U.S. FOOD & DRUG ADMINISTRATION

ICSR Data Quality: Suspect Products

Sonja Brajovic
Medical Officer
Regulatory Science Staff, Office of Surveillance and Epidemiology
CDER | US FDA

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The information within this presentation represents the views of the presenter, not necessarily those of the FDA or any other referenced organization

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Learning Objectives

- Identify the *Technical Specifications* document pertinent to electronic Individual Case Safety Report (ICSR) submissions
- Understand data fields and data sources for ICSR product data elements
- Describe best practices in submitting suspect product information

Specifications for Electronic ICSRs*

Specifications for Preparing and Submitting Electronic ICSRs and ICSR Attachments

Technical Specifications Document

Associated Guidance Documents and Conformance Guide:

Draft Guidance for Industry: Providing Submissions in Electronic Format – Postmarketing Safety Reports (June 2014)

Guidance for Industry and FDA Staff: Postmarketing Safety Reporting for Combination Products (July 2019)

Draft Guidance for Industry: Providing Regulatory Submissions in Electronic Format: IND Safety Reports (September 2019)

Electronic Submissions of IND Safety Reports Technical Conformance Guide (September 2019)

*** Specifications for Preparing and Submitting Electronic ICSRs and ICSR Attachments** *Technical Specifications Document, available at* https://www.fda.gov/media/132096/download

Specifications for Electronic ICSRs: Drug Description

Detailed Description of Drug(s) and Narrative Elements*†

Element	DTD Descriptor 2.2	Length	Element Values for DTD 2.2
B.4.k.1	<drugcharacterization>	1N	1=Suspect 2=Concomitant 3=Interacting 5=Similar
B.4.k.2.1	<medicinalproduct>	70AN	Proprietary Medicinal Product Name
B.4.k.2.2	<activesubstancename>	100AN	Active Drug Substance Names
B.5.1	<narrativeincludeclinical>	20000AN	Case Narrative

* Include <medicinalproduct> and/or <activesubstancename>. FDA cannot process the ICSR without at least one of these elements.

† Appendix I lists various examples of correct drug element formats.

Specifications for Electronic ICSRs: Drug Description (2)

FDA

2. *Medicinal Product Name and Active Drug Substance Name*

FDA validates medicinal product names to the available Structured Product Labeling (SPL),[7] the submitted label (as ICSR attachment), and the Substance Registration System (SRS). These are further described below:

- When the product has an SPL, use the same naming convention as it appears in the SPL when submitting the ICSR.
- When submitting a product label as an attachment to an ICSR, use the name as it appears on the submitted product label.
- If no medicinal product is named and only the active substance is named, use the name of the active substance as it appears in the SRS.[8]

7. The SPL is a document markup standard approved by Health Level Seven (HL7) and adopted by FDA as a mechanism for exchanging product and facility information. See https://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
8. https://www.fda.gov/ForIndustry/DataStandards/SubstanceRegistrationSystem-UniqueIngredientIdentifierUNII/default.htm

Specifications for Electronic ICSRs: Drug Description (3)

Examples of Drug Element Format		Comment
Correct	<medicinalproduct>TYLENOL</medicinalproduct> <activesubstancename>ACETAMINOPHEN</activesubstancename>	The stated proprietary name in the <medicinalproduct> tag is the same as provided for structured product labeling (SPL) listing
Correct	<medicinalproduct>MIRACLE WONDER DRUG</medicinalproduct> <activesubstancename>ACETAMINOPHEN</activesubstancename>	The stated proprietary name is the same as provided in the product label
Incorrect	<medicinalproduct>AMAZING DRUG **OTC®**</medicinalproduct> <activesubstancename>ACETAMINOPHEN **500 mg**</activesubstancename>	Only the brand name and active substance should be listed in the <medicinalproduct> and <activesubstance> tags Any additional information should be captured in the relevant structured fields and not included as prefixes and suffixes in the drug name tags.
Incorrect	<medicinalproduct>NEW DRUG **40 mcg/mL**</medicinalproduct> <activesubstancename>NEWSUBSTANCE **Inj** </activesubstancename>	Only the brand name and active substance should be listed in the <medicinalproduct> and <activesubstance> tags Any additional information should be captured in the relevant structured fields and not included as prefixes and suffixes in the drug name tags.

