Guidelines for Pharmaceutical Manufacturers/Importers, Marketing Authorisation Holders and Parallel Trade Authorisation Holders on Managing Alerts Generated in the Verification and Decommissioning of Medicinal Products in the Bulgarian Medicines Verification System

I.   Legal Framework

Pursuant to the provisions of Directive 2011/62/EC and Delegated Regulation (EU) 2016/161, since February 9th, 2019 all stakeholders in the legal drug supply chain – MAHs, manufacturers, wholesalers, parallel importers, wholesale traders and pharmacies, as well as the Bulgarian Medicines Verification Organization (BgMVO) and the National Competent Authorities are responsible for fulfilling their obligations.

According to the provisions set in Art. 272b of the Medicinal Products in Human Medicine Act (MPHMA) (No. 67 of 2020) all participants in the drug supply chain have the obligation to perform the actions specified in Delegated Regulation (EU) 2016/161; BgMVO is obliged to create and manage a National Repository under Art. 32.1.b of Delegated Regulation (EU) 2016/161, to serve the territory of the Republic of Bulgaria; the national competent authorities are designated as follows: the Bulgarian Drug Agency (BDA) - for the purposes of supervising the operation of the repository and investigating suspected cases of falsification, as well as for the purposes of pharmacovigilance or pharmacoepidemiology and the Ministry of Health, National Health Insurance Fund and the Council, according to Art. 258, para. 1 of MPHMA - for the purposes of payment for medicinal products with public funds.
Manufacturers of prescription medicines and omeprazole must ensure the correct uploading of the data on the serialized packs of medicinal products (Product Master Data (PMD) and Product Pack Data (PPD) into the European hub.

According to Art. 68a of the Medicinal Products in Human Medicine Act (No. 67 of 2020), the holder of a marketing authorization (MAH) is obliged to ensure the uploading of the unique identifier of each pack according to the provisions of Art. 168, para 8.1 in the repository in accordance with Delegated Regulation (EU) 2016/161.
According to MPHMA, Art.160, para.11, Art. 164a and Art 217, Para 6, Onboarding Partners/Marketing Authorisation Holders and Parallel traders are obliged to place on the secondary packaging, and if there is no such - on the primary packaging of the Medicinal Products, defined in Delegated Regulation (EU) 2016/161, the safety features under Art. 168, para 8: to ensure the uploading of the unique identifier (UI) for each pack in the repository in accordance with the Delegated Regulation.

According to Art. 284a Para 2 of MPHMA, if an OBP/MAH fails to fulfil the obligations set in the MPHMA (N 67 of 2020) or in the Delegated Regulation (EU) 2016/161, they shall incur a fine in the amount of BGN 5,000 to 10,000, and in case of repeated violation - a fine in the amount of BGN 25,000 to 50,000.

According to Art. 18 of Delegated Regulation (EU) 2016/161 „Where a manufacturer has reason to believe that the packaging of the medicinal product has been tampered with, or

the verification of the safety features shows that the product may not be authentic, the manufacturer shall not release the product for sale or distribution and shall immediately inform the relevant competent authorities."

II.   Types of alerts

Detailed information on the alerts received in the European Medicines Verification System is included in the document - EMVO_0402 *EMVS Alerts and Notifications*, uploaded in the OBP portal of the European Medicines Verification Organization.

National systems generate and send alerts to the European Hub. The European hub records the alerts and sends them to the MAH's client systems.

The alerts received by the MAHs are as follows:

Alert Code	Alert Message
A2	*"Batch not found". An alert has been raised.*
A3	*"Serial Number not found". An alert has been raised.*
A7	*"Pack Already Dispensed"/"Pack Already Decommissioned". An alert has been raised.*
A24	*"Pack Already Decommissioned". An alert has been raised.*
A52	*"Expiry Date mismatch. An alert has been raised.*
A68	*"Batch Id mismatch". An alert has been raised.*

When scanning the unique identifier (UI), it is possible to receive alerts in the Medicines verification system caused by procedural or technical errors by the MAH or by the end users - wholesalers and pharmacies (Annex 1: Summary table of alerts and possible technical and procedural causes for their generation).

