Title II (DSCSA) – Implementation of Serialization

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FDA GUIDANCE UPDATES AND IMPACTS ON SERIALIZATION

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Disclosures

- The views expressed are my own and not those of FDA or any other entity.
- This presentation does not constitute legal advice. Legal questions should be posed to your own counsel.
- This presentation is based upon my current interpretations of the DSCSA and FDA's activities and guidance, which could change as information develops.

DSCSA Timeline

- **November 27, 2018**
  - Manufacturers and repackagers affix product identifier to each individual package and homogenous case
- **November 27, 2019**
  - Wholesale distributors may only engage in transactions involving products with identifiers (unless grandfathered); must verify product identifier before redistributing saleable returns
- **November 27, 2020**
  - Dispensers may only engage in transactions involving products with identifiers (unless grandfathered); suspect product investigation requirements include verifying product identifier of 3 packages/10% of suspect product and verifying lot numbers

2023

- Transaction Information (TI) and Transaction Statement (TS) transmitted in secure, interoperable, electronic manner in accordance with standards developed by a widely recognized international standards development organization
- Product identifiers transmitted in TI (and not required until then)
- Transaction History (TH) sunsets
- Systems and processes
  - For verification of product identifiers
  - To “promptly respond” with TI and TS in response to appropriate requests
  - To “promptly facilitate the gathering” of information necessary to produce TI back to manufacturer in response to appropriate requests

FDA Activity in the last 12 months

- Final Guidance on Product Identifier Requirements Under the Drug Supply Chain Security Act – Compliance Policy Guidance for Industry (Sept. 20, 2018)
- Final Guidance on Grandfathering Policy for Packages and Homogenous Cases of Product Without a Product Identifier (Sept. 20, 2018)
- Draft Guidance on Verification Systems Under the Drug Supply Chain Security Act for Certain Prescription Drugs (October 25, 2018) (Comments due December 24!)
- Draft Guidance Product Identifiers Under the Drug Supply Chain Security Act - Questions and Answers (Sept. 20, 2018)

FDA Activity in the last 12 months

- Draft Guidance on Waivers, Exceptions, and Exemptions from the Requirements of Section 582 of the Federal Food, Drug, and Cosmetic Act Guidance for Industry (May 9, 2018)
- Draft Guidance on Standardization of Data and Documentation Practices for Product Tracing Guidance for Industry (March 2, 2018)
- Draft Guidance on Definitions of Suspect Product and Illegitimate Product for Verification Obligations Under the Drug Supply Chain Security Act Guidance for Industry (March 2, 2018)
- Public meetings December 5-6, 2017, and February 28, 2018

But…

- Still no licensure regulations, now 3 years late, missed the most recent Semi-Annual Regulatory Agenda November 2018 deadline, and not yet at OMB
- No additional guidance on preemption promised at the February 28, 2018 public meeting

Some good news about serialization…

Grandfathering Final Guidance

- Addresses what product without identifier is “grandfathered” that may continue to sold
- Confirms industry position that product packaged after 11/27/2018 must bear identifier
- Applies to manufacturers and repackagers
- Grandfathering extends to expiry of product
- Clarifies that TS “is one indication that product was in the … supply chain” as of 11/27/2018

Product Identifier Enforcement Discretion Final Guidance

- Originally promulgated in July 2017 to give manufacturers an additional year to serialize
- Final guidance issued same day as Grandfathering Final Guidance
- Two guidances are aligned
- Original draft guidance contained problematic provisions now resolved with alignment

The process works!

- FDA listened to comments submitted
- Big improvements from the product identifier enforcement discretion draft guidance in July 2017 to the grandfathering draft guidance in November 2017
- Both guidances, once finalized, were improvements over their draft versions

Issues on the horizon

- A product without an identifier could be
  - Subject to a waiver, exception or exemption
  - Grandfathered
  - Suspect
- This is just part of the transition and will get better
  - Will likely need to build other business processes and SOPs to address issue
  - Need to think about what you will say to inspectors and auditors who don't "get it"
- Also, some products have been serialized for awhile, but
  - Identifiers may not comply with the DSCSA, may not be readable
  - Manufacturers and repackagers may not have easily accessible records of having affixed those identifiers which has implications for verification of suspect/illegitimate product and saleable returns

