Quality Assurance (QA) for Health Products

QA Information Notice

IN № 2023-04
Version - 10/05/2023

Risk mitigations measures for procuring of Insecticide Treated Net (ITN) product, SafeNet manufactured by Mainpol GmbH

Addressees

• Procurement Agents
• All PRs

Purpose

The Global Fund QA is issuing this notice to support implementation of risk mitigations measures on the procurement of Insecticide Treated Net (ITN) product, SafeNet manufactured by Mainpol GmbH in line with WHO Prequalification Unit recommendations.

This notice is for internal and external dissemination and country teams are expected to communicate this information to their relevant stakeholders as appropriate.

Identification of the product(s) and manufacturer

<table>
<thead>
<tr>
<th>Name of Supplier</th>
<th>Mainpol GmbH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commercial Name(s)</td>
<td>SafeNet</td>
</tr>
<tr>
<td>Packaging &amp; Pack size &amp; Type</td>
<td>All (Size, Colour)</td>
</tr>
<tr>
<td>Batch(es)</td>
<td>All</td>
</tr>
</tbody>
</table>

Background

On April 25, 2023, WHO PQ Unit shared with Global Fund their Letter of Concern for the above product following several quality complaints submitted to them by various organizations regarding Out of Specification (OOS) findings for certain batches of the ITN product, SafeNet manufactured by Mainpol GmbH. The OOS findings pertain to the active ingredient (AI) alpha-cypermethrin content being above or below the specified tolerance.

In accordance with their established procedures, WHO PQT/VCP has opened investigations for each submitted complaint through which the available information was reviewed to consider the identified issue and determine the potential root cause. To date, the investigations have not led to the identification of a specific root cause of the problems. While WHO continues to collaborate with all parties involved to obtain concrete data and information to determine the root cause of the OOS findings, GF QA has decided to issue this notice to recommend risk mitigation measures when procuring the product in line with the risk mitigations suggested by WHO PQ.
Nature of defect(s)

<table>
<thead>
<tr>
<th>Details of defect or problem.</th>
<th>Active Content: Alpha-cypermethrin content being above or below the specified tolerance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is there any evidence or suspicion of a risk to public health?</td>
<td>No concrete evidence of risk to public health but lack of efficacy could be a risk</td>
</tr>
<tr>
<td>Extent of the problem (eg. nb batches).</td>
<td>Not known</td>
</tr>
<tr>
<td>Extent of distribution of the product / batch (es).</td>
<td>Not known</td>
</tr>
<tr>
<td>Number of end-users potentially impacted</td>
<td>Not known</td>
</tr>
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</table>

Next steps

Based on the information available to date and until further notice, the following actions are recommended by GF QA:

- Not to recall the nets already distributed in countries.
- For nets not distributed or in transit, not to suspend the delivery of the placed orders for batches that have already been inspected and passed QC testing in order not to disrupt the supply chain and limit access.
- For orders already sampled and awaiting testing at QC labs or due for inspection sampling and testing to proceed with the inspection, sampling and testing and release the product upon getting complying results. PRs are recalled forwarding any non-compliant results to TGF QA Team.
- For any new procurements or nets due for inspection and sampling, ALL batches to be inspected, increase the sample size by doubling the quantity and all samples to be tested as per full WHO specifications.
- PRs to ensure that the conditions, as specified by the supplier, under which the ITNs are transported and stored are adequately recorded and monitored.

