It’s time to get specific with alcohol testing

N Latex CDT assay helps identify excessive alcohol consumption and assists in patient monitoring in clinical, legal, and workplace settings.

siemens-healthineers.com/n-latex-cdt-assay

SIEMENS Healthineers

CDT: a specific marker for detection of chronic alcohol abuse

Worldwide, almost 3 million deaths result each year from harmful use of alcohol, which is also a causal factor in more than 60 acute and chronic disease and injury conditions. In addition to its consequences for health, alcohol abuse imposes a significant social and economic burden on individuals and society.[1]

Clinicians require an effective and accurate procedure to identify and manage alcohol abuse. Measurement of carbohydrate-deficient transferrin (CDT) has been shown to be a useful tool in identifying changes in transferrin associated with heavy consumption of alcohol. CDT is therefore suggested as a specific biomarker to identify alcohol abuse and monitor abstinence during treatment.[2]

CDT is a variant of transferrin, an iron-transporting glycoprotein present in high concentrations in serum. Different isoforms of transferrin occur in humans. The most prominent, tetrasialotransferrin, consists of three substructural domains: a single polypeptide chain, two iron-binding sites, and two N-linked complex glycan chains terminated with a negatively charged sialic acid molecule (Figure 1).

3 million deaths every year result from harmful use of alcohol

Regular alcohol consumption of more than 50–80 g of ethanol per day for at least 2 weeks can result in a changed glycosylation pattern of transferrin, leading to a higher rate of isoforms lacking one or both carbohydrate chains.[3,4]

These isoforms (disialo- and asialotransferrin) are collectively referred to as carbohydrate-deficient transferrin. With a half-life of approximately 10 days, CDT concentrations usually return to normal levels after 2–4 weeks.

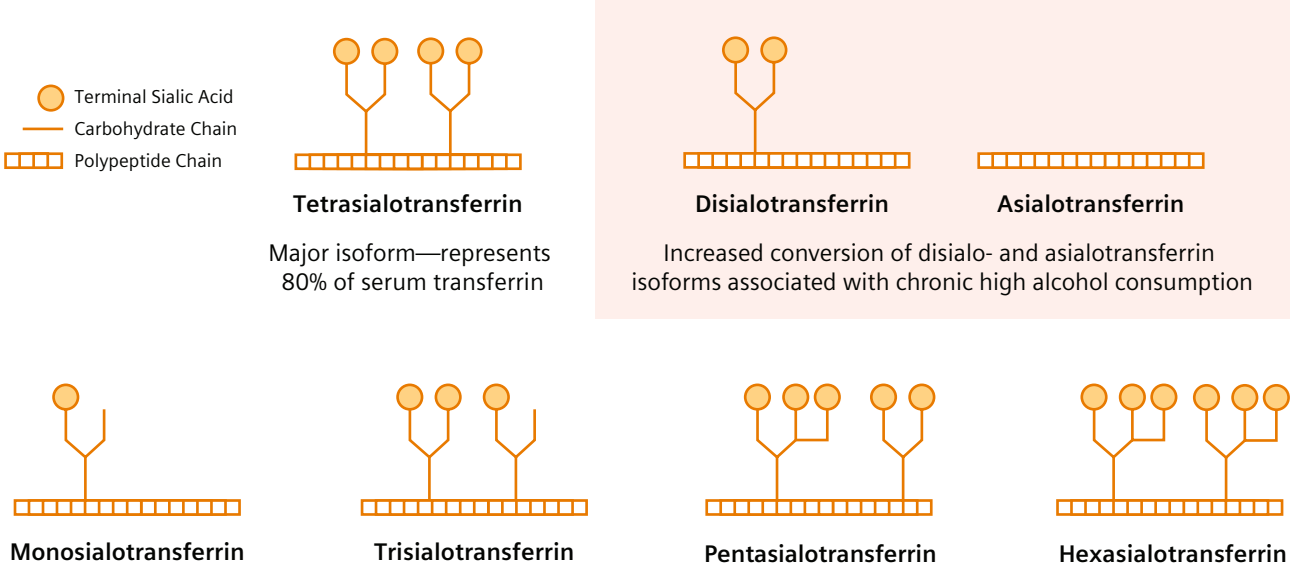


Figure 1. Illustration of different human transferrin glycoforms. Tetrasialotransferrin is the major isoform representing approximately 80% of serum transferrin in healthy adults. Heavy alcohol consumption causes an increase of disialo- and asialotransferrin isoforms.

