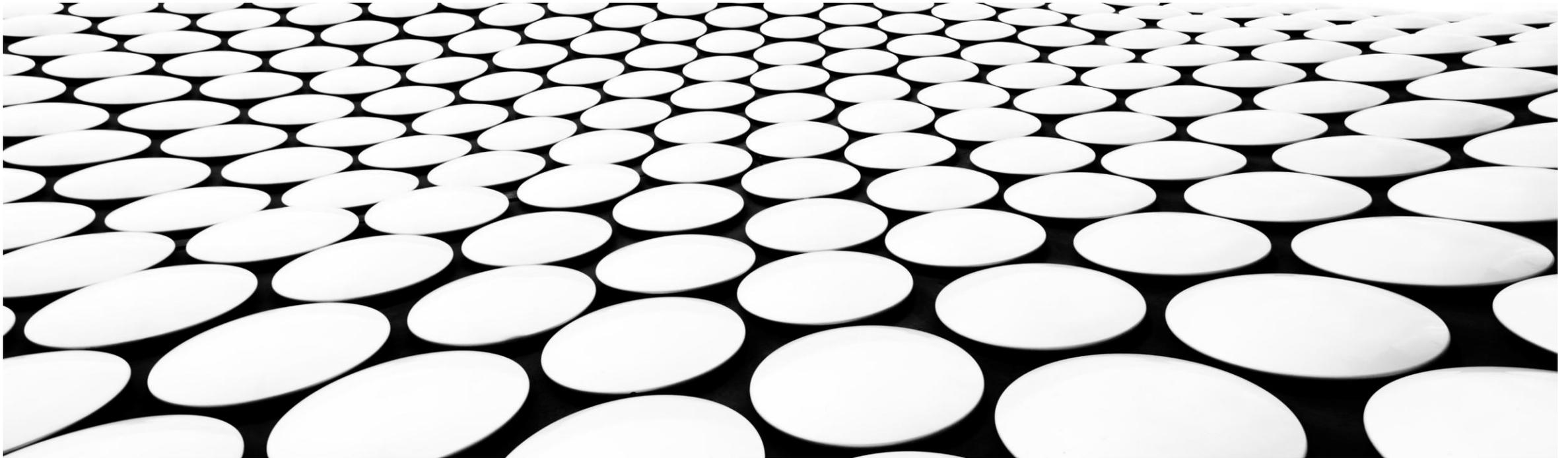

OUTCOME OF GVP INSPECTION IN MALAYSIA VOLUNTARY PHASE (2023-2024): PRELIMINARY KEY FINDINGS & TRENDS



GOOD PHARMACOVIGILANCE PRACTICE (GVP) INSPECTION IN MALAYSIA

- ❑ GVP Inspection is aimed to ensure that the Product Registration Holders (PRHs) or any parties employed by PRHs that are involved in any pharmacovigilance activities comply with the pharmacovigilance obligations and guidance laid out in the Malaysian Guidelines on Good Pharmacovigilance Practices (GVP) for PRHs, as well as post-registration safety-related requirements imposed by the NPRA.

Voluntary Phase of GVP Inspections in Malaysia

- ❑ Initiated by NPRA as part of the progressive implementation of GVP inspections.
- ❑ The voluntary phase allows NPRA to identify and address potential gaps and challenges prior the full implementation of GVP Inspections in the future.

GVP INSPECTION JOURNEY

Attachment training with UK MHRA

2017

Drafting Malaysian GVP Guidelines & GVPI Pilot study (4 PRHs: 3 MNC & 1 Local manufacturer)

2018-2019

Consultation with stakeholders (UPC) on the draft of Malaysian GVP Guidelines

2020-2021

Publish Malaysian GVP Guidelines, 1st Edition

Aug 2021

Announcement of GVPI Voluntary phase, risk-based assessment & publishing Malaysian Guidance Document On Voluntary GVP Inspection

2022

Initiation of GVP Inspection (Voluntary phase)

2023-2024

Keyword:

GVPI: GVP inspection

MNC: Multinational company

PRH: Product registration holder

SELECTION OF PRHS TO BE INSPECTED



*4 PRHs, assessed as lower risk, were not selected for inspection

- Product-related factors
(category of products, patient exposure, special conditions for registration)
- PRHs-related factors
(number of products marketed, any PV concern, discrepancies in PVSS)
- PV system-related factors
(number of ADRs received, experience of RPPV, complexity of PV system)

Keyword:

PRH: Product registration holder

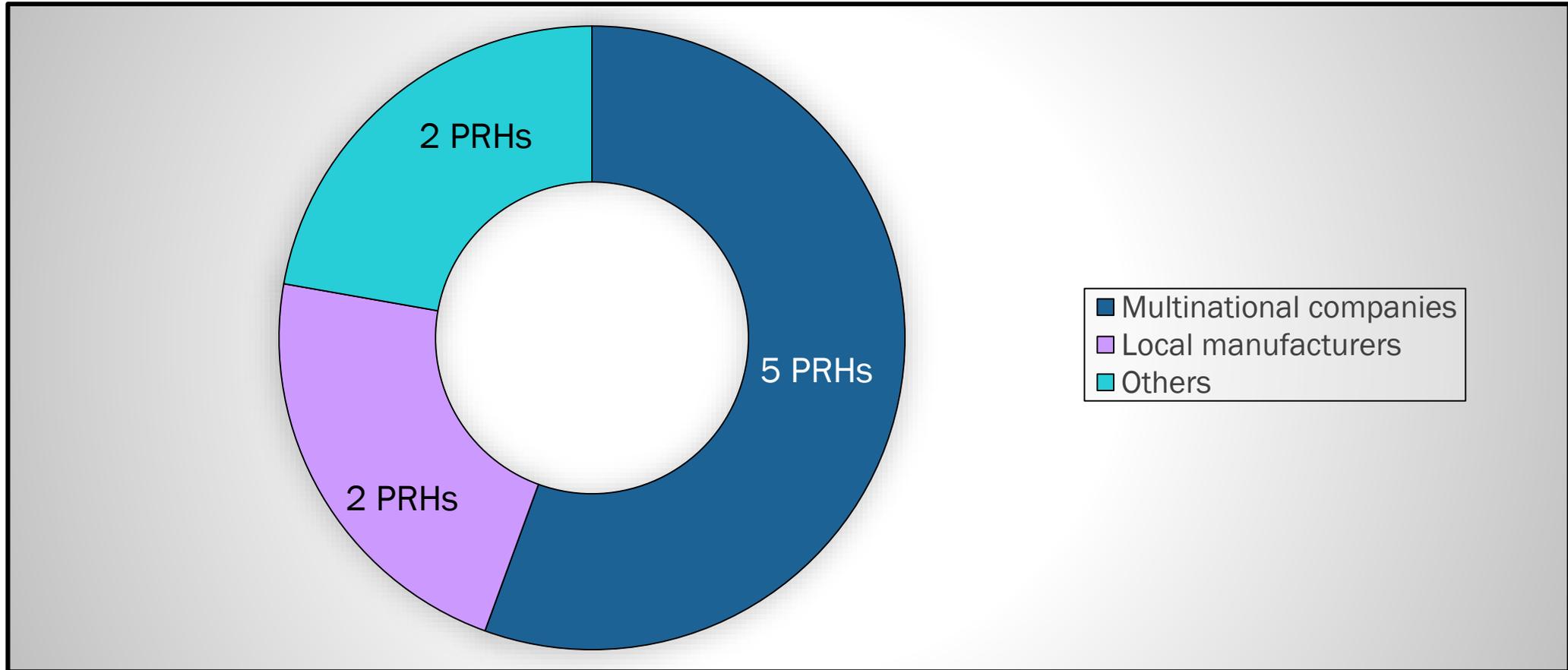
PV: Pharmacovigilance

PVSS: PV System Summary

RPPV: Responsible person for PV

TYPES OF INSPECTED COMPANIES

Total number of PRHs inspected = 9 PRHs (2023: 4 PRHs, 2024: 5 PRHs)



PRH: Product Registration Holder

Others: Refer to companies other than multinational companies / local manufacturers that become the PRH in Malaysia