FAERS Product Dictionary (FPD)

Main Data Sources for FPD

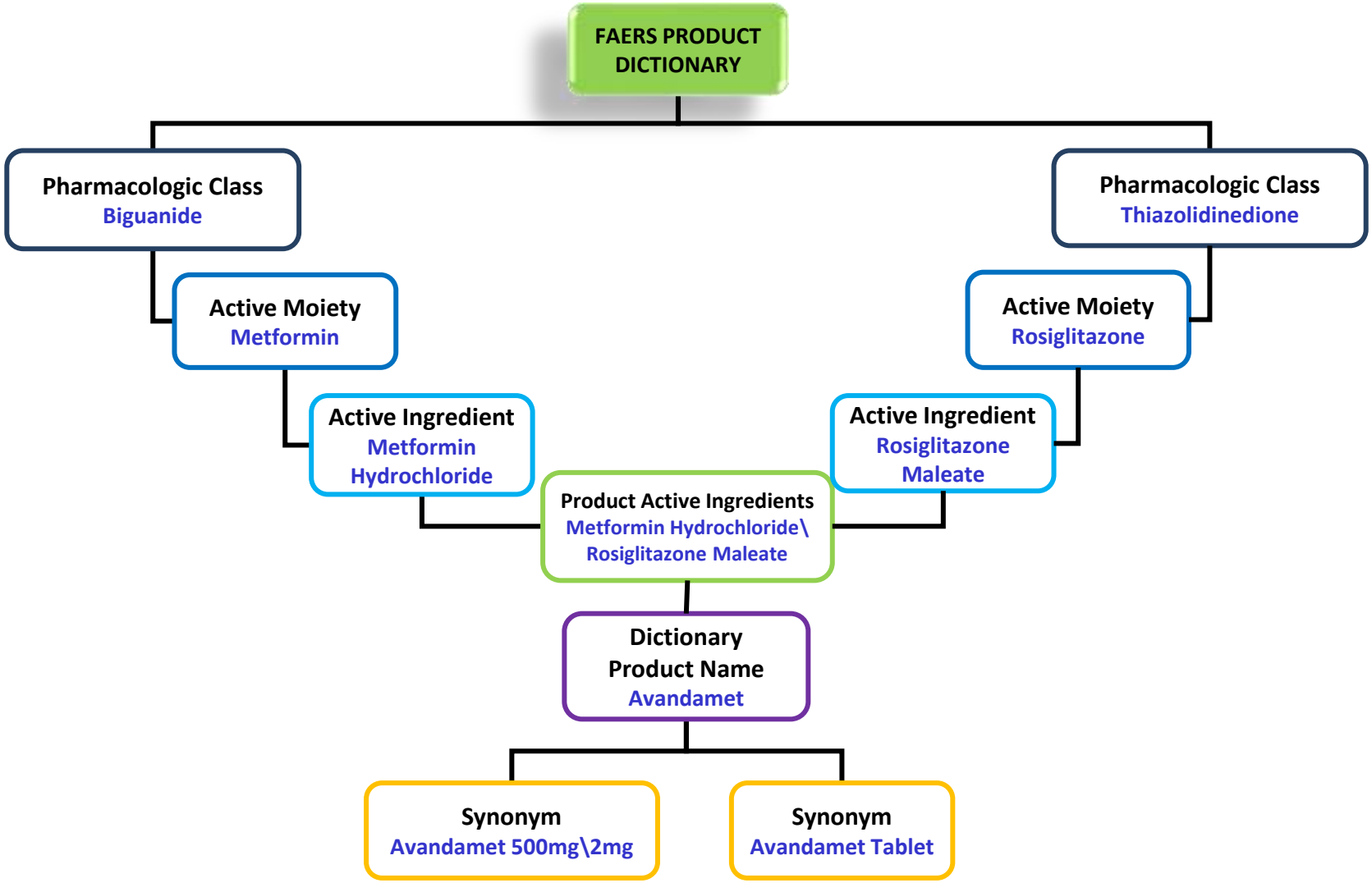
- Substance Registration System (SRS): active ingredient(s) for all products
  - 'Preferred name' for active ingredient, active moiety
  - SRS public database (NLM): https://fdasis.nlm.nih.gov/srs/