Some bad news about serialization…

Product Identifier Q&A
Draft Guidance

- Released September 2018
- Smaller issues
  - Linear bar codes stay (but may be running out of room on the label)
  - 2D barcode should be “near” human-readable if space permits (but if too close, can’t read)
- Much bigger issues
  - Timing – changing what goes on human-readable a few weeks before November 27, 2018 deadline
  - Wouldn’t be an issue if everyone was already following the Draft Q&A
  - But they aren’t

Draft Product Identifier Q&A
Question 3

3.How should machine-readable formats include the product identifier required by the DSCSA?

The product identifier must be included in a 2-dimensional (2D) data matrix barcode when affixed to or imprinted on a package and in a linear barcode or 2D data matrix barcode when affixed to or imprinted on a homogenous case.

What's missing from Question 3?

- What goes in the machine-readable?
- No discussion of how the machine-readable data carrier must "confor[m] to the standards developed by a widely recognized international standards development organization" (§ 581(14))
- No recognition that industry has widely adopted GS1 standards where a product's GTIN (with embedded NDC), serial number, lot number, and expiration date are encoded into the GS1 2D DataMatrix

Draft Product Identifier Q&A
Question 4

4.How should the human-readable portion of the product identifier required by the DSCSA be formatted to appear on the drug package label?

NDC: [insert product's NDC]

SERIAL: [insert product's serial number]

LOT: [insert product's lot number]

EXP: [insert product's expiration date]

Draft Product Identifier Q&A
Question 5

5. **Can the GS1 [GTIN] be used in place of the NDC to comply with the requirements for a human-readable NDC as part of the product identifier?**

> **No.** The product identifier on the [human-readable bar code] product label must contain the NDC. …
>
> "We note that a manufacturer or repackager ***may choose*** to utilize a GTIN to encode the NDC number in the machine-readable portion of the product identifier (2D data matrix barcode)." (emphasis supplied)

Draft Product Identifier Q&A
Questions 4 & 5 – The Problems

- Timing
- Contrary to current industry practice
- Not aligned with GS1 standards on HRI
  - “Choosing” to use the GTIN in your product identifier isn’t optional if you are following GS1 standards
- Implies that you should be serializing the NDC, not the GTIN
  - That’s not what industry has been doing
  - No international standard for serializing the NDC
  - Unlike the GTIN, the NDC isn’t unique at the trade item level
- Massive and expensive operational implications, especially to change machine-readable product identifier

Draft Product Identifier Q&A
Question 4 – Expiration Dates

- Human-readable interpretation of the 2D DataMatrix bar code should represent the expiration date as
  - YYYY-MM-DD with non-zero day if using only numbers, or
  - YYYY-MMM-DD if using alpha for month
- If space is a problem, human-readable may include only a year and month,
  - YYYY-MM if using only numbers, or
  - YYYY-MMM if using alpha for month

Draft Product Identifier Q&A
Question 4 – Expiration Dates

- Especially complicated because no alignment exists in the industry on expiry formatting
- Concerns with process

Temporary Solutions

- Many comments submitted!
  - FDA has incorporated comments submitted on other draft guidances when final guidance issued ; maybe they will here, too
  - But industry takes draft guidance very seriously -- lots of anxiety now about whether, in the meantime, to redo all the serialization just accomplished
- Guidance states “If the NDC is on the label in its FDA-assigned 3-segment format, a company may also voluntarily affix or imprint the associated GTIN on the label.”
  - So maybe keep GTIN where it is in HRI and put HR NDC somewhere else
- Address dispenser concerns about inability to read HRI
- Expiration dates should be clear and unambiguous
- Unfortunately, be prepared to argue with an inspector or auditor
  - It is only a draft
  - Guidances aren’t binding

Implementation of Serialization

FDLI Drug Quality and Security Act Conference

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Grandfathering Issues

- Starting to see serialized product now
- Required to transact solely in serialized product in 2020
- How do you know a product is grandfathered?
  - Reliance on transaction statement
  - Product arrives before data
  - 3Ts are at a central location/3rd party vendor, product at the pharmacy. 3rd party may be verifying
- Burdensome process and patient access issues

