What's new in the Inactive Ingredient Database (IID)?

SBIA 2020: Advancing Innovative Science in Generic Drug Development Workshop
Session 2: Excipient and Formulation Considerations

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Big changes are underway in the IID

- New data standards
- Added transparency
- New excipient levels based on exposure
- New tool for excipient qualification

Learning Objectives

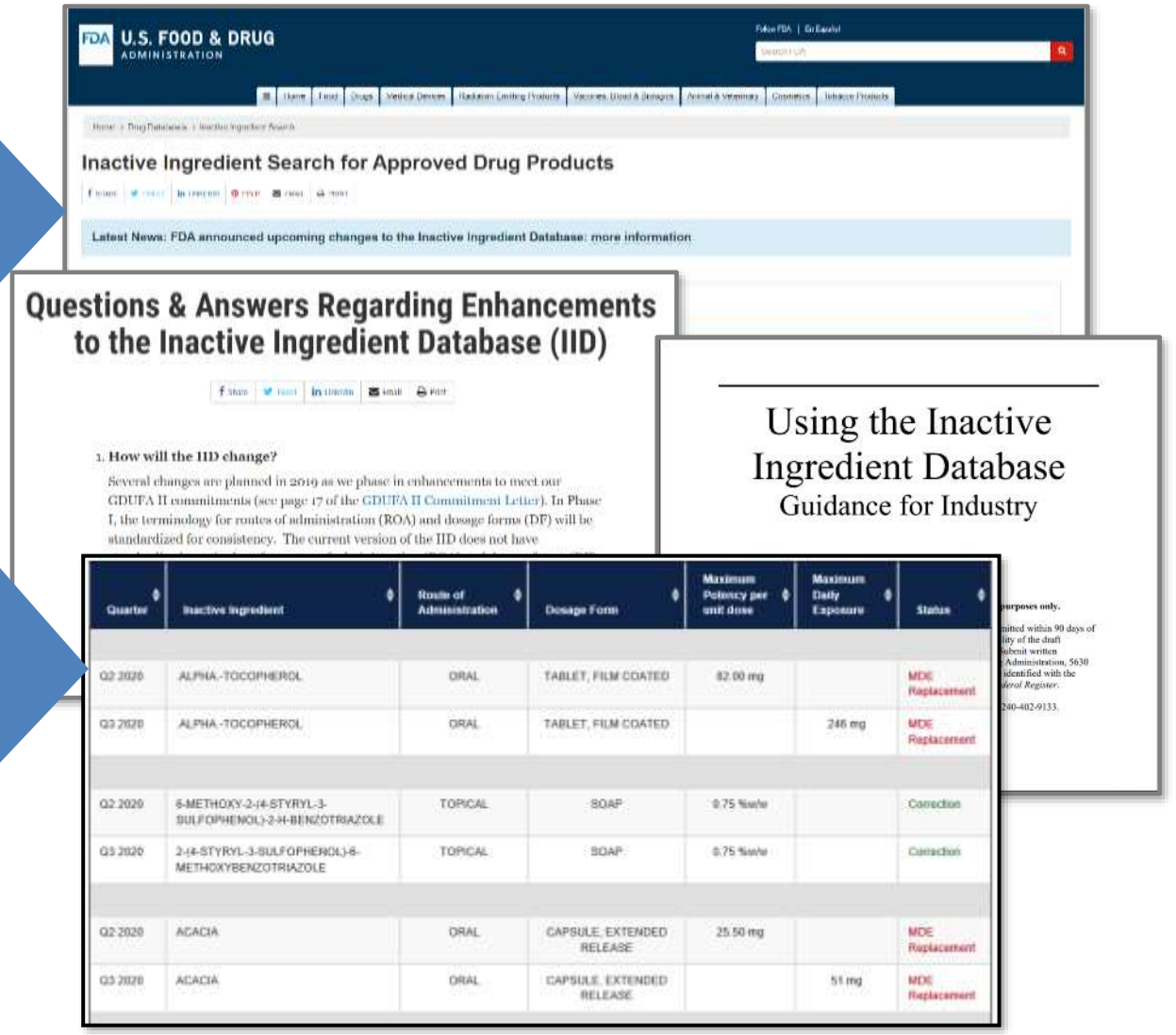
- We will review recent IID enhancements to:
  - Define current IID terms and data
  - Discuss changes that were implemented in 2019 and 2020
  - Explain how to read the new Quarterly IID Change Log
  - Clarify how excipient Maximum Daily Exposure (MDE) is determined and displayed in the IID

