

Urgent Field Safety Notice

ACHC20-06.A.OUS.DM

May 2020

Dimension® clinical chemistry systems

N-acetyl-p-benzoquinone imine (NAPQI) Interference with Dimension® Enzymatic Creatinine (EZCR) Flex® reagent cartridge

Our records indicate that your facility may have received the following product:

Table 1. Dimension® affected product

Assay	Test Code	Catalog Number	Siemens Material Number (SMN)	Lot Number
Enzymatic Creatinine	EZCR	DF270B	10471520	ALL

Reason for Correction

The purpose of this communication is to inform you of an interference identified with the product indicated in Table 1 above and to provide instructions on actions that your laboratory must take.

Siemens Healthcare Diagnostics has become aware that the presence of N-acetyl-p-benzoquinone imine (NAPQI), a metabolite of acetaminophen, may cause interference in certain chemistry assays when testing patient samples. Through spiking studies of NAPQI at 15 mg/L [101 µmol/L], Siemens observed a bias with Dimension EZCR of approximately -12% at a creatinine concentration of 1.02 mg/dL (90 µmol/L). This level of NAPQI correlates to a toxic level of acetaminophen. Titration experiments were subsequently performed to characterize the potential for interference at decreasing concentrations of NAPQI.

Actions to be Taken by Siemens:

The "Limitations of the Procedure" section of the Dimension EZCR assay Instructions for Use (IFU) will be updated to indicate that *'N-acetyl-p-benzoquinone imine (NAPQI) is a metabolite of acetaminophen. NAPQI concentrations of approximately 10 mg/L correlating to toxic levels of acetaminophen demonstrates a ≤10% change in results. NAPQI concentrations greater than this may lead to falsely depressed results for patient samples.'*

The information related to NAPQI provided in this letter supersedes the information in the current Dimension EZCR IFU until it is updated.

The updated IFUs will be uploaded into Document Library where all registered users who opt in to receive alerts will be notified of the updated IFU.

N-acetyl-p-benzoquinone imine (NAPQI) Interference with Dimension® Enzymatic Creatinine (EZCR)

Risk to Health

There is negligible risk to health. At toxic levels of acetaminophen, NAPQI interference may lead to falsely depressed creatinine values, however the magnitude of the bias would not be expected to lead to a clinically significant difference in patient management.

Actions to be Taken by the Customer:

- Be aware of the limitation indicated above.
- Please review this letter with your Medical Director.
- Complete and return the Field Correction Effectiveness Check Form attached to this letter within 30 days.
- If you have received any complaints of illness or adverse events associated with the products listed in Table 1, immediately contact your local Siemens Customer Care Center or your local Siemens technical support representative.

Please retain this letter with your laboratory records and forward this letter to those who may have received this product.

We apologize for the inconvenience this situation may cause. If you have any questions, please contact your Siemens Customer Care Center or your local Siemens Technical Support representative.

Dimension is a trademark of Siemens Healthcare Diagnostics.

N-acetyl-p-benzoquinone imine (NAPQI) Interference with Dimension® Enzymatic Creatinine (EZCR)

Frequently Asked Questions:

1. Which other assays have been evaluated for NAPQI interference?

The assays indicated below were tested on the Siemens ADVIA Chemistry and Atellica CH systems. These assays have identical principles of procedure to the equivalent assays on the Dimension® clinical chemistry system. No significant interference is expected on the following Dimension assays: Cholesterol, Creatinine (Jaffe), Direct HDL, Lactic Acid, Lipase, Triglyceride, and Uric Acid.

Additionally, Direct and Total Bilirubin (DBI and TBI) assays were tested on the Dimension system and showed show no interference ($\leq 10\%$ bias) for NAPQI concentrations of >15 mg/L ($101 \mu\text{mol/L}$) at sample concentrations similar to those published in each product's IFU.

2. Is the Jaffe Creatinine assay impacted in the presence of NAPQI?

Siemens testing has shown that the Jaffe methodology is not impacted by NAPQI interference as the Jaffe methodology uses different reagents and parameters than the EZCR assay.

N-acetyl-p-benzoquinone imine (NAPQI) Interference with Dimension® Enzymatic Creatinine (EZCR)

FIELD CORRECTION EFFECTIVENESS CHECK

N-acetyl-p-benzoquinone imine (NAPQI) Interference with Dimension® Enzymatic Creatinine (EZCR) Flex® reagent cartridge

This response form is to confirm receipt of the enclosed Siemens Healthcare Diagnostics Urgent Field Safety Notice ACHC20-06.A.OUS.DM dated May 2020 regarding NAPQI Interference with Dimension® Enzymatic Creatinine (EZCR). Please read the question and indicate the appropriate answer.