The occurrence of alerts caused by technical reasons should in no case be a barrier for the supply of medicines to patients or lead to problems in the normal supply of medicines in Bulgaria. However, it places even more responsibility on the OBP/MAH to eliminate technical errors in order to identify alerts related to possible falsifications.

III.   Alert processing by the OBP/MAH

1.1 Alerts caused by MAHs errors

The OBP/MAH must ensure that the alerts are not caused by their error, for example caused by the failure to upload a batch in the system, a partially uploaded batch in the system, a batch uploaded with incorrect data or other alerts due to technical or procedural reasons.

If the alerts are found to be the result of technical or procedural errors by the OBP/MAH, the OBP/MAH shall take immediate action to correct the problem. Packs from the batch may not be dispensed until the technical problem has been rectified.

If the OBP/MAH does not have the technical capacity to correct the cause of the alert, the OBP/MAH shall notify the Bulgarian Drug Agency (BDA) and the BgMVO, providing information about the problem, including the reasons for its occurrence, the corrective and preventive actions taken, and shall inform all participants in the drug supply chain of the problem and the ability to generate alerts.

1.2 Alerts caused by errors by the end-users

If the received alert is found to be the result of technical or procedural errors by the end-user, the OBP/MAH may suspend their work related to the alert.

The alerts processed by the OBP/MAH under Section 1.1 and Section 1.2, which are assumed to be the result of technical malfunctions in the barcode reader or the software of the end-user or of technical or procedural reasons by the OBP/MAH may be put together in a table (for a period from one to four weeks) and sent to BgMVO by e-mail to office@bgmvo.org . The information should be included in an Excel sheet (Annex 2: *Sample table for summarizing alerts caused by technical errors*).

1.3 Alerts where the cause cannot be determined

To assist in the investigation of alerts for possible falsification, the OBP/MAH may promptly send inquiries to the BgMVO by e-mail to office@bgmvo.org.

BgMVO shall process the inquiry and respond to it within 5 working days. During this period BgMVO shall contact the end-user to obtain a photo of the unique identifier (UI) of the pack and clarify the reason for the alert.

Inquiries by the MAH to the BgMVO must contain the following information for investigating the alert:

- Alert Date
- Alert ID/ UPRC
- Error Code
- Product Code
- Product Name

- Batch ID
- Serial Number
- SN Length
- Expiry Date
- Market ID
- Comment.

If the investigation confirms the absence of a technical or procedural error by the OBP/MAH or the end-user, the OBP/MAH shall inform the Bulgarian Drug Agency by e-mail to: falsifiedmedicines@bda.bg that there is possible falsification according to Art. 18 of Delegated Regulation (EU) 161/2016. BDA shall investigate the case and take the necessary legal actions.

IV. Inquiries by BgMVO to OBP/MAHs

When asked by a wholesaler or pharmacy about the reason for the generated alert, BgMVO shall investigate the alert. In case no technical error by the end-user is identified, BgMVO shall send an inquiry to the OBP/MAH.

In the case of an **A2 alert (“*Batch not found. An alert has been raised***.”)** and if the OBP/MAH confirms that the scanned batch number was generated by them but not uploaded to the system, the OBP/MAH must take immediate action to upload the batch number in the system and inform BgMVO.

In the case of an **A3 alert** *(“Serial Number not found. An alert has been raised.”*) and if the OBP/MAH confirms that the scanned serial number was generated by them but not uploaded to the system, the OBP/MAH must take immediate action to upload the serial number in the system and inform BgMVO.

In the case of an **A68 alert (“*Batch Id mismatch***. *An alert has been raised.”*)** and if the MAH confirms that the data discrepancy is caused by their error, the OBP/MAH must immediately eliminate the problem by updating the batch number in the system and shall inform BgMVO.

In the case of an **A52 alert** (“*Expiry Date mismatch. An alert has been raised.”*) and if the MAH confirms that there is a discrepancy in the data, the MAH must immediately eliminate the problem by updating the date indicating the expiry date in the system and shall inform BgMVO. Packs from the batch may not be dispensed until the technical problem has been rectified.

In the case of **A7 and A24 alerts**, the MAHs shall send information to the BgMVO in the cases when the reason for the generation of the alerts is repeated attempts to decommission packs that are in the possession of the OBP/MAH. BgMVO shall process the A7 and A24 type alerts on a weekly basis and report to the BDA the alerts caused by a broken drug supply chain.