Introduction to the IID

Online, searchable list of excipients in FDA-approved drug products

Available IID resources:

- IID FAQ
- Draft IID Guidance
- Record of changes by quarter (Change Log)



http://www.accessdata.fda.gov/scripts/cder/iig/index.cfm

IID Basics

IID contains only excipients in NDAs and ANDAs.

SRS preferred terms

Maximum Potency per unit dose

New item: Maximum Daily Exposure (MDE)

Inactive Ingredient	Route	Dosage Form	CAS Number	UNII	Maximum Potency per unit dose	Maximum Daily Exposure (MDE)	Record Updated
.ALPHA.-TOCOPHEROL	ORAL	CAPSULE	1406184	H4N855PNZ1	5mg		
.ALPHA.-TOCOPHEROL	ORAL	SOLUTION	1406184	H4N855PNZ1	1.05mg/1ml		
.ALPHA.-TOCOPHEROL	ORAL	TABLET	1406184	H4N855PNZ1	42.5mg		
.ALPHA.-TOCOPHEROL	ORAL	TABLET, CHEWABLE	1406184	H4N855PNZ1	0.1mg		
.ALPHA.-TOCOPHEROL	ORAL	TABLET, EXTENDED RELEASE	1406184	H4N855PNZ1	1.34mg		
.ALPHA.-TOCOPHEROL	ORAL	TABLET, FILM COATED	1406184	H4N855PNZ1		246mg	Y
.ALPHA.-TOCOPHEROL ACETATE	ORAL	CAPSULE	7695912	9E8X80D2L0	2mg		
.ALPHA.-TOCOPHEROL ACETATE	ORAL	TABLET	7695912	9E8X80D2L0	0.5mg		
.ALPHA.-TOCOPHEROL, DL-	ORAL	CAPSULE	10191410	7QWA1RIO01	1mg		
.ALPHA.-TOCOPHEROL, DL-	ORAL	SUSPENSION	10191410	7QWA1RIO01	0.01mg/1ml		
.ALPHA.-TOCOPHEROL, DL-	ORAL	TABLET	10191410	7QWA1RIO01	0.9mg		
.ALPHA.-TOCOPHEROL, DL-	ORAL	TABLET, CHEWABLE	10191410	7QWA1RIO01	0.02mg		

Displays one record per unique Excipient-RoA-DF combination

CAS and UNII

Flag for new records

SRS is FDA's Substance Registration System
CAS is the Chemical Abstracts Service Registry Number
UNII is a unique code assigned by SRS

Ongoing IID Changes

New Data Standards

SPL is FDA's Structured Product Labeling system.
IID uses SPL terminology for routes of administration and dosage forms.

