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# PRODUCT TESTING FOR LOT RELEASE ACTIVITIES

**12 November 2019**

**Centre for Quality Control**

**National Pharmaceutical Regulatory Agency (NPRA)**

**Ministry of Health, Malaysia**

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# OUTLINE

- Objectives of Extension of Scope
- Current Lot Release Activity
- Proposed Extension of Lot Release  Activity
- Product Testing
- Temperature Monitoring for Sample Submission
- Sample Submission
- Issuance of Lot Release Certificate
- Fee Charges
- Proposed Implementation

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# OBJECTIVES

- **To conduct appearance, particulate contamination & solubility testing on all registered vaccines & plasma products involved with Lot Release activities**

➢**To fulfil WHO recommendation during pre-assessment workshop in April 2017**

➢**To conduct minimum testing since not all NRA/NCL conduct full testing on the product**

➢**Physical appearance test is a mandatory test conducted by the NRA/NCL of ASEAN neighbouring countries**

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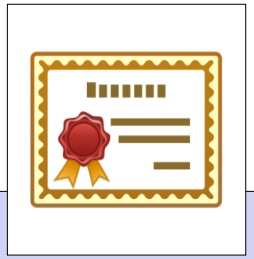
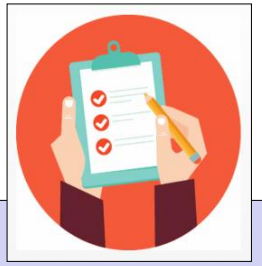
# CURRENT LOT RELEASE ACTIVITIES



**Recognise release certificate from the responsible National Regulatory Authority**



**Evaluation of manufacturer's summary protocol**

**Cold chain inspection upon product arrival at warehouse**

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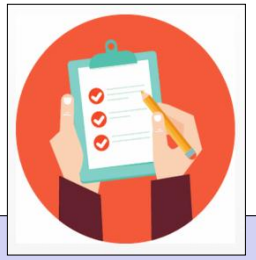
# PROPOSED LOT RELEASE ACTIVITIES

**Recognise release certificate from the responsible National Regulatory Authority**



**Evaluation of manufacturer's summary protocol**

**Cold chain inspection upon product arrival at warehouse**

**Product testing**

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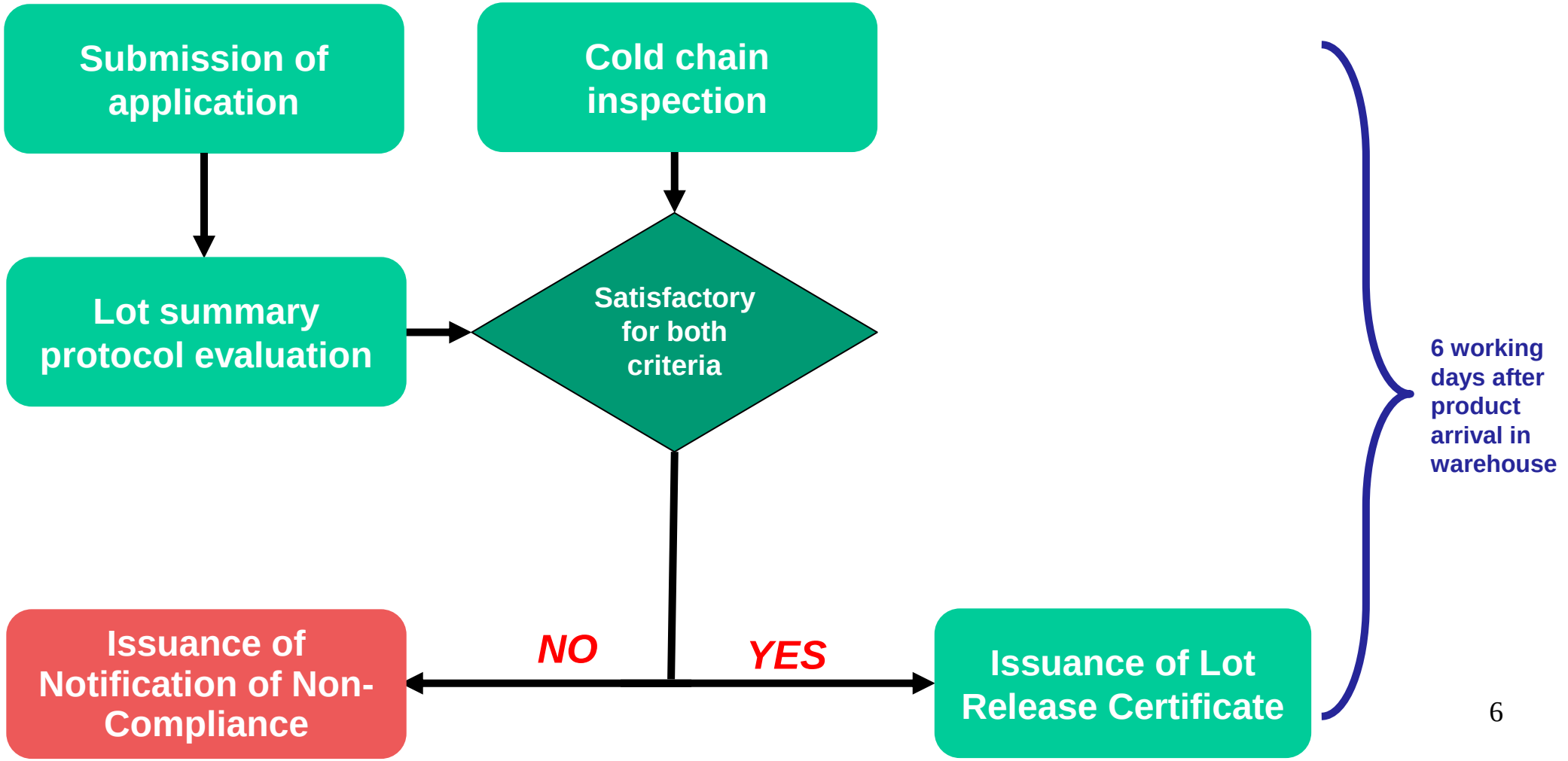
# CURRENT LOT RELEASE PROCESS FLOW