Bar Code Issues

- Manufacturers are not communicating product changes
- Unexpected barcodes can stop automated processes
- Not all stakeholders have 2D technology deployed
- New barcodes are being introduced (GS1 RSS Stacked) where there is not enough room
- Linear NDC’s are being left off in favor of 2D

Bar Code Issues Continued

- Colors are a problem
  - Some manufacturers are attempting to make the DSCSA Product Identifier barcode blend in with the marketing information on their packages by printing it in the same color.
- Placement problems
  - Barcodes were printed too close together, which makes it hard for workers to read whichever barcode they need to read.
  - Smudging, which can result from the ablated waste material being redeposited onto the package in the laser ablation process.
  - Some packages where the prescribing information outset attached to the package was blocking the DSCSA 2D barcode so it was unreadable or difficult to read.

Bar Code Data Content Issues

- Data content problems
  - 2017-Only 6.6% of packages ABC and McKesson scanned contained *usable* 2D barcodes, but 8% more contained *unusable* 2D barcodes. That implies that the *majority* of attempts at compliant 2D barcodes *are not actually usable for compliance*.
  - 2018-ABC and McKesson-20.7% of packages had usable barcodes with all four data elements
  - 2018-15.1% of homogenous cases had usable barcodes with all four data elements
  - If that percentage is maintained as the number of serialized products rises—and there is little reason to believe it won't—this is an indication that we have a serious problem in the industry.

Pending FDA Draft Guidance

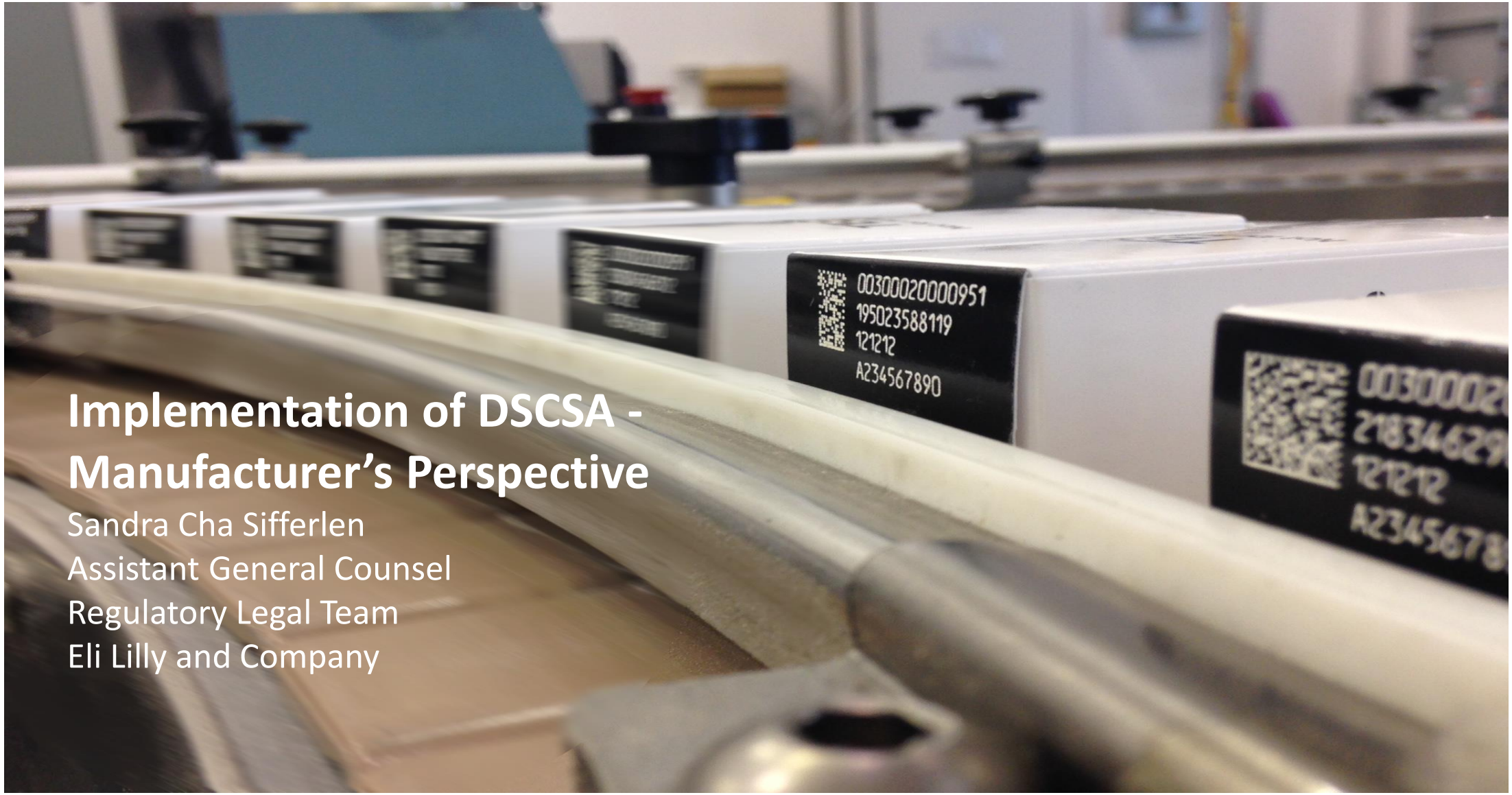
- Draft Guidance PI Q&A
  - Except for circumstances where current regulations already allow for manufacturers and repackagers not to use linear bar codes, the smallest saleable unit must have both the 2D and linear barcode
  - Recommending that the 2D barcode be placed near the human-readable portion, if space permits
  - Manufacturers and repackagers may want to place the PI on individual units even if the smallest saleable unit is a larger package

