# FDA's Inactive Ingredient Database (IID)

**Improvements on the Path to 2020**

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# Pharmaceutical Quality

**A quality product of any kind consistently meets the expectations of the user.**

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**A quality product of any kind consistently meets the expectations of the user.**

**Drugs are no different.**


FDA
Patients expect safe and effective medicine with every dose they take.
www.fda.gov

**Pharmaceutical quality is**

assuring *every* dose is safe and effective, free of contamination and defects.


FDA
It is what gives patients confidence in their *next* dose of medicine.
www.fda.gov

# How can generic drug applicants meet requirements for excipients in FDA regulations?

§314.94(a)(9)(ii) … an applicant must **identify and characterize the inactive ingredients** in the proposed drug product and **provide information demonstrating that such inactive ingredients do not affect the safety or efficacy** of the proposed drug product.

# Audience Poll

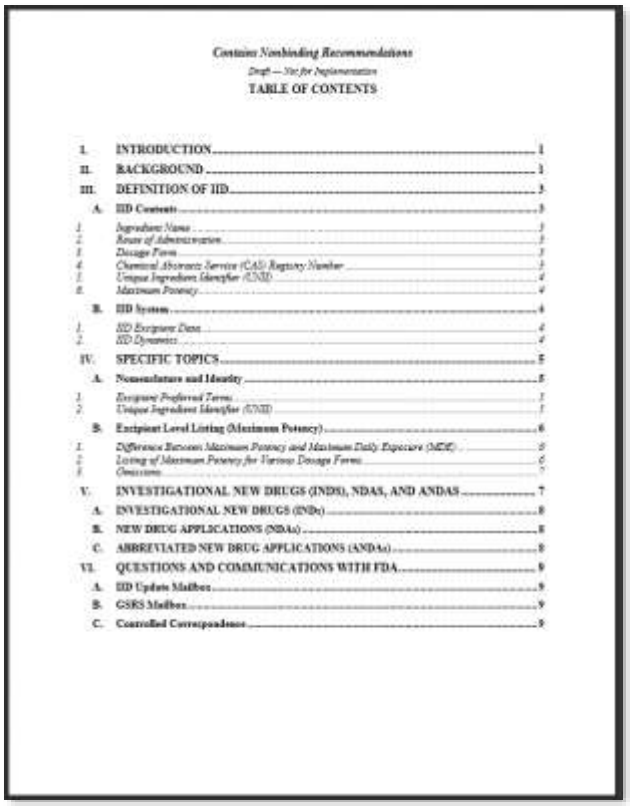
- How many have read the IID guidance?

Using the Inactive Ingredient Database

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

July 2019
Pharmaceutical Quality/CMC



*Contains Nonbinding Recommendations*

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Link to *Using the Inactive Ingredient Database*
https://www.fda.gov/media/128687/download

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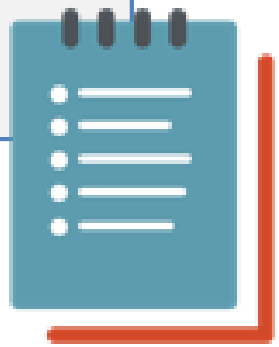
   - New IID draft guidance
3. Changes in 2020
   - IID Data Standards
   - What's MDE?
   - IID Change log
4. Contacting FDA
5. Questions


# IID BASICS

# What is the IID?

- Searchable list
- Excipients in approved products
- Maximum levels of excipients
- Toolbox for development



