

# Preanalytical Notes<sup>®</sup>

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## Urine Specimens – an overview of collection methods, collection devices, specimen handling and transportation

Urine has a long history as a specimen for analysis in clinical laboratories. After blood, urine is the most commonly used specimen for diagnostic testing, monitoring of disease status and detection of drugs. Urine testing using both automated and traditional manual methods, is growing rapidly<sup>1</sup>. As for all clinical laboratory specimens, preanalytical error in urine specimens is often difficult to detect. Because of this, it is important for laboratories to have processes in place to ensure compliance with best practice in specimen collection, handling and transport.

**Urine testing using both automated and traditional manual methods is growing rapidly**

In this article, we present an overview of the various types of collection methods and commonly used collection devices. We then move on to cover recommendations for specimen collection procedures, specimen handling and the use of preservatives.

### Types of Urine Collection Methods

Urine specimens may be collected in a variety of ways.

#### ***Randomly collected specimens***

These are suitable for urinalysis in the clinical chemistry laboratory and for microscopic analysis. However, they are not regarded as specimens of choice because of the potential for dilution of the specimen when collection occurs soon after the patient has consumed fluids. In this situation, analyte values may be artificially low. Of necessity, pediatric

urine specimens for urinalysis and microscopy are often of this type.

#### ***First Morning Specimen***

This is the specimen of choice for urinalysis and microscopic analysis, since the urine is generally more concentrated (due to the length of time the urine is allowed to remain in the bladder) and therefore contains relatively higher levels of cellular elements and analytes. Abnormal constituents are also likely to be present in higher concentration and thus more likely to be detected.

#### ***Midstream Clean Catch Specimens***

Midstream specimens are strongly recommended for microbiological culture and antibiotic susceptibility testing because of the reduced incidence of cellular and microbial contamination. Following instruction from a healthcare professional, patients are required to follow a prescribed procedure commencing with cleansing the urethral area. The patient should then void the first portion of the urine stream into the toilet. These first steps significantly reduce the opportunities for contaminants to enter the urine stream during collection of the clinical specimen. The urine midstream is then collected into a clean container after which the remaining urine is voided into the toilet. This method of collection can be conducted at any time of day or night.

#### ***Timed Collection Specimens***

These specimens may be required for quantitative measurement of certain analytes, including those subject to diurnal variation. Analytes commonly tested using

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timed collection include creatinine, urine urea nitrogen, catecholamines, metanephrines, vanillylmandelic acid (VMA), 5-hydroxyindoleacetic acid, protein, oxalate, copper and 17-hydroxysteroids. A timed collection allows measurement of the excretion of these substances in urine over a specified length of time, usually, but not always, 8 or 24 hours. In this collection method, the bladder is emptied prior to beginning the timed collection. Then, for the duration of the designated time period, all urine is collected and pooled into a collection container, with the final collection taking place at the very end of that period. Half an hour before the end of the collection period, it is helpful to ask the patient to drink a glass of water, so that the last urine specimen can be obtained. If no specimen is produced, then the total volume and time of collection cannot be determined. It is also important to caution the patient not to lose urine specimens to the toilet during defecation. When a 24-hour urine specimen is required for the assay of catecholamines, metanephrines and/or VMA, for the diagnosis of pheochromocytoma which causes persistent or episodic hypertension, it is advisable to monitor the blood pressure of the patient and collect the urine specimen when the blood pressure is high, in order to improve the chance of a positive finding.

Timed specimens should be refrigerated during the collection period, unless otherwise directed by the laboratory. Accurate timing is very important as this information forms a critical part of the calculations performed to determine urine clearance values (e.g. creatinine clearance). Interpretations based on faulty calculations can result in improper diagnoses or medical treatment.

### Collection from Catheters

Urine specimens can be collected from catheters (e.g. Foley catheter) using a syringe, followed by transfer to a specimen tube or cup. Alternatively, urine can be drawn directly from the catheter to an evacuated tube using an appropriate adaptor (Figure 1).



**Figure 1**  
Direct draw  
adaptors for urine  
specimen  
collection from  
Foley catheter

### Supra-pubic Aspiration

This may be necessary when a non-ambulatory patient cannot be catheterised or where there are concerns about obtaining a sterile specimen by conventional means. This procedure involves collection of the specimen by needle aspiration through the abdominal wall into the bladder.

### Pediatric Specimens

These present many challenges. For infants and small children, a special urine collection bag is adhered to the skin surrounding the urethral area. Once the collection is completed, the urine is poured into a collection cup or transferred directly into an evacuated tube with a transfer

straw (refer to Figure 2 below). Urine collected from a diaper is not recommended for laboratory testing since contamination from the diaper material may affect test results.