Inactive Ingredient	Route	Dosage Form	CAS Number	UNII	Maximum Potency per unit dose	Maximum Daily Exposure (MDE)	Record Updated
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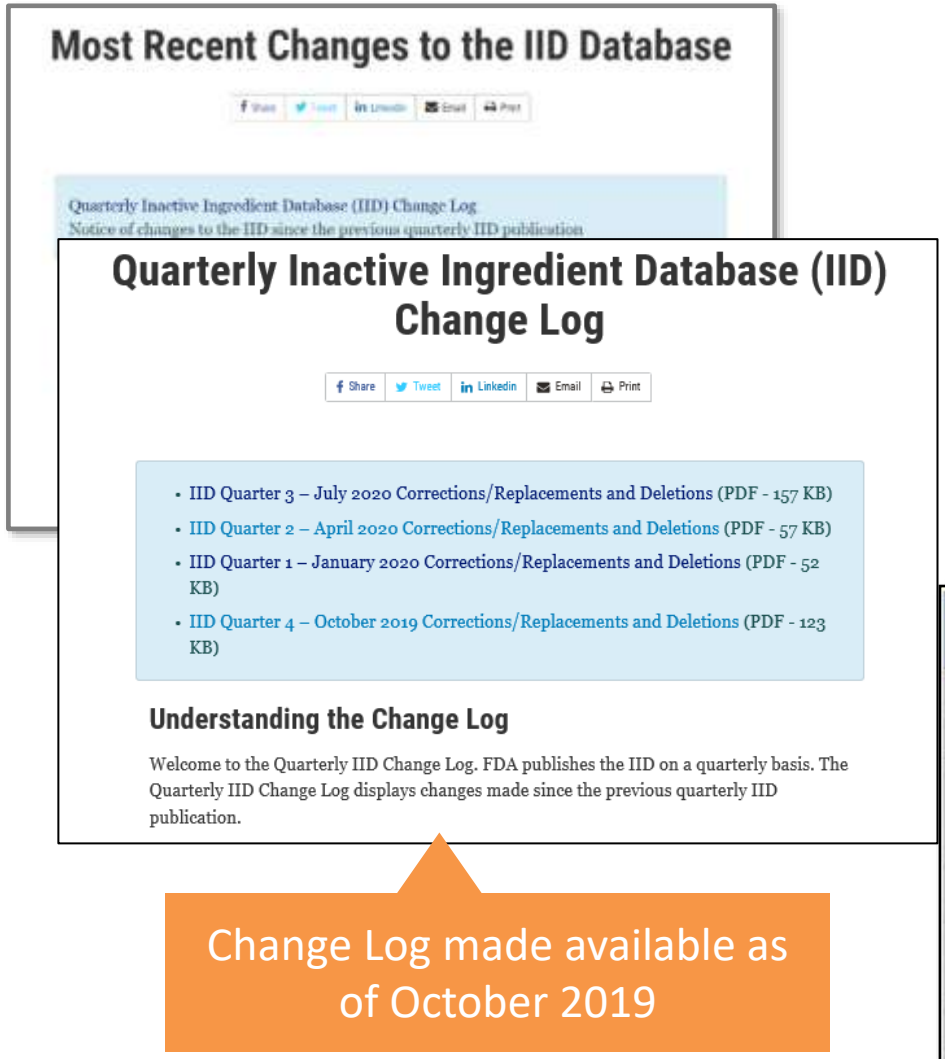
.ALPHA.-TOCOPHEROL, DL-	ORAL	TABLET, CHEWABLE	10191410	7QWA1RIO01	0.02mg		

SPL terms for Route and Dosage Form as of July 2019

A comprehensive list of mapped terms can be found on the IID webpage. Select the link for Most Recent Changes to the IID Database.

