Inactive Ingredient Database (IID) Overview

Excipients and Formulation Assessments of Complex Generic Products: Best Practices and Lessons Learned
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Why is the IID Important to the Generic Drug Program?

Regulatory Requirement

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

IID Provides Evidence of Prior Approved Use

- Prior use in approved products is particularly important for ANDAs
- IID is used by FDA in application filing decisions
- IID is referenced during submission technical assessments
- IID is used by industry in excipient selection

Presentation Outline

1. IID and FDA's Generics Program
2. Introduction – IID Basics
3. IID Enhancements
4. Excipient Maximum Daily Exposure (MDE)
5. Stakeholder Feedback

What is the Inactive Ingredient Database?

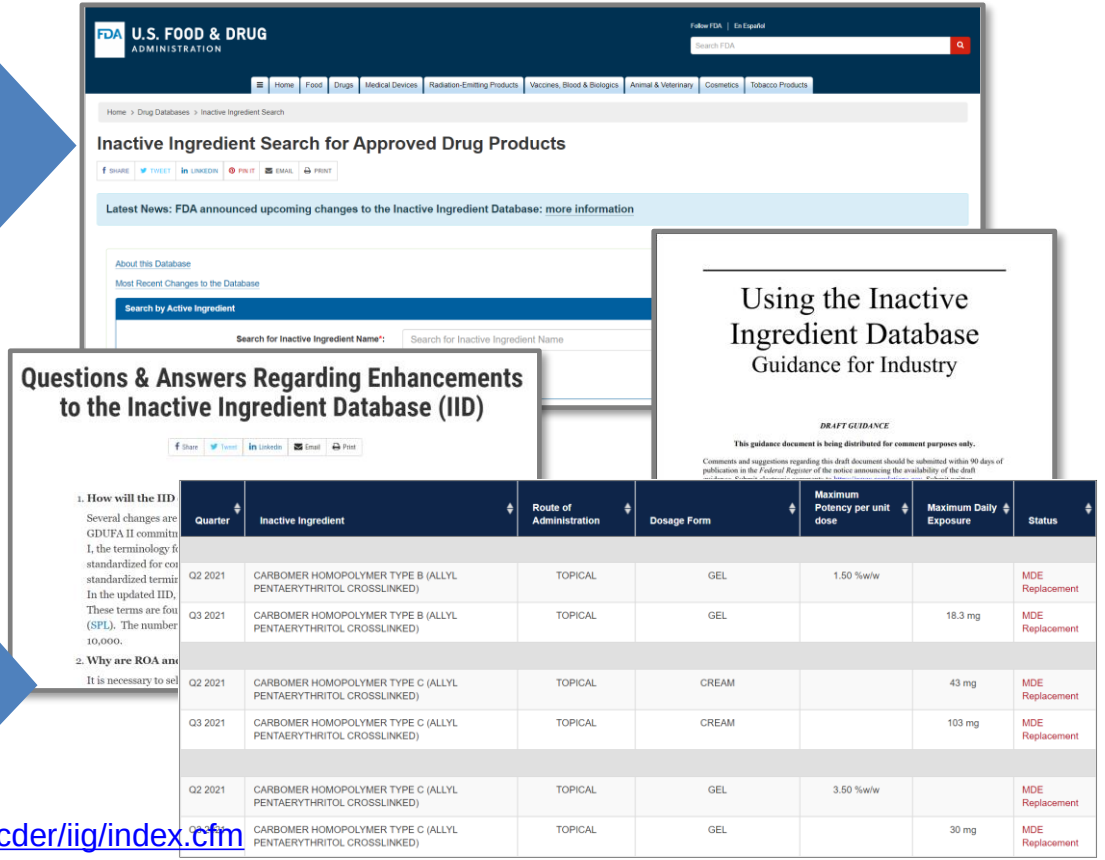
IID Basics

Introduction to the IID

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

Available IID resources:

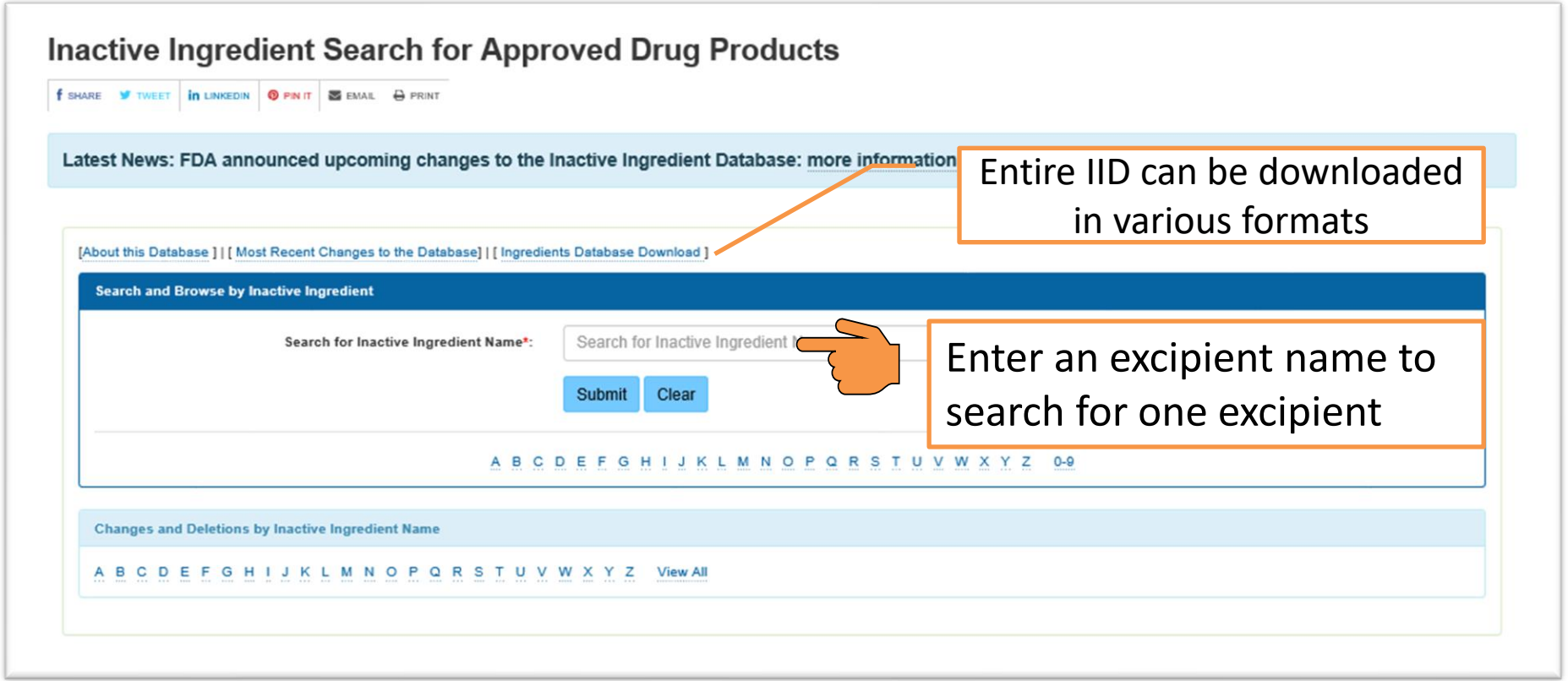
- IID FAQ
- Draft IID Guidance
- IID Quarterly Change Log



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

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/using-inactive-ingredient-database-guidance-industry

Where to find the IID



To access the IID, go to www.accessdata.fda.gov/scripts/cder/iig/index.cfm

IID Basics

Maximum Potency per unit dose

Maximum Daily Exposure (MDE)