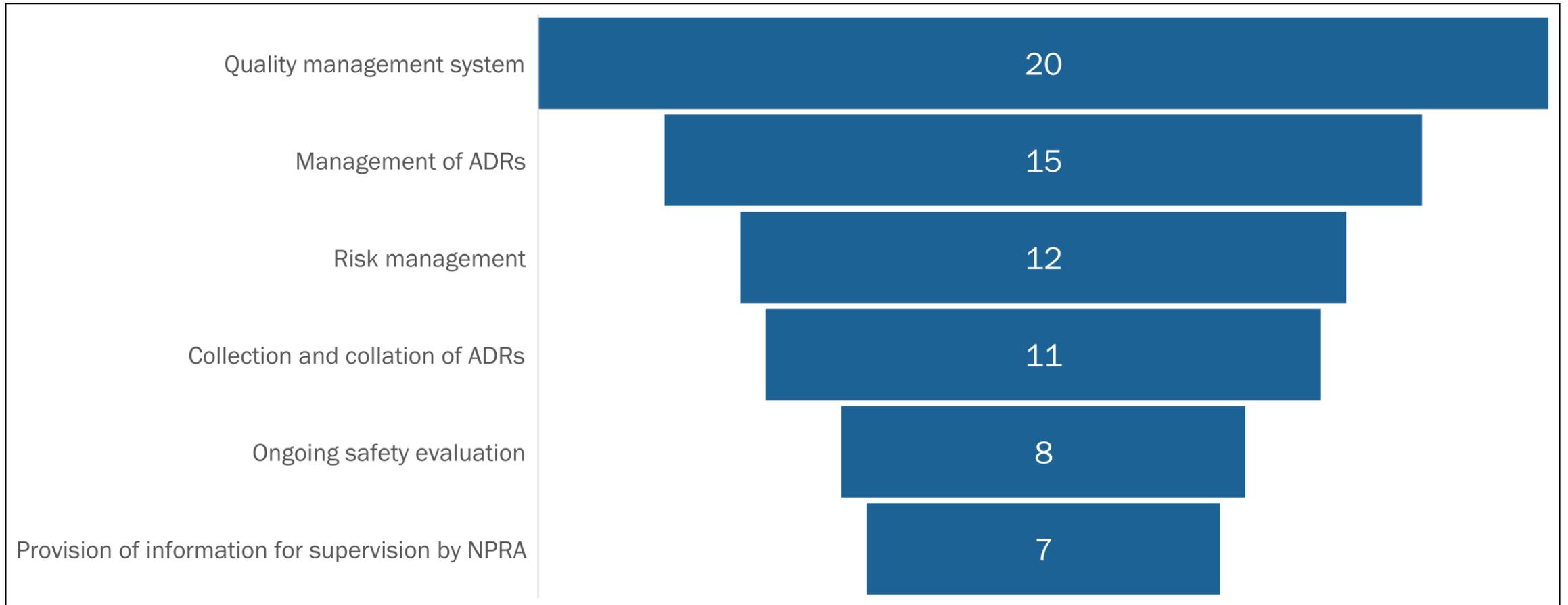
CATEGORISATION OF GVPI FINDINGS BASED ON PV TOPIC

| TOPIC | SUB-TOPIC |
|--|---|
| Collection and collation of adverse drug reactions | Spontaneous sources of safety data, e.g. medical information, product quality complaints, screening of internet, mass media, others |
| | Literature searching, reconciliation from source of ADRs |
| | Solicited sources of safety data (including patient support or market research programmes) |
| | Safety data exchange agreements |
| | Surveillance system for pregnancy & breastfeeding |
| Management of adverse drug reactions | Case processing: data entry, coding, assessment, follow-up and reporting, |
| | Data management, including migration of safety data |
| Ongoing safety evaluation | Signal management |
| | Periodic safety update reports (PSUR)/ Periodic Benefit Risk Evaluation Report (PBRER), Issue-Related Summary Report (IRSR), Monthly Safety Summary Report (MSSR) |
| Risk management | Management of additional PV activities in Part III of the RMP (e.g. PASS, targeted follow-up questionnaires) |
| | Maintenance of authorised product information (Package Insert/RiMUP) |
| | Additional risk minimisation measures in Part V of the RMP |
| | RMP maintenance |
| | Safety communication –DHPC, Emerging safety issue (ESI) notification |
| | Special Conditions for Registration |

CATEGORISATION OF GVPI FINDINGS BASED ON PV TOPIC

| TOPIC | SUB-TOPIC |
|--|---|
| Quality management system | Procedures, record management, PV training, PV contracts, archiving |
| | PV Audit and deviation management, including CAPA management |
| | PV system oversight and governance, including performance monitoring and role of the RPPV |
| | Information technology systems and applications |
| | RPPV, RPPV back-up arrangement, local contact person details, etc |
| Provision of information for supervision by the NPRA, including via inspection | Inspection readiness |
| | PVSS/ PSMF management |
| | Submission of information to the NPRA |

