specifications
ANDA Specifications
ANALYTICS
Specification
Specification Details
Release
Justification
AD
Evaluation
Polymorphic Form
Meets Standard
Adopted from DMF
Yes
Polymorph meets spectral match comparison requirements
Assay
98.0% - 101.0%
Compendial
Yes
Assay limits are consisent with current USP compendial
Identification A
IR spctra match
-Select-
Yes
No further comment needed.
pH of Solution
pH within 4.0 - 6.0
Compendial
Yes
pH meets current USP monograph limits.
SEC
DEF
Missing DS Specification(s)
Does the sponsor's specification monitor all relevant drug substance attributes? *
No
Reference Links, Secondary Comments, IR/Deficiency Input
Specification
Specification Details
AD
Evaluation
Particle Size
No: Specification Required
Defined drug substance particle size is needed since it is poorly water soluble.

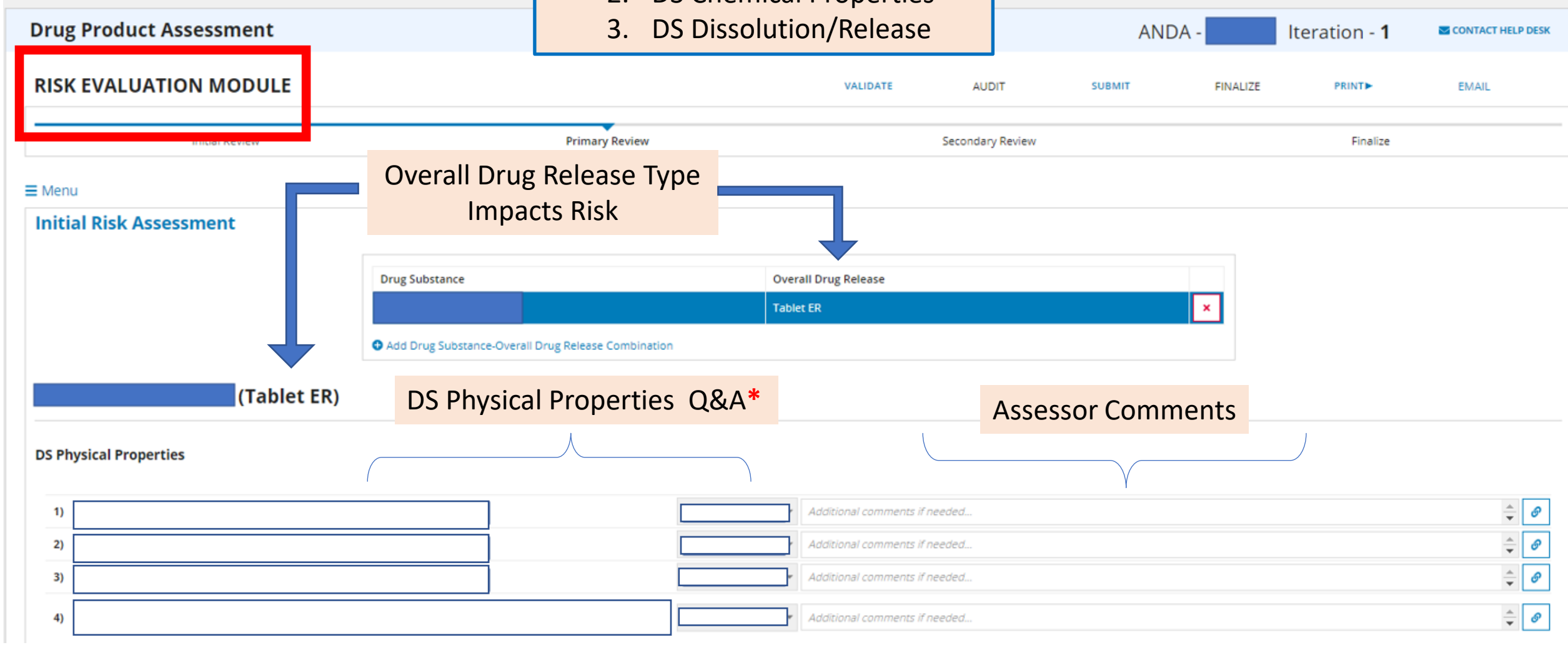

Drug Product Assessment
ANDA [redacted] Iteration - 1
CONTACT HELP DESK
DP MODULE
Navigation – ANDA ID and Assessment Status
VALIDATE
AUDIT
SUBMIT
FINALIZE
PRINT
EMAIL
Initial Review
Primary Review
Secondary Review
Finalize
Menu
ANDA Specifications
P.5.1 Specifications
Release and Stability Acceptance Criteria
DP Specification Evaluation
ANALYTICS
Specification
Specification Details
Release
Stability
Justification
AD
Evaluation
Assay
[redacted]
95% - 105%
90% - 110%
Tightened based on degradation profile
Yes
Test1
SEC
DEF
Dissolution
[redacted]
NLT 80%
NLT 80%
OGD dissolution database
Yes
Test2
SEC
DEF
Disintegration
NMT 10 min
NMT min
Based on pharmaceutical development
Yes
Test3
SEC
DEF
Assay
[redacted]
90% - 110%
90% - 110%
Typical standard 90-110%
Yes
Test4
SEC
DEF
Dissolution
[redacted]
NMT 75%
NMT 75%
OGD dissolution database
Yes
Test5
SEC
DEF
Water Content
NMT 4.0%
NMT 6.0%
Adopted from pharmaceutical developm...
Yes
Test6
SEC
DEF
Missing Drug Product Specifications
Does the sponsor's specification monitor all relevant drug product attributes?
Yes
Reference Links, Secondary Comments, IR/Deficiency Input