Ongoing IID Changes



Change Log made available as of October 2019

Updated from static to searchable and interactive Change Log as of June 2020

How to Read the Quarterly Change Log

Record = Excipient Name + Route + Dosage Form

Inactive Ingredient	Route	Dosage Form
BETADEX	ORAL	TABLET

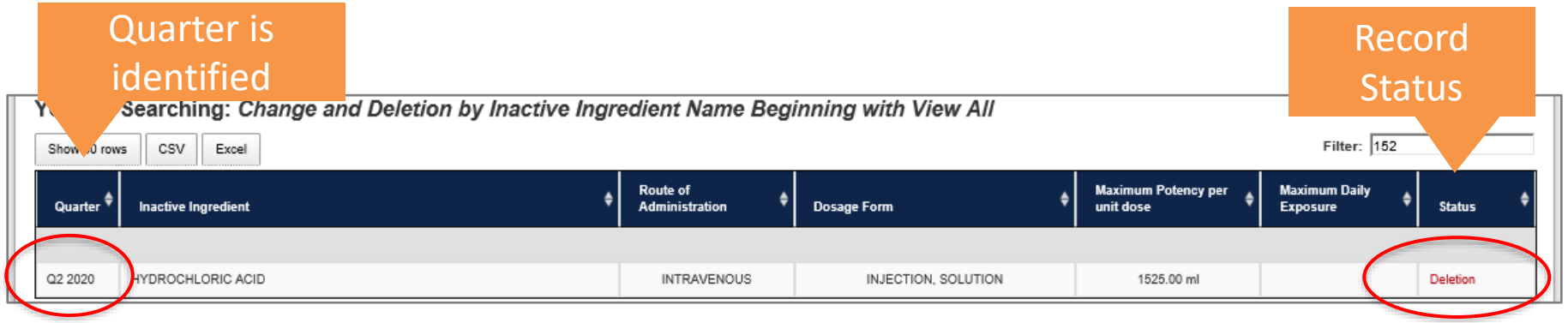
Three types of changes to a record

- Deletions
- Corrections
- MDE Replacements

Quarterly Change Log Terms

Deleted Record

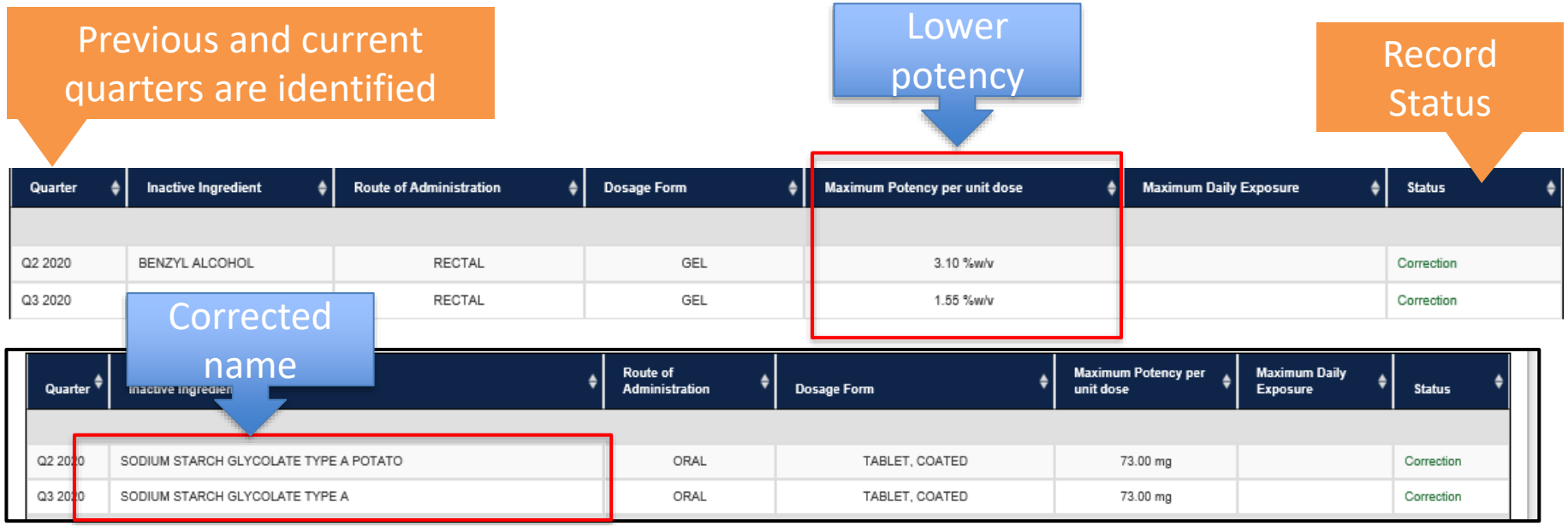
- Record was removed in this IID quarter



