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To customers
struggling with nitrosamine impurities in pharmaceuticals

Measurement Against Nitrosamine Formation

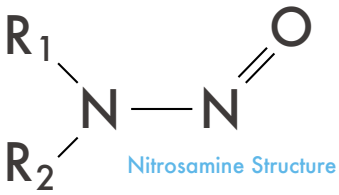
NOx Removal Gas-phase Filter System

■ It is widely known in the pharmaceutical manufacturing industry that amines and nitrogen oxides react to form nitrosamines. Nitrosamines are considered to increase health risks due to their potential carcinogenicity, leading to stricter regulations in pharmaceuticals.

Example of drugs

- Sultan
- Metformin
- Ranitidine
- Rifampicin
- Nizatidine
- NDSRIs：nitrosamine drug substance-related impurities

*antihypertensive drug, acid suppressant, oral antidiabetic drug, etc.

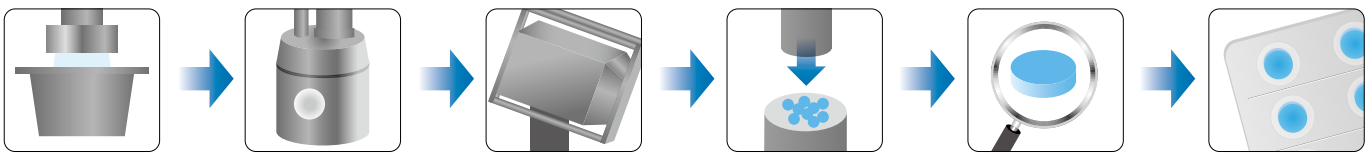


Nitrosamine Structure

Risk of Nitrosamine Contamination

■ There are multiple reasons why nitrosamines can be present in drugs;
It can be related to the drug's manufacturing process or its chemical structure or even the conditions in which they are stored or packaged.

API/Solid dosage form manufacturing process



① Weighing ② Granulation ③ Mixing ④ Tablet compression ⑤ Inspection ⑥ Packaging

■ One of the pharmaceutical manufacturing company in Japan conducted a verification of the removal of nitrogen oxides in the manufacturing process using our gas-phase filter system and confirmed its superiority.

■ For details of the verification, please refer to the article published in OPR&D (Organic Process Research & Development). (Please access from the QR code on the right)

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■ The FDA and EMA have issued notifications for pharmaceutical manufacturers to assess the risk of nitrosamine contamination. Items found to contain nitrosamines exceeding the limit must be reported promptly.
If the limits are exceeded, it is recommended to take mitigation measures such as changing the manufacturing process.

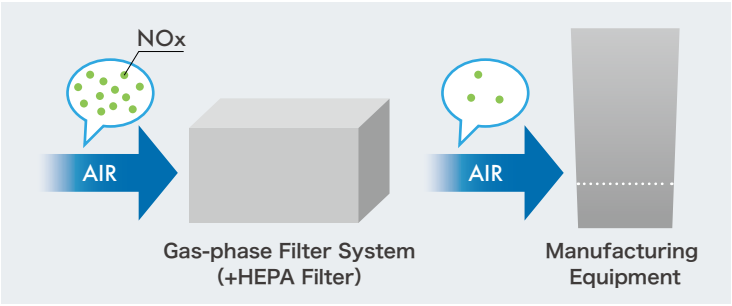
➤FDA：By August 2025　➤EMA：By October 2023

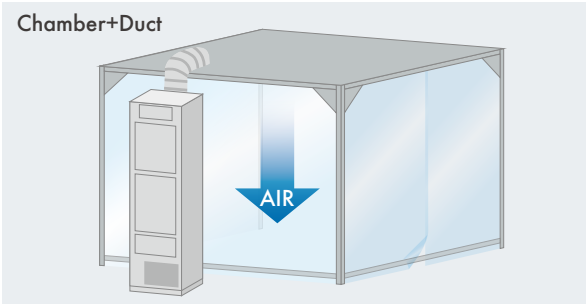
Target and Example of NOx removal system

API manufacturing

Pharmaceutical manufacturing

Equipment maker





Performance evaluation of NOx removal filter system using a test machine（one example）

■ Gas concentration analysis in a room inside the factory

■ Compared the upstream and downstream sides of the filter and confirmed the reduction in NOx levels

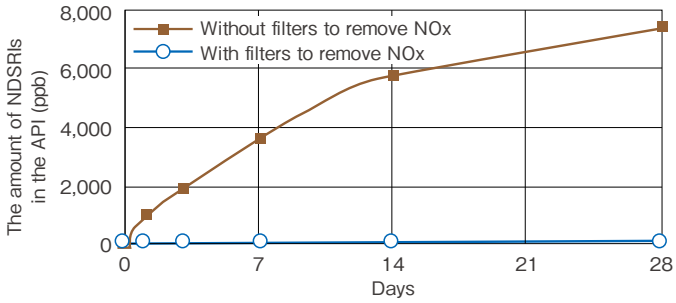
24-hour concentration measurement results

Object	Upstream of Gas-phase filter	Downstream of Gas-phase filter	Removal Efficiency*
NOx	1.27μg/㎥	0.09μg/㎥	92.0%

*Calculate the removal rate from the concentration levels upstream and downstream of the gas-phase filter system

■ Confirmed the change in the content of NDSRIs (nitrosamine impurities) in the active pharmaceutical ingredient with and without the NOx removal filter using a test machine.

Content of NDRIs in the active pharmaceutical ingredient and its changes over time(ppb)



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