- Structured Product Labeling (SPL): US marketed products
  - Product name with active ingredient and moiety from SRS

- Foreign product names
  - WHODrug Global for the Product name
  - SRS for the Preferred name of the active ingredient

- Other sources

FAERS Product Dictionary Example: Multi-Ingredient Product



Examples of Suspect Products in ICSRs Submitted to FAERS

Issues with Reported Suspect Products

Suspect Product name contains additional product attributes/characters in the <*medicinalproduct*> field

- *IMUREL
- GLEEVEC TAB 400MG
- SAMSCA TAB 15MG
- QUTENZA 179 MG, CUTANEOUS PATCH
- LYRICA 50 MG CAPSULE
- LYRICA 50 MG, CAPSULE
- CO-VALSARTAN SANDOZ 80/12.5
- PIOGLITAZONE 15 MG
- PREGABALIN CAPSULES 75 MG

Issues with Reported Suspect Products

Suspect Product name in the <*medicinalproduct*> field or <*activesubstancename*> field is too vague


```
- <drug>
    <drugcharacterization>1</drugcharacterization>
    <medicinalproduct>IMMUNOGLOBULINS</medicinalproduct>
    <obtaindrugcountry>CA</obtaindrugcountry>
    <drugauthorizationcountry>CA</drugauthorizationcountry>
    <drugdosagetext>UNK</drugdosagetext>
    <drugadministrationroute>042</drugadministrationroute>
    <drugindicationmeddraversion>23.0</drugindicationmeddraversion>
    <drugindication>10070592</drugindication>
    <actiondrug>5</actiondrug>
  - <activesubstance>
      <activesubstancename>IMMUNOGLOBULINS</activesubstancename>
    </activesubstance>

    drugcharacterization>1</drugcharacterization>
    <medicinalproduct>CHEMOTHERAPY</medicinalproduct>
    <drugadministrationroute>065</drugadministrationroute>
    <drugstartdateformat>102</drugstartdateformat>
    <drugstartdate>20140115</drugstartdate>
    <actiondrug>4</actiondrug>
      </drug>
    - <drug>
    <drugcharacterization>1</drugcharacterization>
    <medicinalproduct>PAIN MEDICATIONS (MORPHINE AND THE LIKE)</medicinalproduct>
    <drugadministrationroute>065</drugadministrationroute>
    <actiondrug>5</actiondrug>
      </drug>
    - <summary>
```

Issues with Reported Suspect Products

Narrative and structured field(s) do not match

- Ingredient salt stated in narrative, structured field populated only with moiety
  - Issue: Products available as two different salts, or a moiety and a salt (i.e. short-acting versus long-acting) with different safety profiles
  - Example: olanzapine vs. olanzapine pamoate
- Family line of Products: “CURE ALL” and “CURE MUST” with different ingredients
  - Narrative specifies the exact product, but <*medicinalproduct*> field populated only with <CURE> and nothing provided in <*activesubstancename*>
- Inconsistency
  - Narrative: “… received magnesium sulphate”
  - Structured field: “Magnesium sulfonate”


```
- <drug>
    <drugcharacterization>1</drugcharacterization>
    <medicinalproduct>Magnesium-sulfonate</medicinalproduct>
    <drugstructuredosagenumb>4</drugstructuredosagenumb>
    <drugstructuredosageunit>002</drugstructuredosageunit>
    <drugdosagetext>4 gram, UNK</drugdosagetext>
    <drugadministrationroute>040</drugadministrationroute>
    <drugindicationmeddraversion>22.0</drugindicationmeddraversion>
    <drugindication>Product used for unknown indication</drugindication>
    <actiondrug>5</actiondrug>
  - <activesubstance>
      <activesubstancename>Magnesium-sulfonate</activesubstancename>
    </activesubstance>
  </drug>
```