**Figure 2**  
Urine transfer 'straw'  
with adaptor for transfer  
of specimen to evacuated  
urine collection tube

### Urine Collection Devices

An extensive array of urine collection products is available in the market. Information on features, intended use and instructions for use should be obtained from the device manufacturer and reviewed before being incorporated into a specimen collection protocol.

**Healthcare worker safety is enhanced by urine specimen containers with special access ports that allow closed-system transfer of urine**

### Urine Collection Containers (cups for collection and transport)

Urine collection container cups are available in a variety of shapes and sizes with lids that are either 'snap-on' or 'screw-on'. Leakage is a common problem with many products. Some urine specimen containers have closures with special access ports that allow closed-system transfer of urine directly from the collection device to the tube (Figure 3). This feature offers added protection to healthcare workers from exposure to specimens as a consequence of leakage.



**Figure 3**  
Urine collection containers with integrated port for  
transfer of specimen to evacuated urine collection tube

### Urine Collection Containers (24-hour collection)

Urine collection containers for 24-hour specimens commonly have a 3 litre capacity and are amber coloured (to protect light-sensitive analytes such as porphyrins and urobilinogen). As for the urine collection cups above, closure types vary with some containers featuring an integrated port for transfer of an aliquot of the specimen to an evacuated urine

collection tube. This provides the option for the laboratory to receive only the aliquot tube and specimen weight (with the large 24-hour container and contents discarded at the point of collection). When a preservative is required, it should be added to the collection container before the urine collection begins. Commonly used preservatives for 24 hour specimens are hydrochloric acid, boric acid, acetic acid, thymol and toluene. If more than one acceptable preservative is available for the analyte(s) being tested, the least hazardous one should of course be selected. Appropriate warning labels should be placed on the container to alert patients to possible harm arising from contact with the preservatives. This should be reinforced by appropriate instruction from the attending healthcare worker. A corresponding Material Safety Data Sheet (MSDS) should also be provided for the patient.

### Urine Specimen Tubes

Urine specimens may be poured directly into tubes with 'screw-on' or 'snap-on' caps. Additionally, evacuated tubes, similar to those used in blood collection, are now available (Figure 4). These can be filled using a straw device (Figure 2), from urine specimen containers with integrated transfer devices (Figure 3), or from direct sampling devices that are used to access catheter sampling ports (Figure 1). Urinalysis tubes are available in a variety shapes: conical bottom, round bottom, or flat bottom. Conical bottom tubes offer advantages for microscopic examination of urine sediment. The laboratory's tube selection process must include consideration of centrifugation conditions and compatibility with automated instrument systems. Tube fill volumes are typically within the range 4 to 10ml with dimensions of 13 x 75mm and 16 x 100mm (Figure 4).



**Figure 4**  
Evacuated urine specimen tubes

## Urine Specimen Collection and Transportation Guidelines

As for any type of clinical laboratory specimen, certain criteria for collection and transportation of urine specimens must be met to ensure high quality specimens free of preanalytical artifact are obtained consistently. Without this, accurate test results cannot be guaranteed.

- All urine collection and/or transport containers should be clean and free of particles or interfering substances.
- The collection and/or transport container should have a secure lid and be leak-proof. Leak-proof containers reduce specimen loss and risk of healthcare worker exposure to the specimen while also protecting the specimen from contaminants.
- The use of containers that are made from break-resistant plastic is strongly recommended.

- The container material should not leach interfering substances into the specimen.
- Specimen containers must not be re-used.
- Specimen tubes should be compatible with automated systems and instruments used by the laboratory.
- Collection containers and/or specimen tubes should be compatible with pneumatic tube systems where these are used for urine specimen transport. Use of leak-proof containers is essential in this situation.

The CLSI<sup>2</sup> makes the following recommendations for urine collection:

- Primary (routine) specimen containers to have a wide base and a capacity of at least 50 ml.
- 24 hour specimen containers to have a capacity of at least 3 litres.
- Sterile collection containers for all microbiology specimens.
- Specimen containers to have secure closures to prevent specimen loss and to protect the specimen from contaminants.
- Amber coloured containers for specimens required for assay of light sensitive analytes such as urobilinogen and porphyrins.