Return this completed form to Siemens Healthcare Diagnostics as per the instructions provided at the bottom of this page.

1. I have read and understood the Urgent Field Safety Notice provided in this letter. Yes ☐ No ☐

Name of person completing questionnaire:	
Date:	
Title:	
Institution:	Instrument Serial Number:
Street:	
City:	State:
Phone:	Country:

Please send a scanned copy of the completed form via email to XXXX@XXX

Or to fax this completed form to the Customer Care Center at XXXXXX

If you have any questions, contact your local Siemens Healthineers technical support representative.

Urgent Field Safety Notice

ACHC20-06.A.OUS.DV

May 2020

Dimension Vista® Systems

N-acetyl-p-benzoquinone imine (NAPQI) Interference with Dimension Vista® Enzymatic Creatinine (ECREA) Flex® reagent cartridge

Our records indicate that your facility may have received the following product:

Table 1. Dimension Vista® Chemistry Systems affected product

Assay	Test Code	Catalog Number	Siemens Material Number (SMN)	Lot Number
Enzymatic Creatinine	ECREA	K1270A	10700444	ALL

Reason for Correction

The purpose of this communication is to inform you of an interference identified with the product indicated in Table 1 above and to provide instructions on actions that your laboratory must take.

Siemens Healthcare Diagnostics has become aware that the presence of N-acetyl-p-benzoquinone imine (NAPQI), a metabolite of acetaminophen, may cause interference in certain chemistry assays when testing patient samples. Through spiking studies of NAPQI at 15 mg/L [101 µmol/L], Siemens observed a bias with Dimension Vista ECREA of approximately -15% at a creatinine concentration of 1.01 mg/dL [89 µmol/L]. This level of NAPQI correlates to a toxic level of acetaminophen. Titration experiments were subsequently performed to characterize the potential for interference at decreasing concentrations of NAPQI.

Actions to be Taken by Siemens:

The "Limitations of the Procedure" section of the Dimension Vista ECREA Instructions for Use (IFU) will be updated to indicate that '*N-acetyl-p-benzoquinone imine (NAPQI) is a metabolite of acetaminophen. NAPQI concentrations of approximately 10 mg/L correlating to toxic levels of acetaminophen demonstrates a ≤10% change in results. NAPQI concentrations greater than this may lead to falsely depressed results for patient samples.*

The information related to NAPQI provided in this letter supersedes the information in the current Dimension Vista ECREA IFU until updated.

The updated IFUs will be uploaded into Document Library where all registered users who opt in to receive alerts will be notified of the updated IFU.

N-acetyl-p-benzoquinone imine (NAPQI) Interference with Dimension Vista® Enzymatic Creatinine (ECREA)

Risk to Health

There is negligible risk to health. At toxic levels of acetaminophen, NAPQI interference may lead to falsely depressed creatinine values, however the magnitude of the bias would not be expected to lead to a clinically significant difference in patient management.

Actions to be Taken by the Customer:

- Be aware of the limitation indicated above.
- Please review this letter with your Medical Director.
- Complete and return the Field Correction Effectiveness Check Form attached to this letter within 30 days.
- If you have received any complaints of illness or adverse events associated with the products listed in Table 1, immediately contact your local Siemens Customer Care Center or your local Siemens technical support representative.

Please retain this letter with your laboratory records and forward this letter to those who may have received this product.

We apologize for the inconvenience this situation may cause. If you have any questions, please contact your Siemens Customer Care Center or your local Siemens Technical Support representative.

Dimension Vista is a trademark of Siemens Healthcare Diagnostics.

N-acetyl-p-benzoquinone imine (NAPQI) Interference with Dimension Vista® Enzymatic Creatinine (ECREA)

FIELD CORRECTION EFFECTIVENESS CHECK

N-acetyl-p-benzoquinone imine (NAPQI) Interference with Dimension Vista® Enzymatic Creatinine (ECREA) Flex® reagent cartridge

This response form is to confirm receipt of the enclosed Siemens Healthcare Diagnostics Urgent Field Safety Notice ACHC20-06.A.OUS.DV dated May 2020 regarding NAPQI Interference with Dimension Vista® Enzymatic Creatinine (ECREA). Please read the question and indicate the appropriate answer.

Return this completed form to Siemens Healthcare Diagnostics as per the instructions provided at the bottom of this page.