Error Handling with Aggregation and Inference

- Aggregation is not required by the DSCSA, but the statute contemplates its use once serialization occurs
  - Trading partners will need to know which unit-level serial numbers are contained in their shipments so they can include in their TIs and to assist with their receiving verification process.
- It is essential to making the DSCSA work
  - Pharmacies cannot scan or read each individual saleable unit to match the physical supply chain with the virtual supply chain

Error Handling with Aggregation and Inference

- Errors will occur particularly with manual packing
  - PI in the physical supply chain is not in the virtual supply chain and vice versa
    - Operational errors, such as unreadable bar codes
- Estimates of 4.5 billion units per year, so even high rates of accuracy will result in a lot of errors
- Industry is proposing that TS is not a statement of the accuracy of aggregation by manufacturers/wholesalers
  - The commissioned unit-level data from the manufacturer is the source of truth
- Industry proposes that authorized trading partners (ATPs) have controls in place to identify and resolve errors as early as possible, but leave the details up to the individual business
  - Request for FDA guidance to clarify how industry handles errors in inference/aggregation; call to permit stakeholders to resolve errors among themselves and only treat product with such errors as suspect/illegitimate where errors cannot be resolved.



Implementation of DSCSA - Manufacturer's Perspective

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DQSA and DSCSA

- The Drug Quality and Security Act of 2013–
- Title I - the Compounding Quality Act and Title II - the **Drug Supply Chain Security Act (DSCSA)**

- **PRODUCT TRACING – Manufacturer Requirements**
    i. prior to, or at the time of, each transaction in which a manufacturer transfers ownership of a product, manufacturer will provide the subsequent owner with transaction history, transaction information, and transaction statement, in a single document in paper or electronic format; and
    ii. capture TI/TH/TS for each transaction and maintain such information for not less than 6 years after the date of the transaction
- **PRODUCT IDENTIFIER –** manufacturer shall affix or imprint a product identifier to each package and homogeneous case of a product intended to be introduced in a transaction in commerce
- **AUTHORIZED TRADING PARTNERS** – trading partners of a manufacturer may only be authorized trading partners
- **VERIFICATION** – systems to comply with suspect and illegitimate product investigations and notifications