**14 working days before product arrival**



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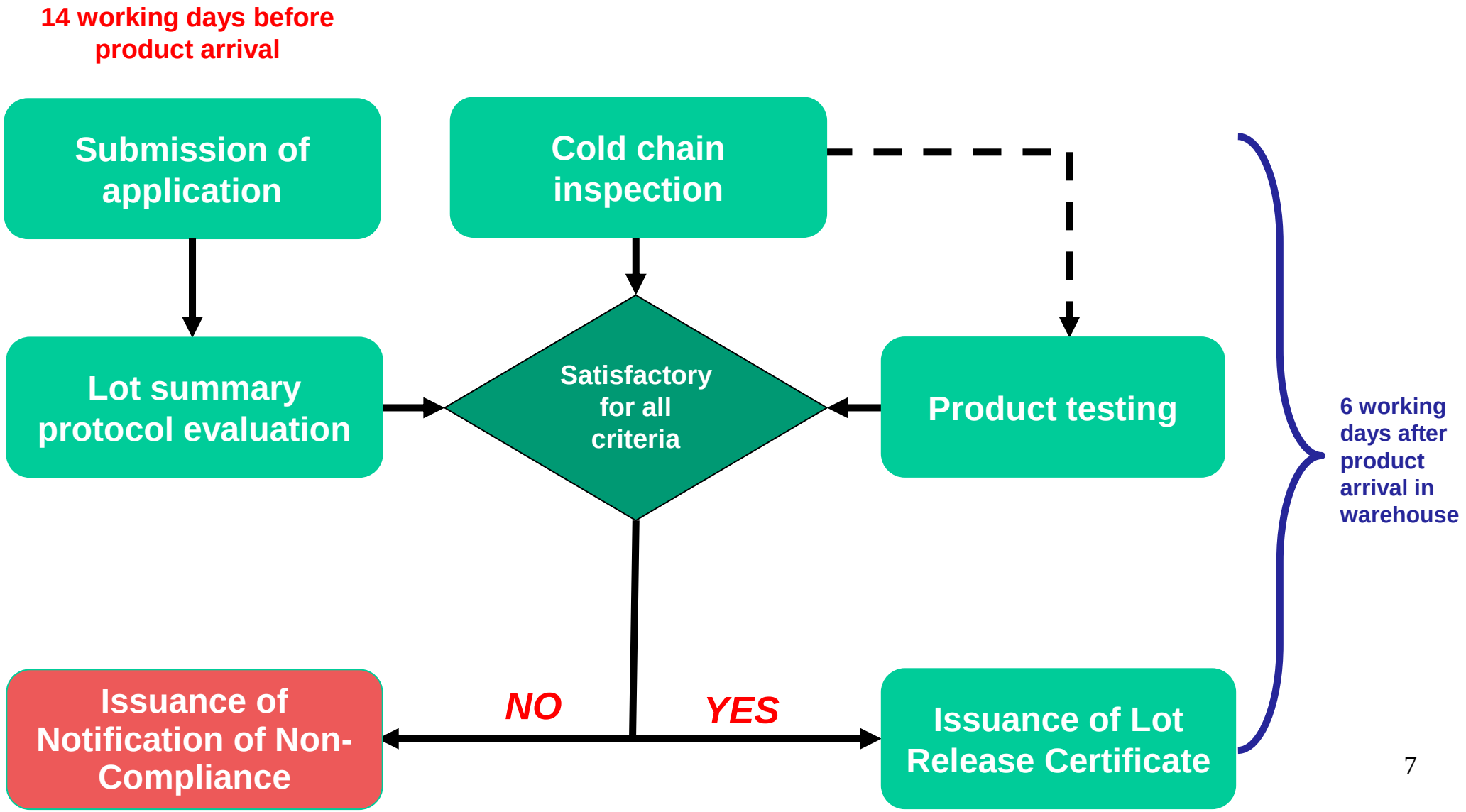
# PROPOSED LOT RELEASE PROCESS FLOW