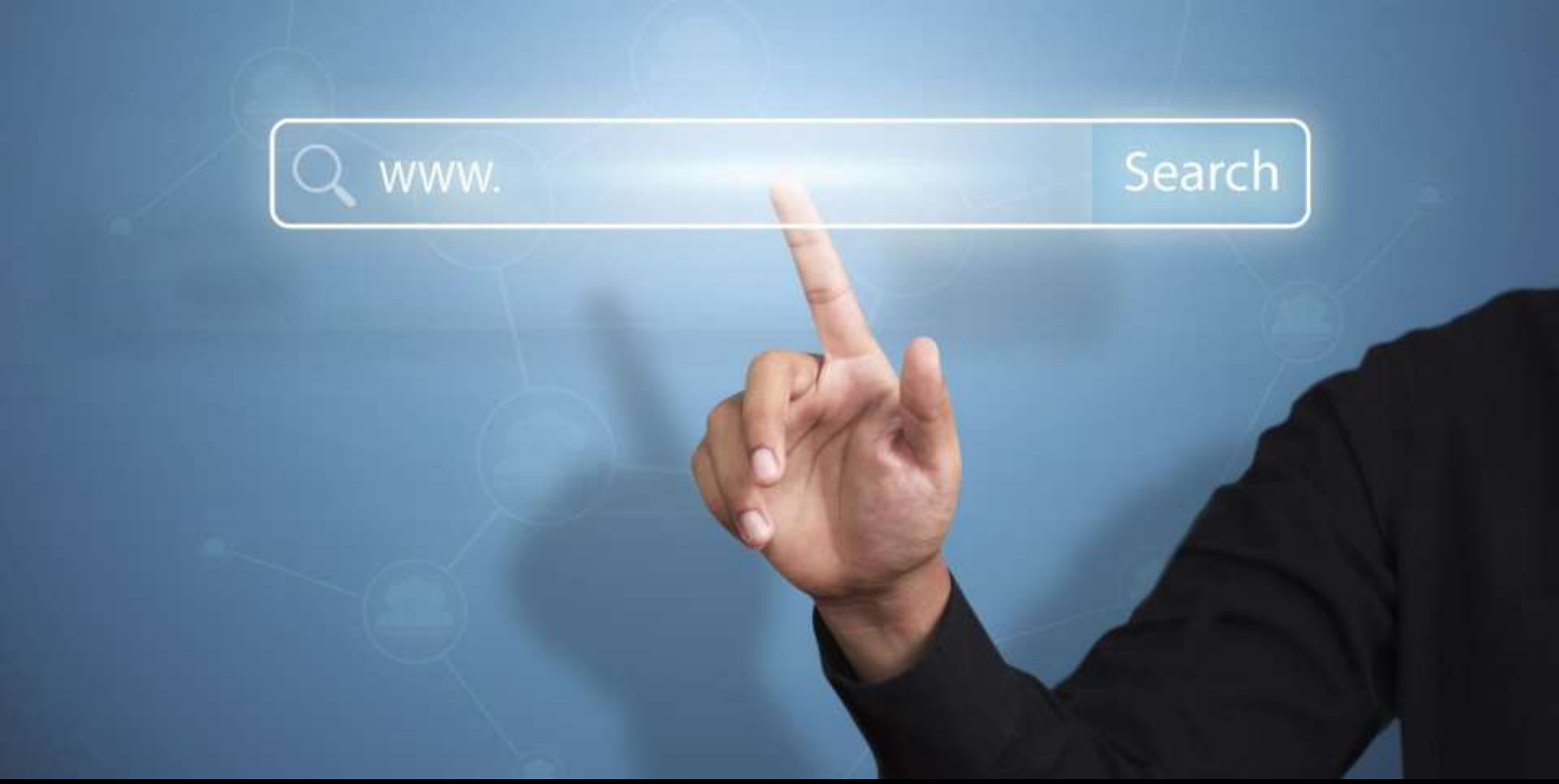
Available at
https://www.accessdata.fda.gov/scripts/cder/iig/index.cfm

# Why was the IID Created?

- To provide evidence of previous safe use of specific excipients in drug products
- To provide information on excipients present in FDA-approved drug products
- To serve as a resource for drug development

