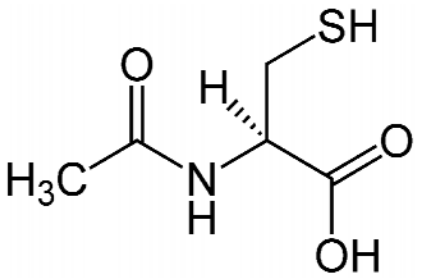
HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Safety Notice

Medical Devices

Interference Of *N*-Acetylcysteine (NAC) with Enzyme-based Assays Used following Paracetamol Overdose



N-Acetylcysteine

Priority 3 – Advisory

HPRA Safety Notice: SN2015(09) **Issue Date: 21 May 2015**

MANUFACTURER / SUPPLIER	HPRA CASE REFERENCE
Several	N/A

ISSUE
The Health Product Regulatory Authority (HPRA) would like to remind customers of the potential inference of *N*-Acetylcysteine (NAC) with enzyme-based assays used in patients diagnosed with paracetamol overdose, as these can result in biased results. The HPRA has been notified of a number of field safety corrective actions (FSCAs) undertaken by manufacturers relating to the above issue.

ACTION OR RECOMMENDATIONS
The HPRA advises that users: 1 Identify these enzyme-based assays used in your laboratories. 2 Check your internal protocols for measuring results such as Paracetamol level, Enzyme Creatinine, Lactate, Glucose, and their respective validation methods.

3	If in doubt, check with the manufacturer of the device if the enzyme assay has the potential to be affected by biased readings as a result of this inference.
4	Consider the need to carry out a review of previously reported assay test results if deemed necessary.

TARGET GROUPS	
A&E Departments	Nursing Managers
Hospital Managers / CEOs	Nursing staff
Laboratory Managers	Intensive Care Units
Laboratory staff	Purchasing Managers
Chief Medical Scientists	Supplies Managers
Medical Scientists	Hospital personnel
Risk Managers	Private Medical Practitioners
Clinical Directors	All wards

BACKGROUND

Paracetamol is a common analgesic and antipyretic drug which, when ingested in excessive concentrations, may lead to acute renal failure and liver damage. Paracetamol overdose is associated with a significant depletion of glutathione. When the intermediate paracetamol metabolite, *N*-acetyl-*p*-benzoquinoneimine (NAPQI) is formed, with the help of gluthatione it binds covalently to sulphydryl groups. But when gluthatione eventually is depleted it binds to proteins and enzymes within hepatocytes initiating an inflammatory response and leading to cell death.

N-Acetylcysteine (NAC) is the antidote for paracetamol overdose as it was shown to be effective in preventing liver damage when given within 8 hours of the overdose. NAC has the ability to serve as a potent sulphydryl donor allowing the restoration of depleted gluthatione. However, when NAC is administered in recommended therapeutic concentrations it can interfere with commonly used enzymatic-colorimetric assays.

Tests which are commercially available that adopt enzyme mechanisms for analyte detection such as:

- The use of Peroxidases as a catalyst in Trinder reactions, and
- The use of Acyl Amidohyrolase and 8-hydroxyquinoline

have been found to produce potential negative bias in the test results.

The level of interference varies depending on the analyte being tested and the assay in use. NAC has a half-life of approximately 6 hours and the significance of the interference is shown to lessen with time and varies with drug plasma level.

In light of this, the HPRA would like to remind lab users of these interferences and to address any concerns with the respective manufacturers.

MANUFACTURER / AUTHORISED REPRESENTATIVE/ DISTRIBUTOR CONTACT INFORMATION

Enquiries to the **manufacturer** should be addressed to the contact details found on the device labelling / instructions for use.

HPRA CONTACT INFORMATION

All **adverse incidents** relating to a medical device should be reported to:

Health Products Regulatory Authority
Kevin O'Malley House
Earlsfort Centre
Earlsfort Terrace
Dublin 2

Telephone: +353-1-6764971
Fax: +353-1-6344033
E-mail: devicesafety@hpra.ie
Website: www.hpra.ie