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# PRODUCT TESTING

**Type of testing conducted depends on the dosage form of the finished products**

| Dosage Form | Testing |
|---|---|
| Solution/Liquid | 1. Appearance<br>2. Particulate contamination (visible particles) |
| Freeze Dried/Lyophilized | 1. Appearance<br>2. Solubility<br>3. Particulate contamination (visible particles) on reconstituted finished product |

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# PRODUCT TESTING (CONT.)

- All testing will be conducted in NPRA laboratory
- Physical appearance and solubility testing will be based on latest approved product test method and specification available in Quest
- Particulate contamination testing will be conducted based on:

  a) EP* (Chapter 2.9.20, Particulate Contamination: Visible Particles)
  b) USP** (Chapter 790, Visible Particulates in Injections)

- Testing will be conducted on **EVERY** batch of the products
- Testing will be conducted for the first shipment of the same lot of products
- However, if temperature excursion detected during cold chain inspection for the same lot on the 2nd/3rd importation, testing will be carried out again as part of the investigations

***European Pharmacopeia**
**** United States Pharmacopeia**

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# TEMPERATURE MONITORING

**TEMPERATURE MONITORING**

Products submitted for testing adhere to the latest approved storage temperature requirements

Temperature monitoring devices or indicators shall be attached together with the products during transportation

The same data logger that was used for the shipment of the product or use different data logger for the sample submission for testing purpose

- Data logger will be deactivated once the samples are received in NPRA and the data logger will be returned to the PRH
- The temperature recording will be downloaded by the PRH and to be sent to NPRA's officer through e mail

**Remark:**
**As we are giving allowance for PRH to use the same data logger accompanying products from country of origin, the time required to set up data logger can be saved.**



**However, if it is still not manageable, the PRH may send the samples any time convenient to them but the timeline to issue the LRC will no longer within 6 working days.**

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# TEMPERATURE MONITORING (CONT.)

NPRA has the absolute rights to reject any products that do not comply with the latest approved storage temperature

Note: CCM card (3M strip) can only be used for international shipment of OPV packed with dry ice. They have no other function (Reference: How to Monitor Temperatures in the Vaccine Management Handbook Module VMH-E2)

For more information on handling of cold chain products, please refer to:

a) Guideline on Good Distribution Practice (GDP) 3rd edition, January 2018
b) Annex 1 of GDP: Management of Time and Temperature Sensitive Product

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# SAMPLE SUBMISSION

- For multidose packaging, random sampling will be done from the secondary packaging and 3 samples will be chosen from 1 secondary packaging
- Sampling for diluent (if applicable) will be conducted randomly
- PRH to pack and send the selected 3 samples (with diluent if applicable) by NPRA inspector with completed sample submission application form
- Sample can be submitted to NPRA within working hours (from 7.30 am to 6.00 pm, from Monday to Friday). Notifying the NPRA officer in charge before sample submission would be an added advantage

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# SAMPLE SUBMISSION (CONT.)