Quarterly Change Log Terms

Corrected Record

- Record was corrected and replaced with a lower potency in this quarter
- Excipient name was corrected



Quarter	Inactive Ingredient	Route of Administration	Dosage Form	Maximum Potency per unit dose	Maximum Daily Exposure	Status
Q2 2020	BENZYL ALCOHOL	RECTAL	GEL	3.10 %w/v		Correction
Q3 2020		RECTAL	GEL	1.55 %w/v		Correction

Quarter	Inactive Ingredient	Route of Administration	Dosage Form	Maximum Potency per unit dose	Maximum Daily Exposure	Status
Q2 2020	SODIUM STARCH GLYCOLATE TYPE A POTATO	ORAL	TABLET, COATED	73.00 mg		Correction
Q3 2020	SODIUM STARCH GLYCOLATE TYPE A	ORAL	TABLET, COATED	73.00 mg		Correction

Challenge Question

What happens if the record is replaced with a higher potency?

It is flagged as "new" in the IID.

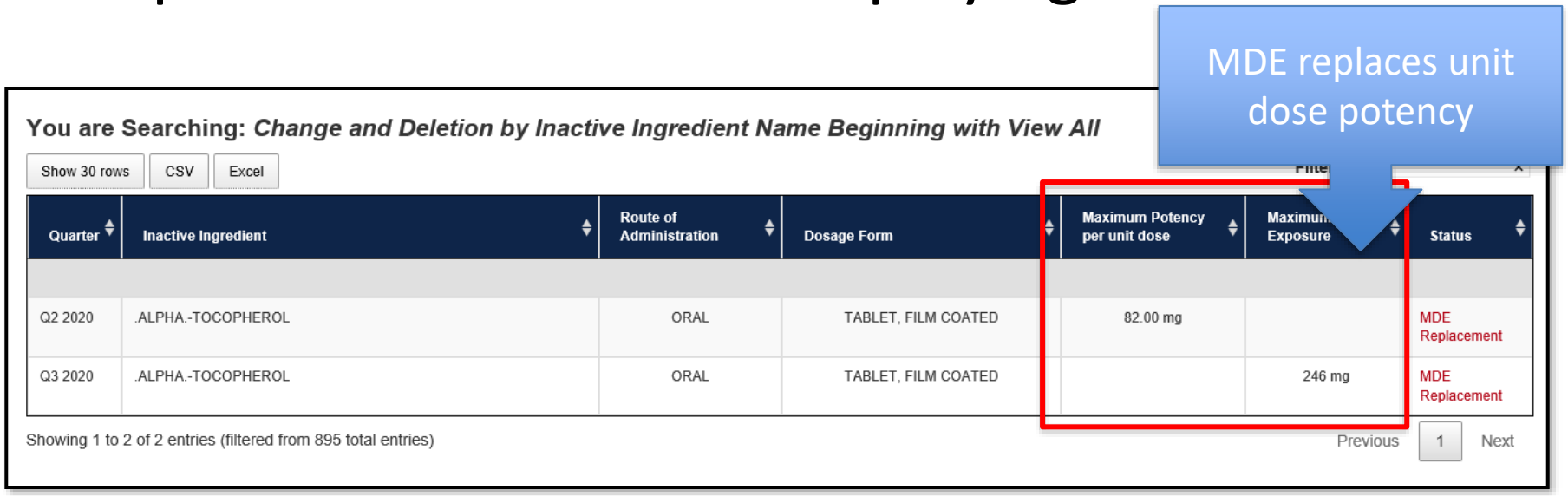
Records corrected with lower potencies appear in the Change Log.