1. I have read and understood the Urgent Field Safety Notice instructions provided in this letter. Yes ☐ No ☐

Name of person completing questionnaire:	
Date:	
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Please send a scanned copy of the completed form via email to XXXX@XXXX

Or to fax this completed form to the Customer Care Center at XXXXXX

If you have any questions, contact your local Siemens Healthineers technical support representative.

N-acetyl-p-benzoquinone imine (NAPQI) Interference with Dimension Vista® Enzymatic Creatinine (ECREA)

Frequently Asked Questions:

1. Which other assays have been evaluated for NAPQI interference?

The assays indicated below were tested on the Siemens ADVIA Chemistry and Atellica CH systems. These assays have identical principles of procedure to the equivalent assays on the Dimension Vista system. No significant interference is expected on the following Dimension Vista assays: Cholesterol, Creatinine (Jaffe), Direct HDL, Lactic Acid, Lipase, Triglyceride, and Uric Acid.

Additionally, Direct and Total Bilirubin (DBIL and TBIL) were tested on the Dimension Vista system and showed no significant interference ($\leq 10\%$ bias) for NAPQI concentrations of >15 mg/L ($101 \mu\text{mol/L}$) at sample concentrations similar to those published in each product's IFU.

2. Is the Jaffe Creatinine assay impacted in the presence of NAPQI?

Siemens testing has shown that the Jaffe methodology is not impacted by NAPQI interference as the Jaffe methodology uses different reagents and parameters than the ECREA assay.

Urgent Field Safety Notice

ACHC20-06.A.OUS.CHC

May 2020

ADVIA® 1800 Chemistry System
ADVIA® 2400 Chemistry System
ADVIA® Chemistry XPT System

N-acetyl-p-benzoquinone imine (NAPQI) Interference with ADVIA® Chemistry Fructosamine (FRUC) and Enzymatic Creatinine_2 (ECRE_2) Assays

Our records indicate that your facility may have received the following products:

Table 1. ADVIA Chemistry Systems Affected Product(s)

Assay	Test Code	REF Number	Siemens Material Number (SMN)	Lot Number
Fructosamine	FRUC	04862501	10361941	ALL
Enzymatic Creatinine_2	ECRE_2	04992596	10335869	ALL

Reason for Correction

The purpose of this communication is to inform you of an interference identified with the products indicated in Table 1 above and to provide instructions on actions that your laboratory must take.

Siemens Healthcare Diagnostics has become aware that the presence of N-acetyl-p-benzoquinone imine (NAPQI), a metabolite of acetaminophen, may cause interference in certain chemistry assays when testing patient samples. Through spiking studies of NAPQI at 15 mg/L [101 µmol/L], Siemens observed a bias with the FRUC assay of approximately -35% at a fructosamine concentration of 356 µmol/L, and a bias with the ECRE_2 assay of approximately -16% at a creatinine concentration of 0.81 mg/dL (72 µmol/L). This level of NAPQI correlates to a toxic level of acetaminophen. Titration experiments were subsequently performed to characterize the potential for interference at decreasing concentrations of NAPQI.

Actions being Taken by Siemens:

The "Limitations of the Procedure" section of the ADVIA Chemistry FRUC assay Instructions for Use (IFU) will be updated to indicate that *'N-acetyl-p-benzoquinone imine (NAPQI) is a metabolite of acetaminophen. NAPQI concentrations of approximately 3 mg/L correlating to supratherapeutic levels of acetaminophen demonstrates a ≤10% change in results. NAPQI concentrations greater than this may lead to falsely depressed results for patient samples. Use of this assay is not recommended for patients being treated for an overdose of acetaminophen.'*

N-acetyl-p-benzoquinone imine (NAPQI) Interference with ADVIA® Chemistry Fructosamine (FRUC) and Enzymatic Creatinine_2 (ECRE_2) Assays

The “Limitations of the Procedure” section of the ADVIA Chemistry ECRE_2 assay IFU will be updated to indicate that *‘N-acetyl-p-benzoquinone imine (NAPQI) is a metabolite of acetaminophen. NAPQI concentrations of approximately 8 mg/L correlating to toxic levels of acetaminophen demonstrates a ≤10% change in results. NAPQI concentrations greater than this may lead to falsely depressed results for patient samples.’*

The information related to NAPQI provided in this letter supersedes the information in the current ADVIA Chemistry FRUC and ECRE_2 IFUs until each is updated.

The updated IFUs will be uploaded into Document Library where all registered users who opt in to receive alerts will be notified of the updated IFU.