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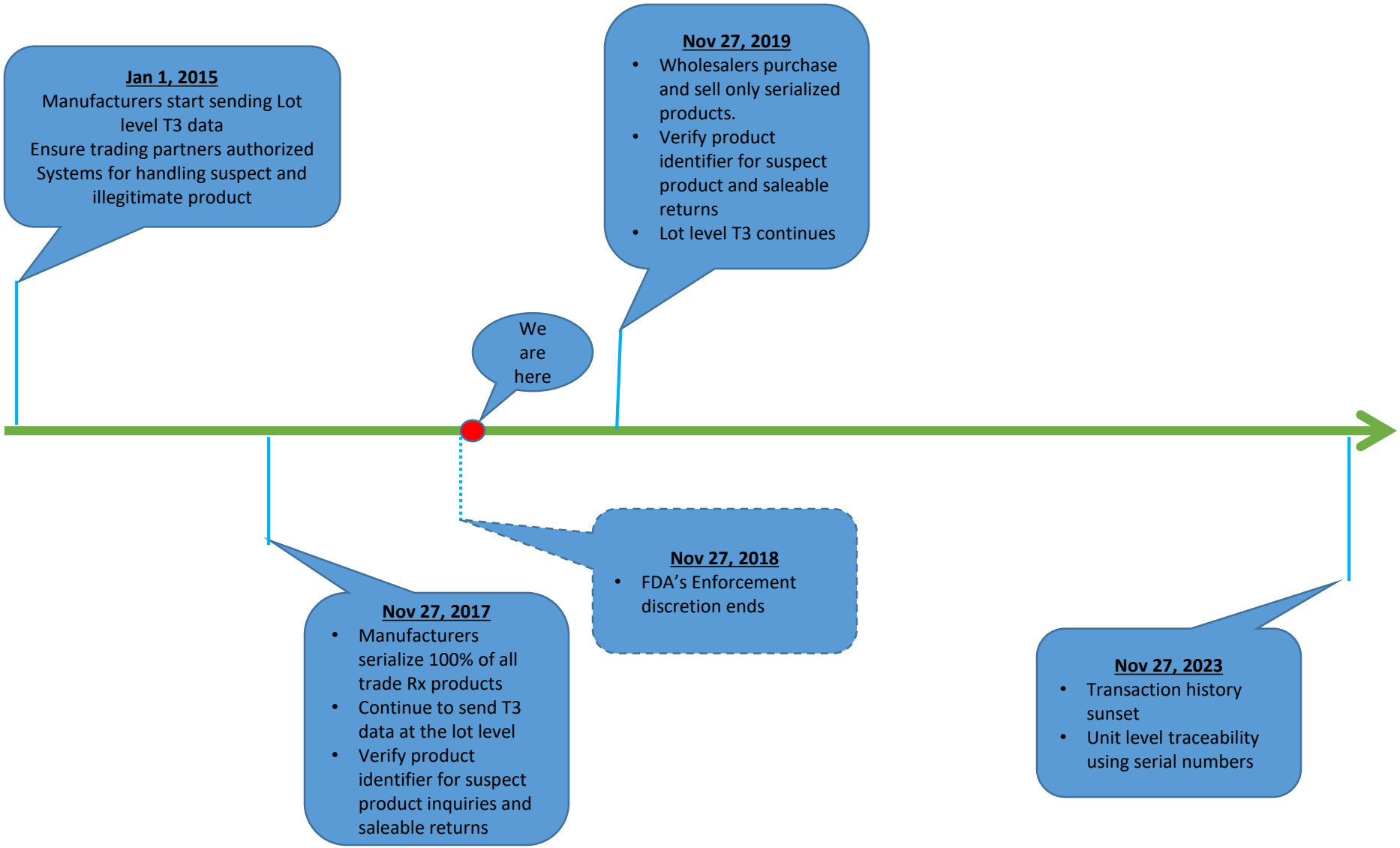
Upcoming phases of DSCSA



New Guidance documents

Guidance document	Release date	Deadline for providing comments
Draft guidance on Product Identifiers Under the DSCSA – Questions and Answers	9/19/18	11/19/18
Final guidance on Product Identifier Requirements Under the DSCSA – Compliance Policy	9/19/18	
Final guidance on Grandfathering Policy for Packages and Homogenous Cases of Product Without a Product Identifier	9/19/18	
Draft guidance of Verification Systems under the DSCSA	10/25/18	12/24/18