Drug Product Assessment
DP DESIGN MODULE
ANDA ID and Assessment Status
ANDA [redacted] Iteration - 1
CONTACT HELP DESK
PRINT
EMAIL
Initial Review
Primary Review
Secondary Review
Finalize
Menu
Dosage Form Tablet IR
P.1.2 Component Composition of ANDA Drug Product
ID
Grade
Function
Quantity/Percent
ANALYTICS
Strength #1 of the Total 3 Strength(s): [redacted] mg
Composition of #1 IR Tablet
Ingredient
Excipient Grade (Optional)
Function
Qty (mg)
%
Function Location (Optional)
[redacted]
USP
API
STARCH
NF, Pre-gelatinized Starch
Binder
MICROCRYSTALLINE CELLULOSE 102
NF
Diluent/Filler
SILICON DIOXIDE
NF, Colloidal Silicon Dioxide
Glidant
SODIUM STARCH GLYCOLATE TYPE A
NF
Disintegrant
LACTOSE MONOHYDRATE
NF, Spray dried
Diluent/Filler
TALC
USP
Anti-adherent
MAGNESIUM STEARATE
NF
Lubricant
Total: 100 100
Strength #1 of the Total 3 Strength(s): [redacted] mg
Previous <<
Copy Content to Next Strength
>> Next
Summary of Component Composition
Component Name
Qty (mg)
(w/w)%
#1 IR Tablet
100
Total Weight
100


Drug Product Assessment
ANDA [redacted] Iteration - 3
CONTACT HELP DESK
STABILITY MODULE
VALIDATE
AUDIT
SUBMIT
FINALIZE
PRINT
EMAIL
Initial Review
Primary Review
Secondary Review
Finalize
DP Exhibit Batch Information
Menu
P.8.2 Evaluation of Stability Data and Expiry Period
DP Batches for Strength(s)
ANALYTICS
Strength
DP Batch #
DS Batch #
Bio Batch
URL of COA at Release
Page #
Yes
No
No
Go
Storage Conditions
Evaluation
Strength #1 of the Total 2 Strength(s):
BILITY DATA PROVIDED FOR THIS STRENGTH
*Storage Condition
25 °C/60% RH
CQAs that are trending significantly
Group
Count
CCS Type
No. Batch(es)
Test Months
Evaluation
Bottle
Significant Trending
Specification of Stability Risk(s)
DP Batch #
Specification
Evaluation
Comment
Assay
Trending
Assay result has decreased by more than 5% within the first twleve months of shefl life.
Impurities
Degradant #3 has increased to the limit of the acceptance criteria (within given method variation)
*Storage Condition
40 °C/75% RH
Prop. Expiry (Months)
Well Within Specifications
Strength #1 of the Total 2 Strength(s):Butalbital 50mg; Acetaminophen 300mg; Caffeine 40mg
Previous <<
Copy Content to Next Strength
>> Next

Initial Risk Assessment

1. DS Physical Properties
2. DS Chemical Properties
3. DS Dissolution/Release



* Developed by Subject Matter Experts in OLDP; support algorithms related to risk assessment.

Initial Risk Assessment
(Continued)

DS Chemical Properties

Q&A

Assessor Comments

DS Chemical Properties

1)			Additional comments if needed...
2)			Additional comments if needed...

DS Dissolution & Drug Release

DS Dissolution & Drug Release

1)			Additional comments if needed...
2)			Additional comments if needed...
3)			Additional comments if needed...
4)			Additional comments if needed...
5)			Additional comments if needed...
6)			Additional comments if needed...

Initial Risk Assessment "Score"

UNLOCK INITIAL RISK ASSESSMENT

Initial Risk Assessment

Risk of Physical Stability	Risk of Chemical Stability	Risk of In Vitro Dissolution
MEDIUM	MEDIUM	HIGH

Revised or “Final” Risk Assessment

Physical Stability

Drug Substance	Overall Drug Release
[redacted]	Tablet ER

[redacted] (Tablet ER)

ANALYTICS

Initial Risk Ranking: Medium MODIFY

Comment

Comment only if you modified the default risk rank

SEC

Risk Mitigation Strategies of Product Design and Measurements

Risk Mitigation of Product Design

	ID	Mitigation Strategy		AD	Reviewer Evaluation						
✓	1			Yes	TEST1		SEC	DEF	+	×	
✓	2			Yes	TEST2		SEC	DEF	+	×	

Risk Mitigation of Measurements

	ID	Mitigation Strategy		AD	Reviewer Evaluation						
✓	1			Yes	TEST3		SEC	DEF	+	×	
✓	2			Yes	TEST4		SEC	DEF	+	×	

Risk Update: Low

Revised or “Final” RISK Update

Comment

Risk Mitigation through Product Design and Measurements reduces initial risk from Medium to Low.

SEC

Drug Product Quality ANDA Assessment with KASA

GUIDANCE

+

ANDA

Analytics – Systematic comparison between multiple assessments

LIFECYCLE

Decision

Three Benefits of KASA for DP Assessment :

1. Provides a *structured approach* to DP Assessment that fully supports the decision on ANDA product quality.

2. Allows collaborative multi-disciplinary view of the Quality Assessment to ensure a *consistent decision-making approach*.

3. Gives FDA internal customers, like OGD & OLDP Post-Marketing Assessors, the ability to *review the DP Lifecycle* using *Analytics* of DS & DP CQAs, Stability, and Risk Evaluation.

Thanks for your Attention.

Challenge Question: KASA for DP Assessment

Which concept does KASA for DP Assessment support that was perhaps not previously in the mindset of assessors?

A. Use of regulation and guidances.

B. Drug Product Lifecycle from the RLD through all its generics.

C. FDA is an Agency that is data-driven.