Issues with Reported Suspect Products

Separate products reported as one multi-ingredient product (which does not exist as a single formulation):

- *"NIVOLUMAB, IPILIMUMAB"*
- *"IDELALISIB W/RITUXIMAB"*
- *"PERTUZUMAB/TRASTUZUMAB"*

➢ Separate products should not be listed together and need to be split

Issues with Reported Suspect Products

Suspect reported as a multi-ingredient of moiety and salts, or different salts (no such true product)

- Example XML Active Ingredient field:
  PREDNISOLONE\PREDNISOLONE ACETATE\PREDNISOLONE BUTYLACETATE\PREDNISOLONE CAPROATE\PREDNISOLONE HEMISUCCINATE\PREDNISOLONE PIVALATE\PREDNISOLONE SODIUM PHOSPHATE\PREDNISOLONE SODIUM SUCCINATE\PREDNISOLONE SODIUM SULFOBENZO\PREDNISOLONE SODIUM TETRAHYDRO\PREDNISOLONE STEAGLATE\PREDNISOLONE VALEROACETATE

- Example Narrative:

  "was on *metoprolol*"


```
  <actiondrug>1</actiondrug>
- <activesubstance>
    <activesubstancename>METOPROLOL</activesubstancename>
  </activesubstance>
- <activesubstance>
    <activesubstancename>METOPROLOL FUMARATE</activesubstancename>
  </activesubstance>
- <activesubstance>
    <activesubstancename>METOPROLOL SUCCINATE</activesubstancename>
  </activesubstance>
- <activesubstance>
    <activesubstancename>METOPROLOL TARTRATE</activesubstancename>
```

Issues with Reported Suspect Products

Non-unique suspect product name coded as the first option displaying in WHO-Insight

- *SERENASE Indication: acute anxiety*

SERENASE	*Haloperidol decanoate*
SERENASE	*Haloperidol*
SERENASE	***Lorazepam***

SERENASE [HALOPERIDOL DECANOATE]	Serenase	depot	Haloperidol decanoate
SERENASE [HALOPERIDOL]	Serenase		Haloperidol
SERENASE [LORAZEPAM]	Serenase		Lorazepam

Same Name/Different Ingredient Issue

Non-unique name (different drug ingredients): recommend to specify the ingredient as an addition to the reported drug name

- *CLAMOXYL [AMOXICILLIN]*
- *CLAMOXYL [AMOXICILLIN/CLAVULANATE POTASSIUM]*
- *SERENASE [LORAZEPAM]*
- *SERENASE [HALOPERIDOL]*

Summary

- Submitted suspect <*medicinalproduct*> and <*activesubstancename*> information is reviewed for data quality and coded internally
- When available, capture the SPL Proprietary name in the <*medicinalproduct*> field, capture the SRS Preferred name active ingredient in the <*activesubstancename*> field
- Ongoing informal feedback/communication with companies

Challenge Question #1

Which of the following statements is true?

A. There are no specifications on how to report drug data in ICSRs

B. A drug name always identifies a specific product

C. Drug information in the narrative and in the structured fields should match

D. It is not necessary to provide a suspect drug in an ICSR

Challenge Question #2

Which of the following statements is NOT true?

A. Suspect drug data submitted in ICSRs to FAERS is validated internally

B. ICSR Product name should match the name in SPL

C. ICSR Active substance name should match the Preferred term name in SRS

D. ICSR Drug data is correct, there are no issues

Challenge Question #2

Which of the following statements is NOT true? Fast forward, future preview:

A. Suspect drug data submitted in ICSRs to FAERS is validated internally

B. ICSR Product name should match the name in SPL

C. ICSR Active substance name should match the Preferred term name in SRS

D. ICSR Drug data is correct, there are no issues

Cannot select, all are true

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