Gain a range of benefits for your lab with CDT testing

Many Areas of Application

A patient's CDT level increases and decreases with the amount of alcohol consumed. CDT was found to be the most specific biomarker for assessment of relapse, and many different applications are possible:[10-12]

Clinical practice

- Differential diagnosis of alcohol-induced versus non-alcohol-induced diseases (e.g., fatty liver, liver cirrhosis, pancreatitis, esophagitis, gastritis, cancer)
- Differential diagnosis of elevated GGT values
- Monitoring effectiveness of detoxification treatments after alcohol abuse
- Accurate assessment of drinking in patients before or after liver transplantation
- Prenatal alcohol exposure

Legal applications

- Regranting or renewal of driver's licenses: CDT is recommended as a biomarker of a "sober" lifestyle in several European countries
- Forensic toxicology: exclusion of potentially alcohol-related accidents or deaths

Workplace testing

- CDT testing can be used to reduce the risk of alcohol-related accidents, trauma, and property damage in safety-sensitive activities.
- In practice, CDT testing for alcohol abuse is used in combination with appropriate questionnaires, patient's medical history and examination, or other laboratory parameters or tests to complement the clinical assessment.

Activities of common liver enzymes can be used to screen for ethanol-induced liver dysfunction and provide information on the risk of comorbidities.

Gamma glutamyl transferase (GGT) is a popular test widely accepted as a marker for alcohol abuse. However, studies have demonstrated its lack of specificity.[5]

Liver enzymes such as aspartate amino transferase (ASAT), alanine amino transferase (ALAT), and mean corpuscular volume (MCV) are also frequently used, but an increase in the serum levels of these parameters might not be specific for alcohol abuse.

Compared to other markers, CDT can be used to diagnose alcohol abuse and is superior to e.g., GGT in terms of sensitivity as well as specificity:[6-10]

- ✓ CDT seems not to be affected by liver diseases other than those induced by alcohol abuse (except biliary cirrhosis and chronic active hepatitis).
- ✓ CDT is not influenced by common chronic diseases or medication. Research data included hypertension, asthma/bronchitis, diabetes mellitus, adipositas/lipid metabolism disorder, angina pectoris, depression, and disorders of the digestive tract.
- ✓ CDT indicates the effectiveness of alcohol detoxification earlier than e.g., GGT or MCV.
- ✓ While other markers such as ethanol or ethylglucuronide (EtG) have a short detection window, CDT formation requires a sustained long-term elevation in blood-alcohol concentration. Therefore, CDT is minimally affected by single acute episodes of alcohol intake.
- ✓ Medication for treatment of excessive alcohol consumption, such as disulfiram, is reported not to influence the CDT level.

There are only a few causes of false-positive/-negative CDT results: genetic transferrin variants, which influence CDT results, and the extremely rare congenital disorders of glycosylation (CDG) syndrome.

N Latex CDT assay from Siemens Healthineers:

Get the first highly specific direct immunoassay that does not require pretreatment*

N Latex CDT assay supports streamlined lab worfklows

N Latex CDT assay is the first immunoassay* for directly quantifying CDT in serum with high specificity through a fully automated procedure.[4]

- No sample pretreatment
- No column separation step
- High specificity (relative specificity compared to HPLC; Figure 5)
- No sample splitting

- Minimized errors due to less manual work
- Reduced hands-on time

- First results within 20 minutes (total assay time)
- Random access with other protein assays

- Automatic calculation of %CDT from CDT and transferrin results
- Parallel measurement of CDT in combination with N antiserum to human transferring from a patient sample by means of immuno-nephelometry

*as of indicated print date

Siemens Healthineers N Latex CDT direct immunoassay supports improved clinical and patient outcomes

- **Highly specific monoclonal antibody that directly detects CDT.**
  Sample splitting by assaying transferrin twice—before and after a time-consuming column separation step—is not necessary (Figure 2).
- **No indication of false-positive results due to genetic variants.**
  Trisialotransferrin levels are frequently elevated in other non-alcohol-related liver diseases. However, as it is not a CDT isoform, N Latex CDT results are not affected by trisialotransferrin (Figure 3).
- **Reliable results: excellent recovery between labs, systems, and lots (Figure 4).**
  With the N Latex CDT assay, CDT can be determined as %CDT compared to total transferrin. This calculation minimizes the influence of transferrin levels, iron status, and mild to moderate limitations of liver function on CDT results. To obtain %CDT values, the transferrin concentration of the sample must be determined as well.

  On Atellica® NEPH 630 and BN™ systems, CDT and transferrin can be measured simultaneously and the %CDT presented as the final result in addition to the mg/L (or selected unit) CDT result.
- **Recommended cutoff: 2.5% CDT.**
- **No gender-specific reference range.**

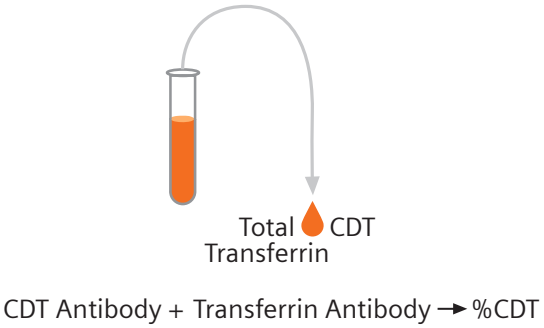


Figure 2. Direct CDT immunoassay. Direct quantification of CDT with highly specific antibodies. Calculation of %CDT by measuring CDT and transferrin simultaneously.