Risk to Health

In a patient being treated for acetaminophen toxicity, the potential exists to report a falsely depressed fructosamine which may affect consideration for intervention. It is extremely unlikely, however, that fructosamine would be used to assess glycemic status in an acetaminophen overdose situation. For a patient being treated for acetaminophen toxicity, glucose would be used to inform the physician of a patient’s glycemic status.

At toxic levels of acetaminophen, NAPQI interference may lead to falsely depressed creatinine values. The magnitude of the bias would not be expected to lead to a clinically significant difference in patient management.

Actions to be Taken by the Customer:

- Be aware of the limitations indicated above.
- Please review this letter with your Medical Director.
- Complete and return the Field Correction Effectiveness Check Form attached to this letter within 30 days.
- If you have received any complaints of illness or adverse events associated with the products listed in Table 1, immediately contact your local Siemens Customer Care Center or your local Siemens technical support representative.

Please retain this letter with your laboratory records and forward this letter to those who may have received this product.

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ADVIA is a trademark of Siemens Healthcare Diagnostics.

N-acetyl-p-benzoquinone imine (NAPQI) Interference with ADVIA® Chemistry Fructosamine (FRUC) and Enzymatic Creatinine_2 (ECRE_2) Assays

Frequently Asked Questions:

1. Which other assays have been tested for NAPQI interference?

Cholesterol_2 (CHOL_2), Creatinine Concentrated (CRE_2c, Jaffe method), Direct Bilirubin_2 (DBIL_2), Direct HDL Cholesterol (DHDL), Glucose Oxidase (GLUO), Lactate (LAC), Lipase (LIP), Total Bilirubin_2 (TBIL_2), Triglycerides_2 (TRIG_2), and Uric Acid (UA) have been tested on the ADVIA Chemistry system and did not show any significant interference ($\leq 10\%$ bias) up to NAPQI concentrations of 15 mg/L (101 $\mu\text{mol/L}$).

2. Is the Jaffe Creatinine (CRE_2c) assay impacted by the presence of NAPQI?

Siemens testing has shown that the Jaffe CRE_2c assay is not impacted by NAPQI interference. The Jaffe methodology uses different reagents and parameters than the ECRE_2 assay.

N-acetyl-p-benzoquinone imine (NAPQI) Interference with ADVIA® Chemistry Fructosamine (FRUC) and Enzymatic Creatinine_2 (ECRE_2) Assays

FIELD CORRECTION EFFECTIVENESS CHECK

N-acetyl-p-benzoquinone imine (NAPQI) Interference with ADVIA® Chemistry Fructosamine (FRUC) and Enzymatic Creatinine_2 (ECRE_2) Assays

This response form is to confirm receipt of the enclosed Siemens Healthcare Diagnostics Urgent Field Safety Notice ACHC20-06.A.OUS.CHC dated May 2020 regarding NAPQI Interference with the ADVIA® Chemistry Fructosamine (FRUC) and Enzymatic Creatinine_2 (ECRE_2) assays. Please read the question and indicate the appropriate answer.

Return this completed form to Siemens Healthcare Diagnostics as per the instructions provided at the bottom of this page.

1. I have read and understood the Urgent Field Safety Notice instructions provided in this letter. Yes ☐ No ☐

Name of person completing questionnaire:	
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Urgent Field Safety Notice

ACHC20-06.A.OUS

May 2020

Atellica CH® Analyzer

N-acetyl-p-benzoquinone imine (NAPQI) Interference with Atellica® CH Fructosamine (Fruc) and Enzymatic Creatinine_2 (ECre_2) Assays

Our records indicate that your facility may have received the following products:

Table 1. Atellica® CH Affected Product(s)

Assay	Test Code	Siemens Material Number (SMN)	Lot Number
Fructosamine	Fruc	11097637	ALL
Enzymatic Creatinine_2	ECre_2	11097533	ALL
Japan Enzymatic Creatinine	ECreJ	11319121 (Japan only)	ALL

Reason for Correction

The purpose of this communication is to inform you of an interference identified with the products indicated in Table 1 above and to provide instructions on actions that your laboratory must take.

Siemens Healthcare Diagnostics has become aware that the presence of N-acetyl-p-benzoquinone imine (NAPQI), a metabolite of acetaminophen, may cause interference in certain chemistry assays when testing patient samples. Through spiking studies of NAPQI at 15 mg/L [101 µmol/L], Siemens observed a bias with the Fruc assay of approximately -34% at a fructosamine concentration of 336 µmol/L, and a bias with the ECre_2 assay of approximately -17% at a creatinine concentration of 0.81 mg/dL (72 µmol/L). This level of NAPQI correlates to a toxic level of acetaminophen. Titration experiments were subsequently performed to characterize the potential for interference at decreasing concentrations of NAPQI.