Inactive Ingredient	Route	Dosage Form	CAS Number	UNII	Maximum Potency per unit dose	Maximum Daily Exposure (MDE)	Record Updated
CARBOMER HOMOPOLYMER TYPE C (ALLYL PENTAERYTHRITOL CROSSLINKED)	TOPICAL	CREAM		4Q93RCW27E		103mg	Y
CARBOMER HOMOPOLYMER TYPE C (ALLYL PENTAERYTHRITOL CROSSLINKED)	TOPICAL	CREAM, AUGMENTED		4Q93RCW27E	1%w/w		
CARBOMER HOMOPOLYMER TYPE C (ALLYL PENTAERYTHRITOL CROSSLINKED)	TOPICAL	EMULSION		4Q93RCW27E	0.6%w/w		
CARBOMER HOMOPOLYMER TYPE C (ALLYL PENTAERYTHRITOL CROSSLINKED)	TOPICAL	GEL		4Q93RCW27E		30mg	Y
CARBOMER HOMOPOLYMER TYPE C (ALLYL PENTAERYTHRITOL CROSSLINKED)	TOPICAL	LOTION		4Q93RCW27E	0.5%w/w		
CARBOMER HOMOPOLYMER TYPE C (ALLYL PENTAERYTHRITOL CROSSLINKED)	TOPICAL	OINTMENT, AUGMENTED		4Q93RCW27E	2.25%w/w		

record

Flag for new records

Displays one row per unique Excipient-RoA-DF combination

CAS is the Chemical Abstracts Service Registry Number
UNII is a unique code assigned by SRS

What are the IID's limitations?

- Does not provide the context of use for excipients
- Does not tell ANDA applicants what is in an RLD
- Does not include excipients in BLAs and OTC monograph products
- Does not provide a link between maximum potency and MDE

IID Enhancements

IID Enhancements under GDUFA

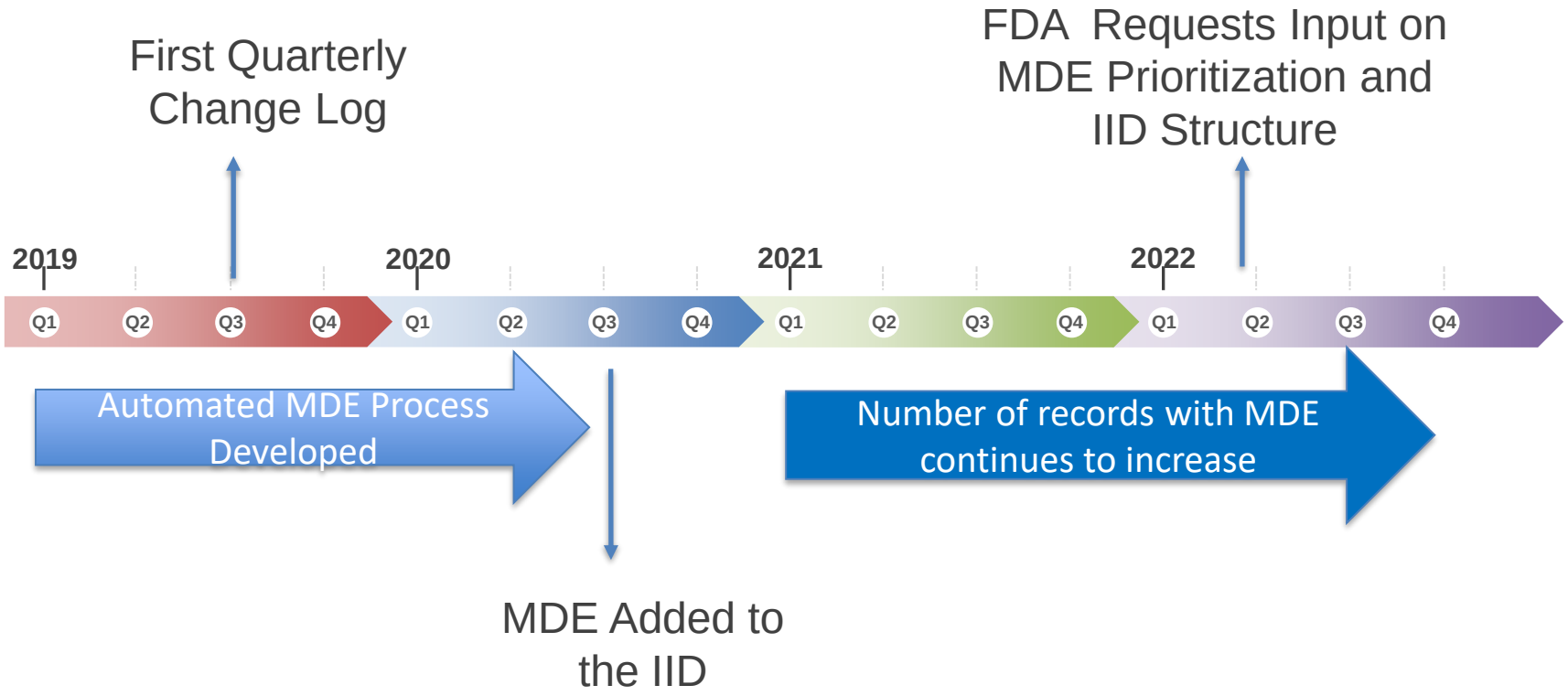
Commitment to enhance the IID brought gradual changes in 2018-2022