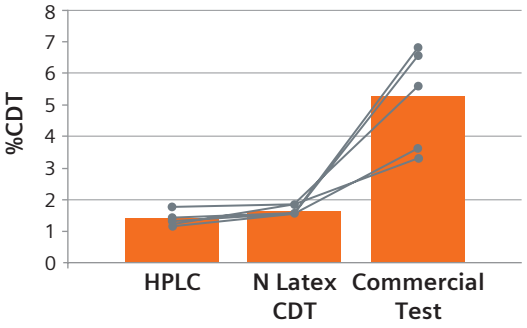


Figure 3. Comparison of %CDT results for genetically determined transferrin variants CD and C2C3 sera (n = 5 samples).[5] Genetic transferrin variants did not interfere with the N Latex CDT assay.

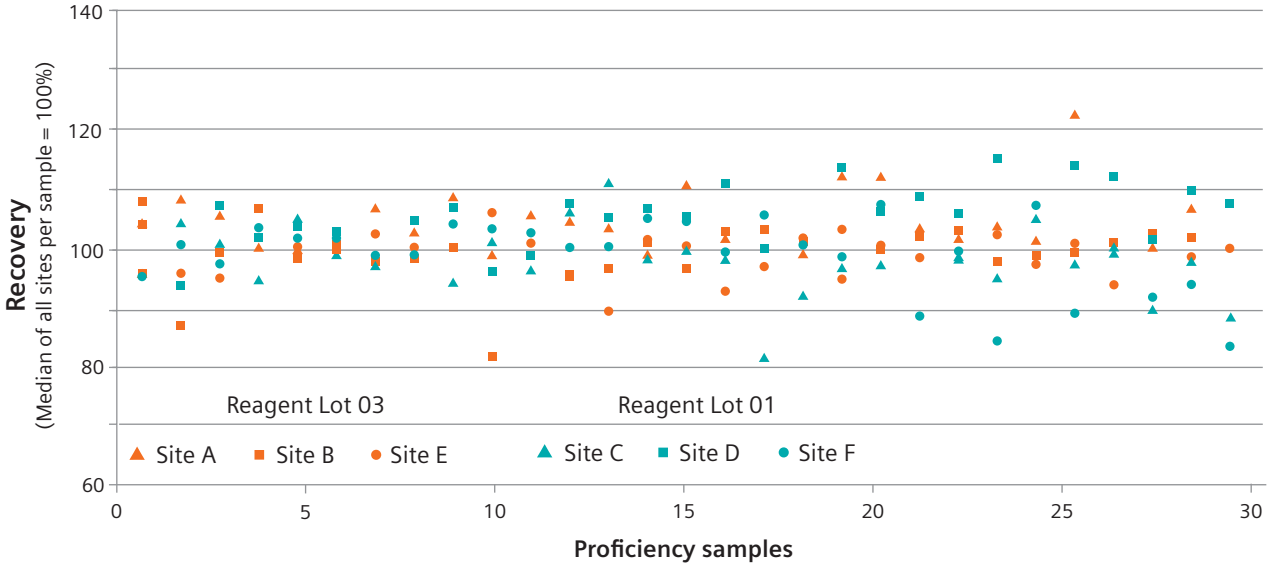


Figure 4. Proficiency panel recovery results for the N Latex CDT assay (%CDT). Overall recovery for %CDT (N Latex CDT assay) in six different laboratories using two different lots of reagents and three BN ProSpec® and three BN™ II Systems.

Confidently test for CDT according to the IFCC recommendation

Methods for CDT determination

There are a variety of methods available for the determination of CDT: While mass spectrometry is not common for routine testing, high-performance liquid chromatography (HPLC), capillary electrophoresis (CE), and immunonephelometry have been widely adopted.

An international working group (IFCC WG-CDT) has defined disialotransferrin as the reference analyte and HPLC as the reference measurement procedure for harmonization of CDT testing across all methods. Based on this reference, a multi-level serum CDT calibrator set has been developed to allow manufacturers of CDT methods to make their method traceable to this IFCC reference material.

The N Latex CDT assay has been developed using diasialotransferrin-specific HPLC as its reference—the same method now established as the IFCC reference method—to determine the relative specificity and sensitivity (Figure 2).