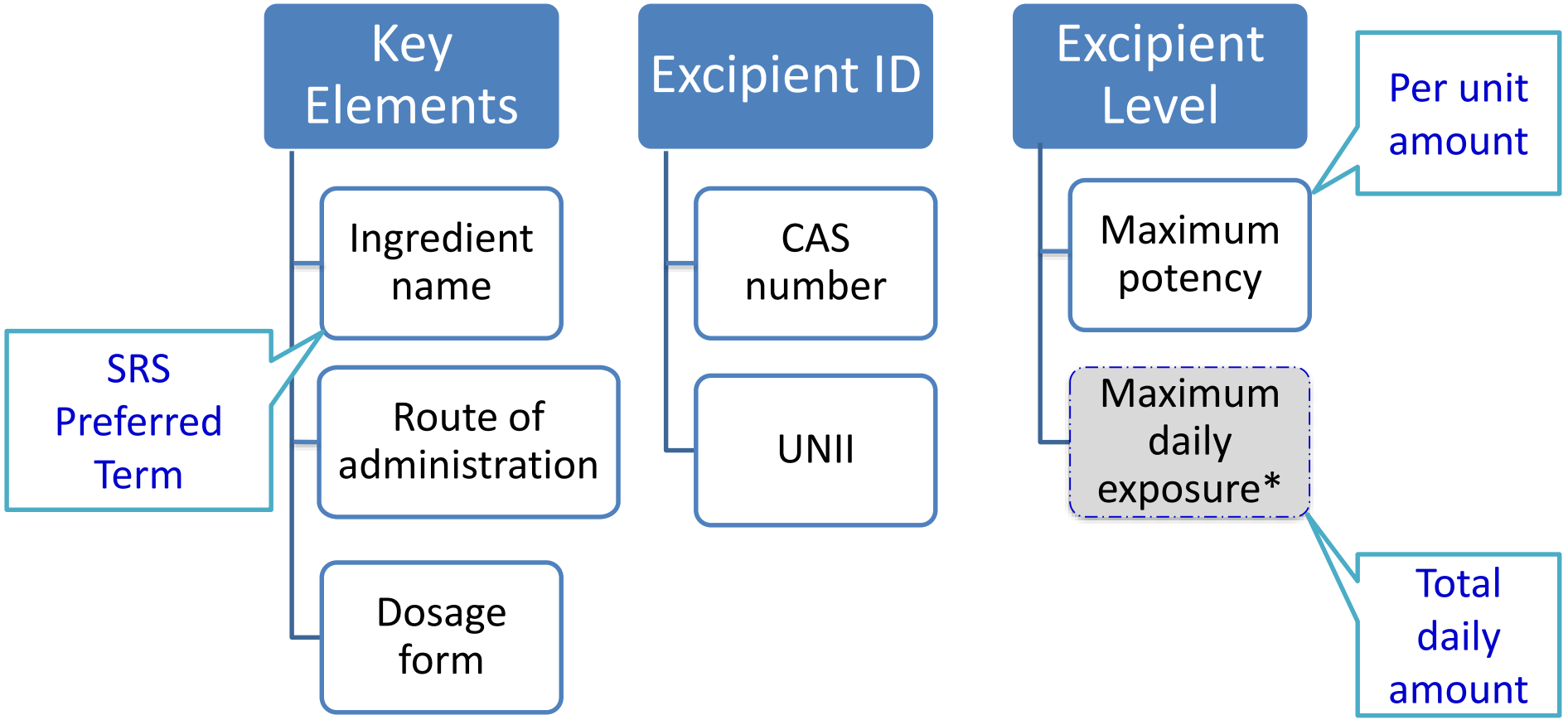
# Who Uses the IID?

- All segments of the pharmaceutical industry
- FDA when performing application assessments
  - Filing assessment
  - Quality assessment
  - Pharm/Tox assessment




# UNDERSTANDING THE IID

# Data Available in the IID




SRS = FDA's Substance Registration System
Ingredients are assigned preferred terms and UNIIs by SRS

# Navigating the IID

Search term

Search filter

**Search Results for: betadex**

Show 30 rows | CSV | Excel

Filter: oral

| Inactive Ingredient | Route | Dosage Form | CAS Number | UNII | Maximum Potency per unit dose | Record Updated |
|---|---|---|---|---|---|---|
| BETADEX | ORAL | TABLET | 7585399 | JV039JZZ3A | 133.33mg | |
| BETADEX | ORAL | TABLET, FILM COATED | 7585399 | JV039JZZ3A | 41.25mg | |
| HYDROXYPROPYL BETADEX | ORAL | CAPSULE | 128446355 | 1I96OHX6EK | 0.6mg | |
| HYDROXYPROPYL BETADEX | ORAL | SOLUTION | 128446355 | 1I96OHX6EK | 400mg/1ml | |
| HYDROXYPROPYL BETADEX | ORAL | TABLET | 128446355 | 1I96OHX6EK | 143.76mg | |
| HYDROXYPROPYL BETADEX | ORAL | TABLET, ORALLY DISINTEGRATING | 128446355 | 1I96OHX6EK | 15mg | |