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.

Reauthorization of the Generic Drug User Fee Amendments (GDUFA) for fiscal years 2018-2022, See page 17, section G of the GDUFA II Commitment Letter

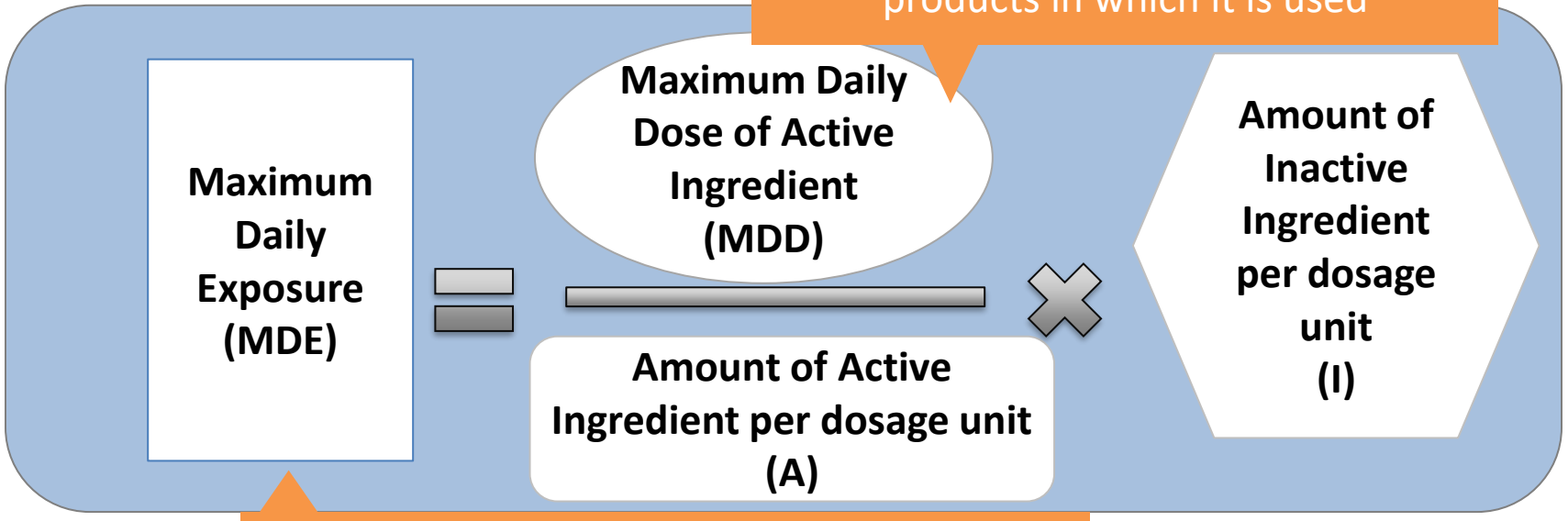
IID Enhancements 2019-2022



Excipient Maximum Daily Exposure

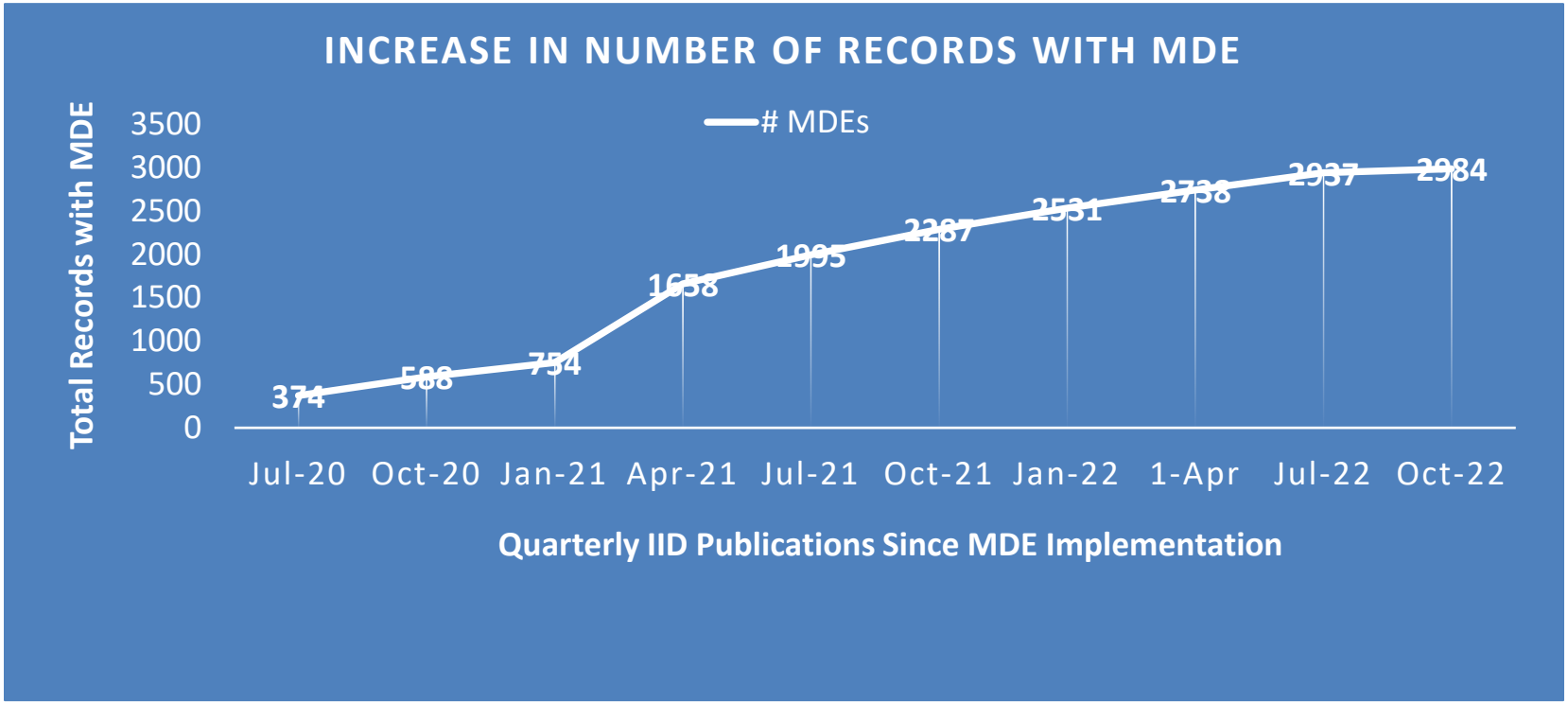
Excipient Maximum Daily Exposure

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 the Maximum Daily Intake (MDI) for oral drugs

Increase in Records with MDE Since 2020



Stakeholder Input on Next Steps

Docket Number: [FDA-2022-N-0236]

Stakeholder Feedback

Should dosage forms be eliminated?

- Most stakeholders said dosage form should be retained.
- Dosage form is important for development of new formulations.
- Route of administration is sufficient for oral products.

Which excipient categories should we prioritize?

- Focus on the most common excipients; those used in most products.
- Excipients unique to certain complex dosage forms.
- Specific excipient types: flavors, emulsifiers, polymers, surfactants.

Which excipients are of highest priority for MDE?

- Most stakeholders did not identify specific excipients by name.
- There was no majority opinion on which excipients to prioritize.

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

Many Thanks to the FDA IID Team

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