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DSCSA Implementation

Phase I

- ✓ Preemption of state pedigree laws
- ✓ Transaction Information, Transaction History and Transaction statement (TI, TH, TS) a.k.a T3 data
- ✓ lot level “product tracing”
- ✓ “Product Identifier” applied by manufacturer, includes SNI, lot # & expiration date
- ✓ Application of unique serial numbers from November 2017
- ✓ Illegitimate product notifications – Form 3911
- ✓ “Verification” of suspect and illegitimate product and saleable returns

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DSCSA Implementation

Phase II

- ✓ Unit level “Traceability” from Nov 2023
- ✓ Transaction history sunsets
- ✓ Self-effectuating provisions
- ✓ New FDA authority and responsibilities

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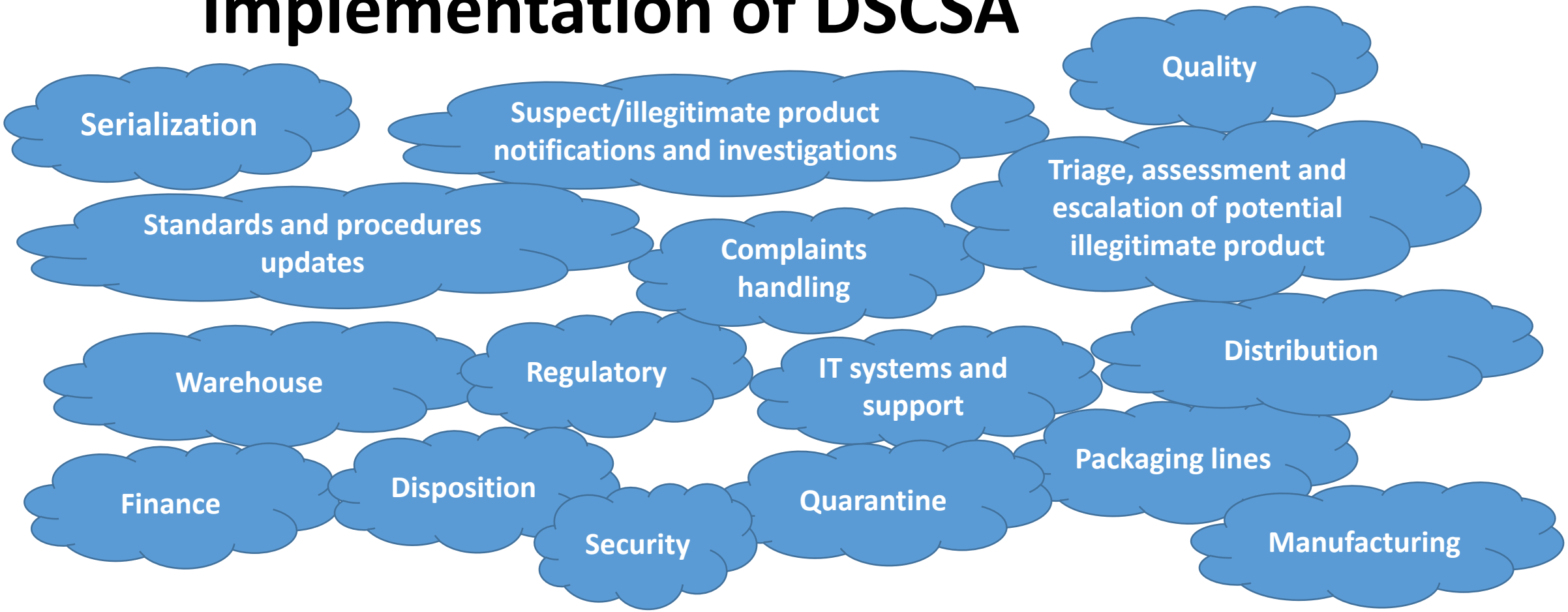
Implementation of DSCSA



Product Protection and Patient Safety

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Implementation of DSCSA

Strong cross-functional team

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Illegitimate product determination

- **Illegitimate product determination**. If trading partners determine a product is illegitimate, they must notify FDA and immediate trading partners
- Form 3911
- No more than 24 hours after the determination is made.
- **"High risk" determination – for manufacturers only**. Manufacturers have additional responsibility to notify FDA and immediate trading partners within 24 hours if a manufacturer has "reason to believe" that its trading partners may possess "a product manufactured by, or purported to be a product manufactured by, the manufacturer" and "there is a high risk that such product is an illegitimate product."