TOTAL NUMBER OF FINDINGS ACCORDING TO PV TOPICS



COMMON GVP INSPECTION FINDINGS ACCORDING TO PV TOPIC

| PV Topic | Common findings |
|-------------------------------------|---|
| Quality management system | <ul style="list-style-type: none"> • No SDEA/PV agreement with third parties involved in PV activities (e.g. distributor/ product owner) • Lack of PV training to PV/ non-PV personnel involved in PV activities • Not conducting PV audit on third parties/ own subsidiaries involved in PV activities |
| Collection & collation of ADR/AEFIs | <ul style="list-style-type: none"> • Lack of surveillance system on special situation populations (e.g. pregnant woman, breastfeeding, etc.) • Deficiencies in reconciliation procedure & conducting reconciliation from sources of safety data (third parties, patient-support program, etc.) • No procedure and activity regarding literature screening for local ADR reports |
| Management of ADR | <ul style="list-style-type: none"> • Failure to submit valid ADR reports within timelines • Lack in conducting & documenting follow-up activities for incomplete ADR reports • Failure to submit follow-up ADR reports to NPRA • Deficiencies in the procedure for handling duplicated ADR reports • Deficiencies in managing/updating local ADR log or databases causing missing data during information/data request |

Note: The findings presented above are examples based on those identified during the voluntary phase of GVP inspections and do not reflect all findings from the voluntary inspections.

COMMON GVP INSPECTION FINDINGS ACCORDING TO PV TOPIC

| PV Topic | Common findings |
|--|--|
| Risk Management | <ul style="list-style-type: none"> • Not submitting <i>Risalah Maklumat Ubat untuk Pengguna</i> (RiMUP) to the NPRA • No procedures for Direct Healthcare Professional Communication (DHPC) Letter management • No procedure and not submitting emerging safety issue (ESI) notification to NPRA, including those issues received from third parties • No monitoring of the timeline from the date the variation was approved until implementation of safety updates to package insert |
| On-going safety evaluation | <ul style="list-style-type: none"> • No procedure on preparation and management of Issue Related Safety Summary (IRSR) for generic products • No evidence of performing any signal detection activities • Late submission of Periodic Benefit Risk Evaluation Report (PBRER) |
| Provision of information for supervision by the NPRA, including via inspection | <p>Lack of PSMF content:</p> <ul style="list-style-type: none"> • Inaccurate and inconsistent information with procedures or related documents • Not describing/listing all third parties involved in PV activities • Inaccurate list of registered products in the annex • Description on required sections are not clear • Unable to demonstrate PV system performance for key PV activities |

Note: The findings presented above are examples based on those identified during the voluntary phase of GVP inspections and do not reflect all findings from the voluntary inspections.

Good Observations during GVP Inspection

1

All PRHs demonstrated strong commitment to the program including preparation of CAPA report for identified findings

2

Some PRHs have successfully developed their own PV system without external guidance, demonstrating that the Malaysian GVP Guidelines, 1st Edition is a practical & effective framework

3

The majority of PRHs were able to provide the requested documents/response within the specified timelines (before, during & after the inspection)

Good Observations during GVP Inspection

4

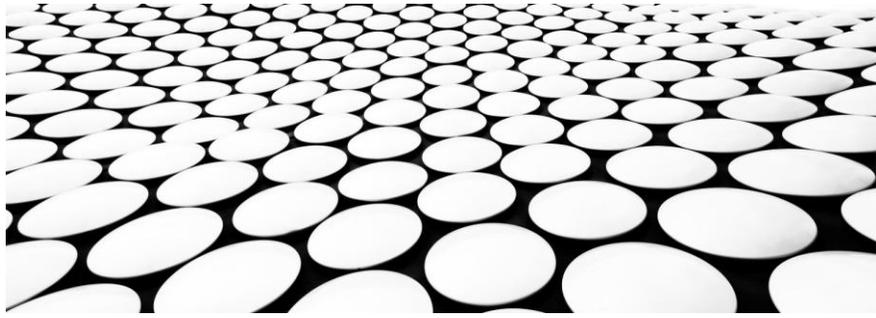
All PRHs demonstrated professionalism during interviews & maintained courteous conduct throughout inspection

5

All PRHs demonstrated a positive attitude by making full efforts to comply to the requirements

6

All inspections were conducted according to the inspection plan and PRHs adhered to the scheduled timeline



SUMMARY

- ❑ The majority of findings were related to the Quality Management System (QMS), followed by the Management of Adverse Drug Reactions (ADRs) & Risk Management topics.
- ❑ A higher number of findings were also observed in areas such as the Collection and Collation of ADRs, particularly among local manufacturers.
- ❑ NPRA acknowledges the excellent commitment demonstrated by all inspected PRHs in successfully completing the inspection.