Contacts

This Notice does not require specific written response from PR. Please direct the respective answers and any questions about this matter to the technical contact listed below:

<table>
<thead>
<tr>
<th>Organisation</th>
<th>Name / Function</th>
<th>E-mail address</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global Fund</td>
<td>Stephen Kimatu, Specialist-Vector Control Products, Quality Assurance team</td>
<td><a href="mailto:Stephen.Kimatu@theglobalfund.org">Stephen.Kimatu@theglobalfund.org</a></td>
</tr>
<tr>
<td>Global Fund</td>
<td>Aziz Jafarov, Manager, Global Sourcing Health Technologies</td>
<td><a href="mailto:Azizkhon.Jafarov@theglobalfund.org">Azizkhon.Jafarov@theglobalfund.org</a></td>
</tr>
<tr>
<td>Global Fund</td>
<td>Kate Kolaczinski, Senior Vector Control Specialist, Malaria Disease Team</td>
<td><a href="mailto:Kate.Kolaczinski@theglobalfund.org">Kate.Kolaczinski@theglobalfund.org</a></td>
</tr>
</tbody>
</table>
Annex 1. WHO Prequalification Unit-Letter of Concern

Dear Mr Perez,

WHO Prequalification Unit
Vector Control Product Assessment: Letter of Concern

According to the established procedures for the prequalification of vector control products, the World Health Organization (WHO) reserves the right to notify stakeholders about the outcome of investigations relating to post-prequalification activities, including handling of complaints, for any prequalified vector control product. Additionally, failure of manufacturers to maintain compliance with the relevant WHO specifications may lead to the requirement for corrective and preventative actions to be established by the manufacturer in cooperation with WHO prequalification assessment and inspection teams to ensure compliance or the manufacturer must submit the necessary application/information to establish new/revised specifications.

Several complaints, submitted by the Pan American Health Organization (PAHO) and the United Nations Development Programme (UNDP), have been received regarding Out of Specification (OOS) findings for certain batches of the Insecticide Treated Net (ITN) product SafeNet manufactured by Mampol GmbH. In general, the OOS findings were submitted to share results pertaining to the active ingredient (AI) alpha-cypermethrin content being above or below the specified tolerance.

In accordance with the established procedures, WHO PQTC/VCPE opened investigations for each submitted complaint through which the available information was reviewed to consider the identified issue and determine the potential root cause. In one case, the Active Ingredient (AI) content was found to be above the established tolerance during the post-shipment testing, while in an another report, the AI content was found to have decreased significantly during 2 years of storage under conditions declared to be in line with manufacturer recommendations.

To date, the investigations have not led to the identification of a specific root cause of the problems due to limitations in the availability of information, specifically, the consistency and completeness of information received. The contributing factors include:
- No clear data submitted or in some cases no data submitted at all
- Summary reports submitted without raw data
- Testing protocols used by independent laboratories not submitted
- Lack of reviewable information regarding ITN transport and storage conditions
- Inconsistent access to testing results pre- and post-shipment and post storage
- Incomplete information shared with the manufacturer by complainants

However, due to the number of complaints received and unexplained reasons for the inconsistency in product characteristics/OOS findings, WHO is issuing this letter of concern to alert stakeholders of complaints received and potential issues related to the product.

Organisation mondiale de la Santé • Всемирная организация здравоохранения • Organización Mundial de la Salud
Mr R Perez, Albershausen

19 April 2023
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WHO continues to collaborate with all parties involved to obtain concrete data and information to determine the root cause of the OOS findings. Among specific actions to be taken, WHO will be conducting an on-site inspection of the new manufacturing site on 15-17 May 2023, observe pre-shipment testing, and review documentation. WHO will request the manufacturer to submit updated batch data on the physical/chemical characteristics of the product as currently formulated at the declared manufacturing site(s) in order to characterize the potential inter/intra-batch variability in the manufacturing process.

In the meantime, WHO is advising that Member States, procurement agencies and other stakeholders who are planning the procurement of this product, or have recently purchased the product, consider the advice below:

- Expand the number of samples for pre-/post-shipment testing, focused on AI content and Wash Resistance Index (clauses 2.2 and 2.3) of the WHO specification 454/LN/1.
- Responsible parties should monitor the conditions under which the ITNs are transported and stored, for example, temperature and humidity

Yours sincerely,

[Signature]
Debs Mubangizi
Unit Head
WHO Prequalification Unit