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Form 3911

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Drug Notification

Form Approved: OMB No. 0910-0806
Expiration Date: December 31, 2018
See PRA Statement on page 2.

Refer to instruction sheet (Form FDA 3911 Supplement) for more information.

1. Type of Report *(Select one)*: ☐ Initial Notification ☐ Follow-Up Notification ☐ Request for Termination

2. Incident Number *(Provide this number, assigned by FDA, if you selected Follow-up Notification or Request for Termination above; see instructions.)*

3. Date of Initial Notification to FDA *(mm/dd/yyyy)*	4. Date Company Determined Product Was Illegitimate *(mm/dd/yyyy)*	5. Classification of Notification *(Select from list)*

Description of Product

6. Name of Product as It Appears on Label

7. Primary Ingredients(s) *(if known)*

8. Drug Use *(Select from list)*	9. Drug Description *(Select from list)*

10. Strength of Drug	11. Dosage Form *(Select from list)*

12. Quantity of Drug *(Number and Unit)*	13. NDC Number *(if applicable)*	14. Serial Number *(if applicable)*

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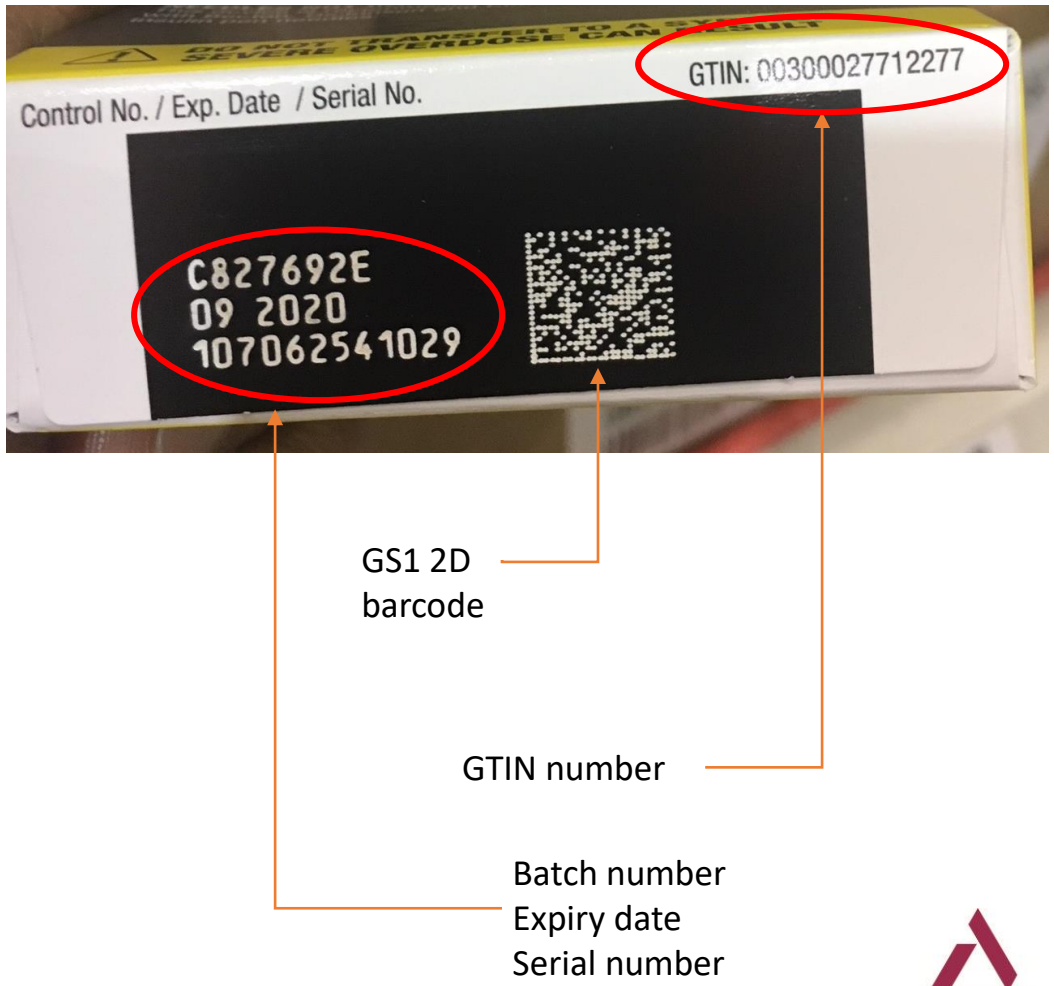
Serialization