- Timeline for sample submission:

| LOCATION OF WAREHOUSE | WITHIN (WORKING DAYS) FROM THE DATE OF COLD CHAIN INSPECTION |
|---|---|
| **Within Klang Valley** | **ONE (1)** |
| **Outside Klang Valley** | **TWO (2)** |

- Samples submitted for testing will be stored based on latest approved storage temperature of the product in NPRA laboratory

- Samples can be hand delivered by PRH or via courier service

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# ISSUANCE OF LOT RELEASE CERTIFICATE

- Lot release certificate will be issued by NPRA if **ALL** the criteria below are **SATISFACTORY**:

  - evaluation of lot summary protocol
  - cold chain inspection
  - product testing

- Based on the current practice, lot release certificate will be issued within 6 working days from the product arrival in warehouse (subjected to the satisfactory status of lot summary protocol evaluation and cold chain inspection)

- This timeline (6 working days from the product arrival in warehouse) for the lot release certificate issuance **shall be maintained** for the additional lot release activity which involves product testing

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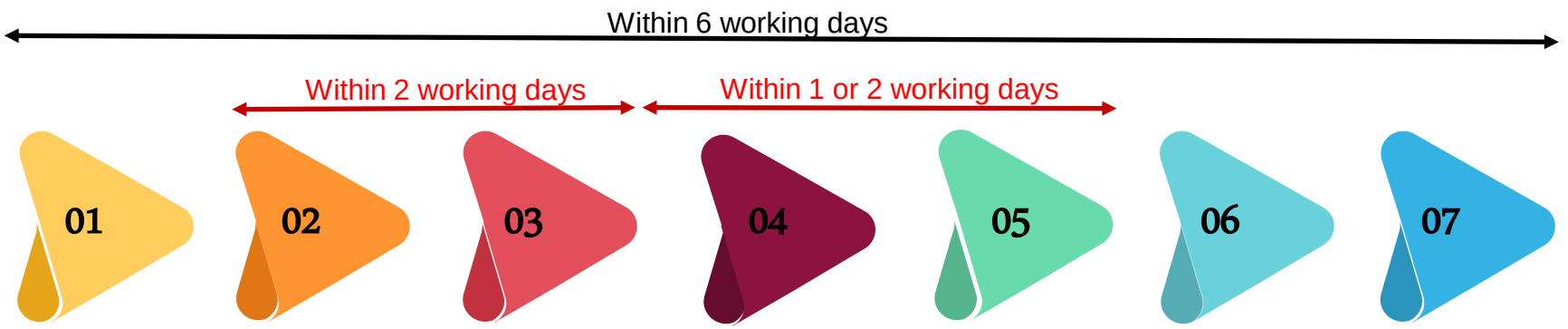
# ISSUANCE OF LOT RELEASE CERTIFICATE (CONT.)




**01** Product arrival at warehouse

**02** Warehouse re-palletise the pallet shipper

**03**
- NPRA conduct cold chain inspection & sampling
- One data logger will continue recording the sample temperature
- NPRA seal the sample and attach data logger onto it

**04** PRH/ warehouse send sealed sample in cool box to NPRA

**05**
- NPRA will stop the data logger upon receiving
- Data logger will be hand over to PRH / warehouse for downloading

**06** PRH / warehouse email the data logger reading to NPRA

**07** Lot Release Certificate will be issued if all criteria found to be satisfactory:
1. LSP review
2. Cold chain inspection
3. Sample testing within specification

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# FEE CHARGES

- **NO** fee implementation for product testing until further notice by NPRA

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# PROPOSED IMPLEMENTATION

| DATE | ACTIVITY |
|---|---|
| December 2019 – March 2020 | Pilot Study (*) |
| April 2020 | Implementation of Extension of Lot Release Activities |

*** ALL registered vaccines and plasma products imported are subjected to this pilot study**

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