In addition, the N CDT Standard SL is calibrated with reference to the IFCC CDT calibrator set to ensure traceability.[13,14] While traceability has been established, each method for quantification of CDT might provide different reference values and cutoffs, since the N Latex CDT assay measures asialo-, monosialo-, and disialotransferrin.[13] Therefore, a conversion formula (immunoassay <=> HPLC reference methods) has been in place since this method was introduced.[2]

Carbohydrate-deficient transferrin (CDT) includes asialo-, monosialo-, and disialotransferrin isoforms of transferrin.

CDT values should be expressed as %CDT to compensate for variations in the total transferrin concentrations.

The N Latex CDT assay employs diasialotransferrin-specific HPLC as its reference—the same method now established as the IFCC reference method.

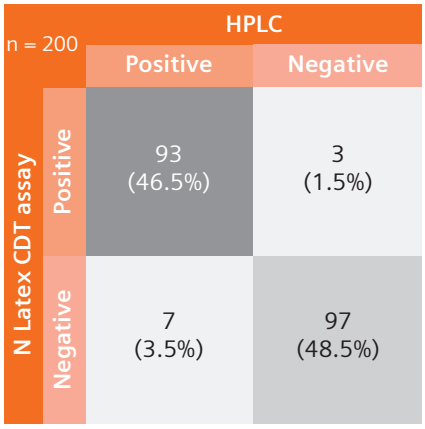


Figure 5. Results of an external evaluation of the N Latex CDT assay, based on a cutoff value of 2.5% CDT.

Relative specificity and sensitivity based on a cutoff value of 2.5% CDT for the BN System method and 2.0% CDT for the HPLC (disialo-specific) method:

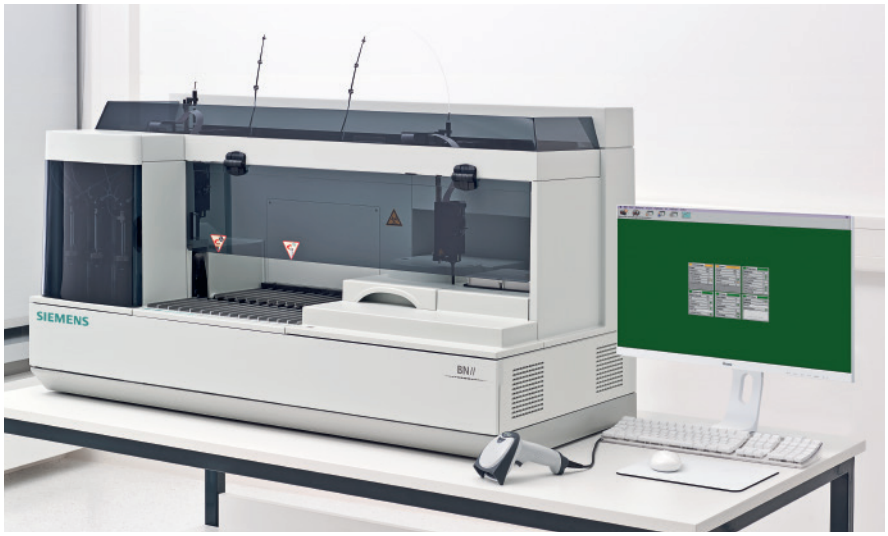
Relative sensitivity (%)
Positive (N Latex CDT)/Positive (HPLC) *100
Relative sensitivity = 93.0%

Relative specificity (%)
Negative (N Latex CDT)/Negative (HPLC) *100
Relative specificity = 97.0%

Take advantage of a powerful combination: The N Latex CDT assay is available on the Atellica NEPH 630 and BN Systems

The N Latex CDT assay is designed for use on the Atellica NEPH 630 and BN Systems, taking advantage of nephelometric technology.

Atellica NEPH 630 System
Dedicated, compact system offering a consolidated menu of specialty and routine plasma-protein testing.



BN II System
Fully automated analyzer providing confidence in results for mid- to high-volume plasma-protein testing.

Contact your local Siemens Healthineers representative today to streamline your CDT testing with the N Latex CDT assay.

The products/features mentioned here are not commercially available in all countries. For regulatory reasons, their future availability cannot be guaranteed. Please contact your local Siemens Healthineers organization for further details.

At Siemens Healthineers, our purpose is to enable healthcare providers to increase value by empowering them on their journey toward expanding precision medicine, transforming care delivery, and improving patient experience, all made possible by digitalizing healthcare.

An estimated 5 million patients globally benefit every day from our innovative technologies and services in the areas of diagnostic and therapeutic imaging, laboratory diagnostics, and molecular medicine, as well as digital health and enterprise services.

We are a leading medical technology company with over 120 years of experience and 18,000 patents globally. Through the dedication of more than 50,000 colleagues in 75 countries, we will continue to innovate and shape the future of healthcare.

Product availability may vary from country to country and is subject to varying regulatory requirements. Please contact your local representative for availability.

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