- Solution based on GS1 standards:
  - Packaging lines capable of printing GS1 2D barcodes encoded with the following four standard data elements:
    - GTIN, batch number, expiry date and serial number
  - The information is also printed in the human readable text
  - Serialization starts at the “smallest saleable unit”, i.e. the smallest unit that a pharmacy can purchase
  - Aggregation of serial numbers from the smallest saleable units to the case and cases to pallet is part of the core solution, irrespective of the market requirement – this is done to keep a consistent process and also for internal efficiency in the manufacturing and shipping warehouses



Implementation Approach

Single Technical Solution

- Single technical solution, centrally supported, locally operated.
- Prioritized based on market deadlines.
- Aggregate at the case and pallet level, even if not required by the market.

Data Management

- Central serial number repository.
- Utilize enterprise system for data.
- Utilize a data broker for contract manufacturer produced data (feeding into Lilly enterprise).
- Utilize a data broker for transmitting to downstream partners and MoH systems.

Operating in a Serialized State

- Modify existing systems to handle serialized products.
- New lines will be built with serialization integrated.
- Warehouse Management systems designed to work with serialization processes.

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Thoughts on implementation

- Single global solution helped in consistency of processes and provided efficiency in managing changes for new markets and software updates.

- Built a pilot packaging line during the initial stages of the program which tremendously helped in the quick deployment at the packaging sites. New recipes/classes are built, tested and qualified on the pilot line first which minimized the line down time at the packaging sites during implementation.

- Took a broad approach and integrated serialization from level-1 throughlevel-5 systems and made sure serialization is incorporated to all the processes starting from the packaging line all the way to the distribution warehouse in a streamlined fashion.

- Cross-functional teamwork needed, impacting multiple organizations and spanning multiple geographies. Departments starting from manufacturing, warehousing, distribution and affiliate supply chain went through OCM (Organizational Change Management) to incorporate serialization and traceability into their business processes.

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And a few learnings -

- Any opportunities for standards vs. specific requirements aids in implementation. Requirements that deviate from GS1 standards create an impact to the serialization solutions and take time and effort to implement. Deviating from a harmonized approach also creates implementation challenges without added benefit for patient protection.

- Early engagement, first within the company and also with industry and regulators help to highlight importance of harmonization.

Looking forward

- Multi-faceted approach will always be needed
- Continued need for strong cross-functional teams
- 2019 then 2023 challenges ahead (verification systems, interoperability)
- Global harmonization
- Governance – Ensure appropriate people access system, verification standards in place, handling of vendors, security of systems to prevent hacking, data integrity, antitrust concerns
- Guidance needed now to put systems and standards in place for 2019 and 2023
- Security of the supply chain and protection of patient safety

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рахмат
danke
謝謝
ngiyabonga
teşekkür ederim
spas
Баярлалаа
mersi
kia ora
barka
welalin
tack
mahalo
tapadh leat
спасибо
faafetai lava
vinaka
blagodaram
dank je
misaotra
matondo
paldies
grazzi
спасибі
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thank you
gracias
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nanni
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dhanyavad
mauruuru
köszönöm
asante
manana
obrigada
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bedankt
hvala
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didi madloba
ありがとう
tanemirt
grazie
najis tuke
terima kasih
rahmet
ευχαριστώ
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shukriya
mercé
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kam sah hamnida
rahmat
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