**Questionnaire for Risk Assessment of the Presence of Nitrosamine in Raw Materials Used in the Manufacture of Medicines**

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| **Material Comercial Name** | Click here to enter text. |
| **Material Type / Generic Name** | Click here to enter text. |
| **Manufacturer Name** | Click here to enter text. |
| **Production Site Address** | Click here to enter text. |
|  |
| **Nitrosamines are substances classified as probable cancer-causing agents in humans. In 2018, the presence of these substances was detected in various blood pressure medicines known as "sartans" and, in 2019, impurities of the same type were detected in batches of the active pharmaceutical ingredient ranitidine.****Therefore, in alignment with health authorities of several countries, ANVISA (Brazilian Health Authority) recommends a reassessment of the synthesis routes of raw materials used in the manufacture of medicines to ensure that the amounts of nitrosamines in pharmaceutical products do not present risks to patients.****This questionnaire must be answered by a qualified person of the manufacturers of raw materials and has the objective of knowing the manufacturing processes of these materials and to identify possible sources of contamination by nitrosamines.****Please, answer the following questions according to the manufacturing process of the material identified above:** |

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| 1) Is Sodium Nitrite (NaNO2) or any other nitrite or nitrosating agent: |  |  |  |
| - Used in any steps in the manufacturing process as reagents / catalyst?  | ☐**YES** | ☐**NO** |  |
| - Known to be used in the preparation of raw materials or intermediates used in the manufacturing process? | ☐**YES** | ☐**NO** | ☐**Unavailable information** |
| - Known to be used in the preparation of reagents / catalysts / processing aids used in the manufacturing process? | ☐**YES** | ☐**NO** | ☐**Unavailable information** |
| - Known to be generated as impurities during the manufacturing process? | ☐**YES** | ☐**NO** | ☐**Unavailable information** |

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| 2) Have your company analysed the material for identification and quantification of: |  |  |  |
| * Nitrites?
 | ☐**YES** | ☐**NO** |  |
| * Nitrates?
 | ☐**YES** | ☐**NO** |  |
| * Nitrosamines?
 | ☐**YES** | ☐**NO** |  |
| If any answer in this section is **YES**, please inform the results, test methodology and if the tests were performed in-house or by a third-party contractor. |
| 3) Does the manufacturing process of the material use water? | ☐**YES** | ☐**NO** |  |
| If so, is this water prepared by distillation, ion Exchange or reverse osmosis? | ☐**YES** | ☐**NO** |  |
| If this water is not prepared using one of the processes mentioned above. Inform (in ppm) the maximum level permitted for: |  |  |  |
| * Nitrites
 | **Click here to enter text.** |
| * Nitrates
 | **Click here to enter text.** |
| 4) Is there any secondary and/or tertiary amine present in the material manufacturing process as: |  |  |  |
| * Raw material?
 | ☐**YES** | ☐**NO** |  |
| * Package material?
 | ☐**YES** | ☐**NO** |
| * Intermediate?
 | ☐**YES** | ☐**NO** |  |
| * Reagent?
 | ☐**YES** | ☐**NO** |  |
| * Processing aids?
 | ☐**YES** | ☐**NO** |  |
| * Catalyst / Base?
 | ☐**YES** | ☐**NO** |  |
| * Solvent?
 | ☐**YES** | ☐**NO** |  |
| If **YES**, are those amines present in which step of the manufacturing process? | ☐ **BEFORE** the step on which any nitrosating agent mentioned in section 1 is added. |
|  | ☐ The **SAME** step on which any nitrosating agent mentioned in section 1 is added. |
|  | ☐ **AFTER** the step on which any nitrosating agent mentioned in section 1 is added. |
| Please, inform below the chemical name / structure of the amine (s):**Click here to enter text.** | ☐ **Not applicable** |

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| 5) Is there any amide, primary amine or ammonium salt used or present in the material manufacturing process as: |  |  |  |
| * Raw material?
 | ☐**YES** | ☐**NO** |  |
| * Package material?
 | ☐**YES** | ☐**NO** |
| * Intermediate?
 | ☐**YES** | ☐**NO** |  |
| * Reagent?
 | ☐**YES** | ☐**NO** |  |
| * Processing aids?
 | ☐**YES** | ☐**NO** |  |
| * Catalyst / Base?
 | ☐**YES** | ☐**NO** |  |
| * Solvent?
 | ☐**YES** | ☐**NO** |  |
| * Washing fluid?
 | ☐**YES** | ☐**NO** |  |
| Please, inform below the chemical name / structure of the substances:**Click here to enter text.** | ☐ **Not applicable** |  |
| 6) Are recycled and / or recovered nitrogen containing solvents used in the manufacturing process of the material? | ☐**YES** | ☐**NO** |  |
| 7) Are the equipment used in the maufacturing process of the material dedicated? | ☐**YES** | ☐**NO** |  |
| If **NO**, are the equipment used to manufacture any other products that require nitrites, nitrosating agents or material with identified risk of formatting nitrosamines? | ☐**YES** | ☐**NO** | ☐ **Not applicable** |

**Issued by:**

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| --- | --- |
| Name | **Click here to enter text.** |
| Job title | **Click here to enter text.** |
| Signature |  |