Records replaced with higher potencies appear with a "Y" flag on the primary IID page.

Quarterly Change Log Terms

MDE Replacement

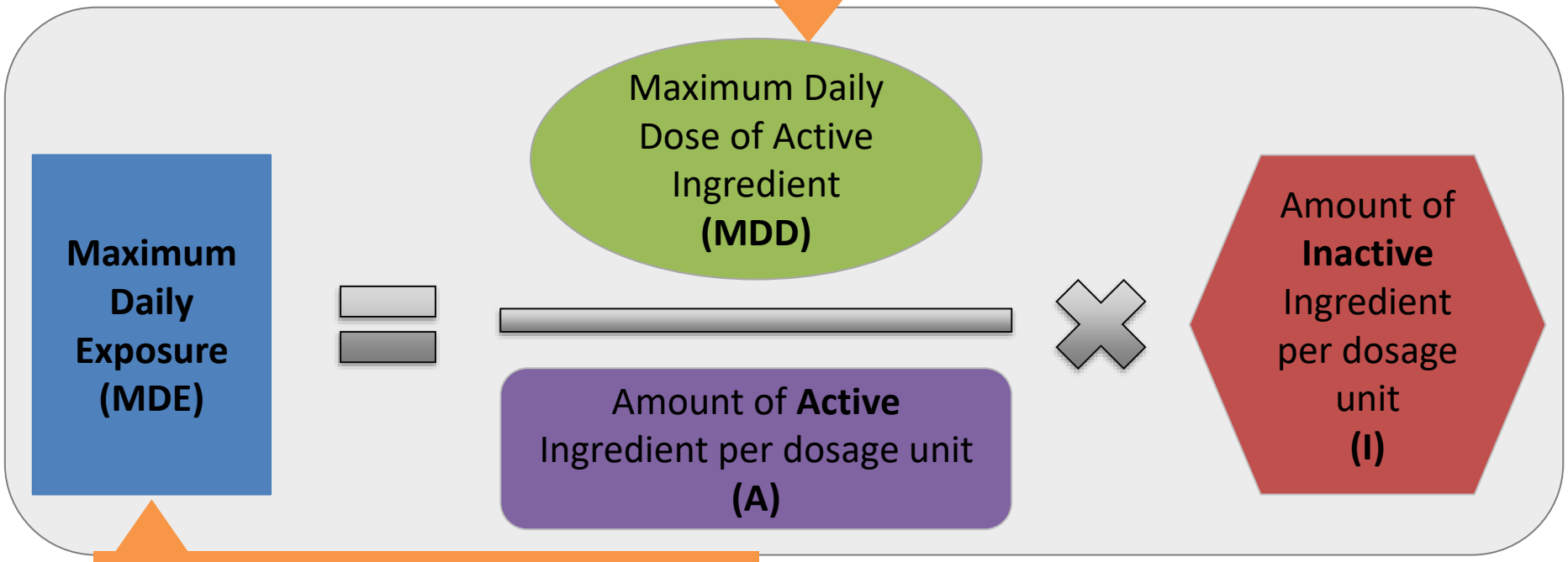
- Record displaying maximum potency was replaced with a record displaying MDE.



Maximum Potency = highest excipient amount in one unit
Maximum Daily Exposure = highest excipient amount in a daily dose