If the OBP/MAH does not have the technical possibility to correct the cause of the alert, the OBP/MAH shall notify the Bulgarian Drug Agency (BDA) and BgMVO, providing

information about the problem, including the reasons for its occurrence, the corrective and preventive actions taken, and shall inform all participants in the drug supply chain of the problem and the ability to generate alerts.

If the MAH confirms that the data on the packaging have not been generated by them, the MAH shall inform the BgMVO by e-mail to office@bgmvo.org and the BDA by e-mail to falsifiedmedicines@bda.bg that there is possible falsification. BDA shall investigate the case and take the necessary legal actions.

ANNEX 1: *Summary table of alerts and possible technical and procedural causes for their generation*

	A2	A3	A7/ A24	A32	A52	A68
	"Batch not found. An alert has been raised."	*"Serial Number not found. An alert has been raised."*	*"Pack Already Dispensed"/ "Pack Already Decommissioned. An alert has been raised."*	*"Duplicate Serial Number"*	*"Expiry Date mismatch. An alert has been raised."*	*"Batch Id mismatch. An alert has been raised."*
MAH Errors in batch	Batch data not uploaded. Batch data uploaded with errors.	Batch uploaded with incomplete data.	Updates of product data.	Not applicable, because the European Hub does not allow MAHs to upload duplicated serial numbers.	In most cases, the issue impacts the whole batch. All end-users who are scanning packs that belong to this batch will generate alerts. This will result in high number of alerts.	Batch number uploaded with errors in the system.
End-user Errors in hardware	Device does not read correclty the UI (unique identifier) on the pack at scanning.	Device does not read correclty the UI (unique identifier) on the pack at scanning.	Double-click of scanning device which generates two or three consecutive alerts within a few seconds.	Double-click of scanning device at bulk verification.	Scanning device misreads expiry date on the pack. The number of alerts is small - one to two alerts.	Device does not read correclty the UI (unique identifier) on the pack at scanning.
End-user Errors in software	Parsing issues - software does not extract correctly the information from the UI (unique identifier). Field with batch number contains data from previous scans. Additional information in the UI (unique identifier) of the pack that is not required for the Bulgarian market. **NB!** IT provider-related errors can impact many end-users using the services of the same provider.	Parsing issues - software does not extract correctly the information from the UI (unique identifier). Field with batch number contains data from previous scans. Additional information in the UI (unique identifier) of the pack that is not required for the Bulgarian market. **NB!** IT provider-related errors can impact many end-users using the services of the same provider.	System loop at which the software scans a few times the same serial number and generates consecutive alerts within a few seconds.	-	In rare cases, the IT provider's software can cause a change in the last two digits of the expiry date which will generate a small number of alerts - one to two alerts. The calendar used in the development of the IT provider's software can also be the reason for the generation of alerts.	Parsing issues - software does not extract correctly the information from the UI (unique identifier). Field with batch number contains data from previous scans. Additional information in the UI (unique identifier) of the pack that is not required for the Bulgarian market. **NB!** IT provider-related errors can impact many end-users using the services of the same provider.
End-user Human errors	Error due to manual entry of the UI (unique identifier) in the system.	Error due to manual entry of the UI (unique identifier) in the system.	Multiple attempts to change pack status or to dispense pack.	End-user scans twice the same pack at bulk verification.	Manual verification does not require entry of the expiry date. Despite of this, if the expiry date is entered with errors, it will generate alert A52.	Error due to manual entry of the UI (unique identifier) in the system.

Notes
1) Alert A7/A24 becomes critical when changes in the pack state are performed by different organisations.
2) Alert A32 becomes critical when two physical packs are present with the same serial number.

ANNEX 2: *Sample table for summarizing alerts caused by technical errors*

Alert Date	Alert ID	Error Code	Product Code	Product Name	Batch ID	Serial Number	SN Length	Expiry Date	Market ID	Root Cause (choose from a drop-down menu)	Comment
22.07.20	BG-KUA-J29-MMH-Z0W-T1F	A3	4055610342719	Medicinal compound	HL00111	253678291010	12	241130	BG	Problematic batch	The batch is manufactured befor 9th of Fenruary 2019.
....	....	....	....	....	....	....	....	.....	....	Scanner/ software	.....