Maximum potency (per dosage unit)

# New Draft Guidance for Industry
## *Using the Inactive Ingredient Database*

- Provides advice to Industry for IND, NDA and ANDA submissions
- Explains how FDA's uses IID in phases of assessment
- Explains sources of IID data

Draft guidance provides an opportunity for industry to give input through the guidance docket

Link to the guidance: https://www.fda.gov/media/128687/download

Comment on the guidance at https://www.regulations.gov. Enter Docket No. FDA-2019-D-2397

# Advice from the IID Guidance

- Excipient grades
  - Always specify excipient grade
  - Reference the same grade in IID or explain the link between IID grade and proposed grade
- Flavors, colors and excipient mixtures
  - Provide a quantitative breakdown of mixtures
  - Reference FDA regulations for colors additives
  - When referencing GRAS status or FDA food regulations, be sure they are relevant considering product use

Controlled correspondence may be submitted to FDA to ask about acceptability of an excipient and its level in a specific proposed generic drug product under development.


# COMING SOON BY OCT 2020

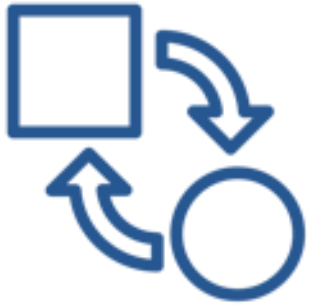
# GDUFA II Commitments

1. By October 1, 2020, FDA will complete enhancements to the Inactive Ingredient Database so users can perform electronic queries to obtain accurate **Maximum Daily Intake and Maximum Daily Exposure** information for each route of administration for which data is available.
2. FDA will update the Inactive Ingredient Database on an ongoing basis, and **post quarterly notice of updates made**. **Such notices will include each change made** and, for each change, the information replaced.

GDUFA II Commitment Letter
Generic Drug User Fee Amendments (GDUFA) was reauthorized on August 18, 2017

# How will the IID Evolve?

- IID Changes
  - Switch the metric measured from maximum potency to maximum daily exposure (MDE)
  - Select a single data standard for routes of administration, dosage forms, and units of measure (new data standards)
  - IID will identify changes and the information replaced
    - Update the IID on an ongoing basis, and post quarterly notice of updates made



# What is Maximum Daily Exposure (MDE)?

- **Maximum daily exposure (MDE)** is the maximum amount of excipient based on the **Maximum Daily Dose (MDD)** of the drug product
- MDE will replace maximum potency in the IID
- Applicants can reference excipient MDE to justify proposed excipient levels in ANDAs


## Implemented July 2019

- Improved IID accuracy and consistency
- Routes of administration (ROA) and Dosage Forms (DF) aligned with Structured Product Labeling (SPL)
- Units of measure (mg, %w/w, mg/mL) are standardized for each dosage form

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

# IID Change Log

The future **IID Change log** will track the following changes:

- Replacements
- Deletions
- Corrections

The main **IID page** will display the following:

- Excipient maximum potency or MDE for each excipient
- Identification of new entries and increases in maximum potencies and MDEs


CONTACT US

# Communication Channels

- Comments about the draft guidance *Using the Inactive Ingredient Database* should be submitted by 10/09/2019 to Docket No. FDA-2019-D-2397 at https://www.regulations.gov
- Information about recent changes to IID, go to IID Website FAQs
- Questions about information in the IID, contact us at our mailbox IIDUpdate@fda.hhs.gov
- Questions/corrections about excipient names, contact the GSRS staff at fda-srs@fda.hhs.gov
- Questions related to generic drug development should be submitted through controlled correspondence. Go to the draft guidance for industry at the following link https://www.fda.gov/media/109232/download

# Summary

- IID should be referenced in ANDAs
- IID is a list of excipients and their levels in FDA-approved drug products
- IID is used as a tool in drug development
- A guidance on using the IID is now available
- July 2019 IID included new data standards
- IID will change further in 2020 to include maximum daily exposure and a change log
- Applicants can contact FDA with excipient inquiries


Questions?
www.fda.gov

# Acknowledgements

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Thank you


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U.S. FOOD & DRUG
ADMINISTRATION