Excipient Maximum Daily Exposure

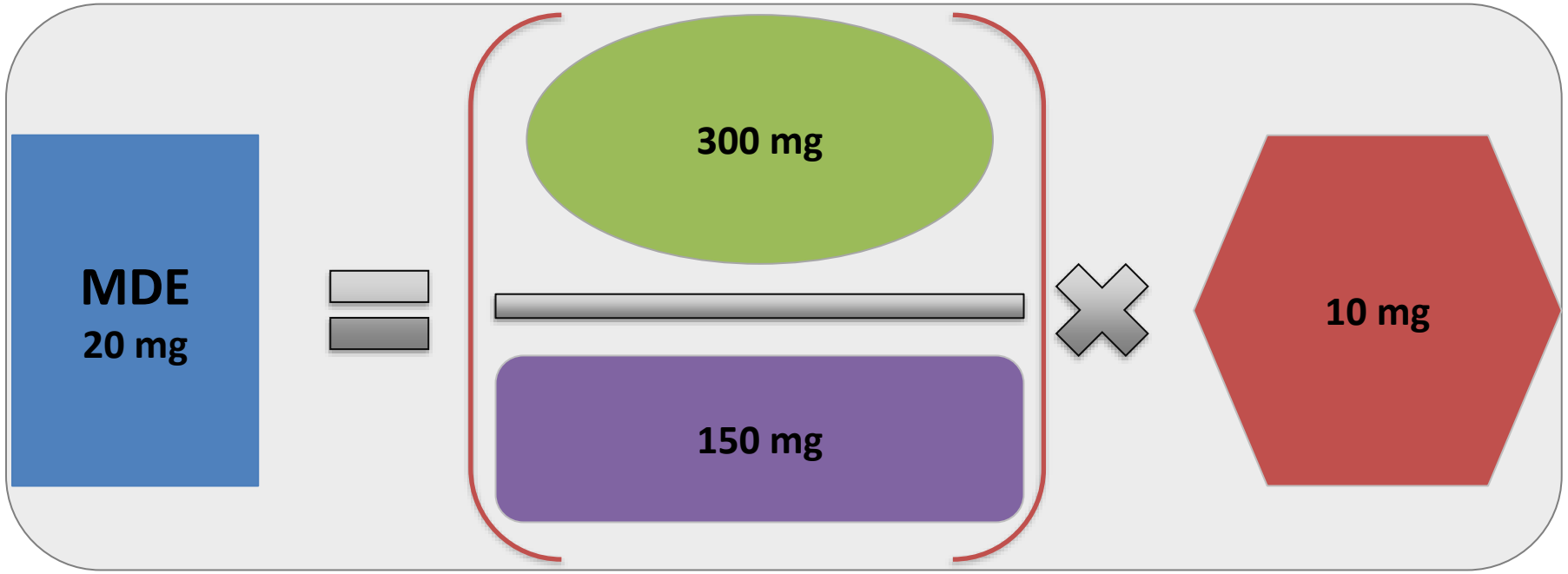
The Maximum Daily Exposure (MDE) of an Inactive Ingredient is based on the Maximum Daily Dose (MDD) of products in which it is used



MDE is also called Maximum Daily Intake (MDI) in oral drugs

Sample MDE Calculation

Oral tablet X has MDD **300 mg/day**
Tablet strength is **150 mg** (A)
Each tablet contains **10 mg** of excipient A (I)
MDE of excipient A = **20 mg**



Using MDE in ANDAs

Transition from Maximum Potency to MDE

MDE values can be used to justify the amount of excipient a patient will receive when given the highest daily dosing regimen.

- MDE will replace maximum potency.
- MDE values will be added gradually to the IID.
- MDE values are expected to increase as data is obtained.
- MDE will typically be displayed in mg (mg/day).

Summary

- IID adopted new data standards in July 2019
- IID began reporting quarterly changes in Oct. 2019
- Quarterly Change Log identifies
  - Deletions
  - Corrections
  - MDE replacements
- New IID entries and higher potencies are flagged with “Y” in the IID
- IID began reporting MDE in July 2020
- More MDEs will appear in the IID as data is gathered

Contact Information

- Questions and concerns about IID entries, send to IIDUpdate@fda.hhs.gov
- Nomenclature corrections and questions about excipient names, send to fda-srs@fda.hhs.gov
- Questions about excipients used in development of generic products should be submitted through Controlled Correspondence. Refer to http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM411478.pdf

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Thank you SBIA


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