Actions being Taken by Siemens:

The "Limitations of the Procedure" section of the Atellica CH Fruc assay Instructions for Use (IFU) will be updated to indicate that '*N-acetyl-p-benzoquinone imine (NAPQI) is a metabolite of acetaminophen. NAPQI concentrations of approximately 3 mg/L correlating to supratherapeutic levels of acetaminophen demonstrates a ≤10% change in results. NAPQI concentrations greater than this may lead to falsely depressed results for patient samples. Use of this assay is not recommended for patients being treated for an overdose of acetaminophen.*

N-acetyl-p-benzoquinone imine (NAPQI) Interference with Atellica® CH Fructosamine (Fruc) and Enzymatic Creatinine_2 (ECre_2) Assays

The “Limitations of the Procedure” section of the Atellica CH ECre_2 assay IFU will be updated to indicate that *‘N-acetyl-p-benzoquinone imine (NAPQI) is a metabolite of acetaminophen. NAPQI concentrations of approximately 8 mg/L correlating to toxic levels of acetaminophen demonstrates a ≤10% change in results. NAPQI concentrations greater than this may lead to falsely depressed results for patient samples.’*

The information related to NAPQI provided in this letter supersedes the information in the current Atellica CH Fruc and ECre_2 IFUs until each is updated.

The updated IFUs will be uploaded into Document Library where all registered users who opt in to receive alerts will be notified of the updated IFU.

Risk to Health

In a patient being treated for acetaminophen toxicity, the potential exists to report a falsely depressed fructosamine which may affect consideration for intervention. It is extremely unlikely, however, that fructosamine would be used to assess glycemic status in an acetaminophen overdose situation. For a patient being treated for acetaminophen toxicity, glucose would be used to inform the physician of a patient's glycemic status.

At toxic levels of acetaminophen, NAPQI interference may lead to falsely depressed creatinine values. The magnitude of the bias would not be expected to lead to a clinically significant difference in patient management.

Actions to be Taken by the Customer:

- Be aware of the limitations indicated above.
- Please review this letter with your Medical Director.
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Atellica is a trademark of Siemens Healthcare Diagnostics.

N-acetyl-p-benzoquinone imine (NAPQI) Interference with Atellica® CH Fructosamine (Fruc) and Enzymatic Creatinine_2 (ECre_2) Assays

Frequently Asked Questions:

1. Which other assays have been tested for NAPQI interference?

Cholesterol_2 (Chol_2), Creatinine_2 (Crea_2, Jaffe method), Direct Bilirubin_2 (DBil_2), Direct HDL Cholesterol (D_HDL), Glucose Oxidase (GluO), Lactate (Lac), Lipase (Lip), Total Bilirubin_2 (TBil_2), Triglycerides concentrated (Trig), and Uric Acid (UA) have been tested on the Atellica CH and did not show any significant interference ($\leq 10\%$ bias) up to NAPQI concentrations of 15 mg/L (101 $\mu\text{mol/L}$).

2. Is the Jaffe Creatinine (CRE_2c) assay impacted by the presence of NAPQI?

Siemens testing has shown that the Jaffe CRE_2c assay is not impacted by NAPQI interference. The Jaffe methodology uses different reagents and parameters than the ECre_2 assay.

N-acetyl-p-benzoquinone imine (NAPQI) Interference with Atellica® CH Fructosamine (Fruc) and Enzymatic Creatinine_2 (ECre_2) Assays

FIELD CORRECTION EFFECTIVENESS CHECK

N-acetyl-p-benzoquinone imine (NAPQI) Interference with Atellica® CH Fructosamine (Fruc) and Enzymatic Creatinine_2 (ECre_2) Assays

This response form is to confirm receipt of the enclosed Siemens Healthcare Diagnostics Urgent Field Safety Notice ACHC20-06.A.OUS dated May 2020 regarding NAPQI Interference with Atellica® CH Fructosamine (Fruc) and Enzymatic Creatinine_2 (ECre_2) Assays. Please read the question and indicate the appropriate answer.

Return this completed form to Siemens Healthcare Diagnostics as per the instructions provided at the bottom of this page.

1. I have read and understood the Urgent Field Safety Notice instructions provided in this letter. Yes ☐ No ☐

Name of person completing questionnaire:	
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