**Specimens for urinalysis, culture and sensitivity testing should be tested within 2 hours of collection<sup>2</sup>**

### Urine Specimen Preservation

For urinalysis and culture and sensitivity testing, CLSI Guidelines recommend testing within two hours of collection<sup>2</sup>. Different time limits may apply to specimens required for molecular testing of infectious agents (e.g. testing for *Neisseria gonorrhoeae*, *Chlamydia trachomatis*). For this type of testing, laboratories should ensure they are able to comply with specimen transportation conditions prescribed by the assay manufacturers. Where compliance with these and/or CLSI recommendations is not possible, consideration should be given to the use of a preservative. For chemical urinalysis and conventional (culture based) microbiological testing, unpreserved specimens exceeding the two hour limit that have not been refrigerated should not be accepted for analysis due to potential bacterial overgrowth leading to disintegration of cells and casts\*, invalidation of bacterial colony counts and errors in chemical urinalysis. When specimens for such testing are directly transferred from a collection cup to a tube containing a suitable preservative, a stable environment is provided for the specimen until testing can be conducted. Preservatives are also available for some molecular tests (e.g. BD UPT urine specimen tube for use with BD ProbeTec™ ET assay system). When a decision to use a preservative is taken – for any type of testing, potential interference with assay methods should be considered. Laboratories should validate all test procedures intended to be used for preserved specimens. Specimens may need to be split if various tests requiring different preservatives are requested.

\* bacterial growth increases the pH of the urine leading to lysis of red blood cells and white blood cells. Increased pH (alkalinity) can also cause casts to dissolve.

**The correct specimen-to-additive ratio must be maintained to ensure correct function of the preservative**

Where preservatives are used, the correct specimen-to-additive ratio must be maintained. Care therefore needs to be taken when manually transferring specimens to a specimen tube containing a preservative. Use of the indicated fill lines on the tubes can assist with ensuring the correct fill volume. Under-filling the tube will lead to a high concentration of preservative in the specimen, while over-filling the tube will overly dilute the preservative. In both cases, the function of the preservative may be compromised. The evacuated tube system is designed to achieve correct fill volume and thus ensure optimal specimen-to-additive ratio and proper preservative function. Evacuated systems also reduce the potential for exposure of the healthcare workers to the specimen.

**Chemical preservatives should be non-mercuric and environmentally friendly**

Chemical preservatives should be non-mercuric and environmentally friendly. The US Environmental Protection Authority (EPA) cites mercuric oxide used in urinalysis preservatives as a source of mercury contamination in medical laboratories. Additional information on this topic is available from the EPA website: <http://www.epa.gov>

### **Preservatives for Chemical Urinalysis**

A variety of urine preservatives is available that allow urine to be maintained at room temperature while still providing urinalysis test results comparable to those achieved with fresh specimens or those stored under refrigerated conditions. Commonly used preservatives for chemical urinalysis specimens include tartaric acid, boric acid, chlorhexidine, ethyl paraben, thymol and sodium propionate (and 'cocktails' of these). Preservation times are typically within the range 24 to 72 hours. Claims for the duration of stability for specific analytes should be obtained from the manufacturer.

### **Preservatives for Culture and Antibiotic Susceptibility Testing**

The most common preservative used for this testing is boric acid. This preservative may be used in tablet, powder or lyophilised form.

Preservatives for culture and antibiotic susceptibility testing are designed to maintain the specimen in a state equivalent to that which would be achieved with refrigeration by deterring the proliferation of organisms that could result in a false positive culture or bacterial overgrowth. Careful attention must be given to the formulation of these preservatives to achieve this objective. There is evidence to suggest that non-pH buffered boric acid may be harmful to certain organisms and that buffered boric acid preservatives can reduce the harmful effects of the preservative on the organisms<sup>3</sup>. Preserved urine specimens can be stored at room temperature until the time of testing. Product claims regarding duration of preservative potency should be obtained from the manufacturer.

## **Urine Specimen Reception in the Laboratory**

In addition to routine checks and precautions taken for all specimens received in the clinical laboratory, the following additional 'check items' apply to urine specimens.

### **Labels**

If the collection container is used for transport, the label should be placed on the container and not on the lid, since the lid can be mistakenly placed on a different container. Note that some labels are unsuitable for specimens stored under refrigerated conditions because of a lack of adhesion at low temperatures.

### **Volume**

It is important for specimen collection personnel to ensure there is sufficient volume to perform the required tests. For specimens in preservative tubes, the fill volume must be correct. As above, under-filling or over-filling these tubes may adversely affect test result accuracy.

### **Collection Date and Time**

Collection time and date must be shown on the specimen label. For timed specimens, both the start and stop times of the collection must be shown. The time at which the specimen was received in the laboratory must also be documented for verification of proper handling and transport after collection.

### **Collection Method**

The method of collection should be confirmed when the specimen is received in the laboratory to ensure the type of specimen submitted meets the needs of the required test(s). An example of an optimum specimen/test match would be a first morning specimen for urinalysis and microscopic examination.

### **Specimen Preservation**

If the specimen is not received within two hours of collection, specimen reception personnel must confirm that a tube containing an appropriate preservative has been used. Confirmation that the specimen receipt time is within the allowable time for the particular preservation tube used must also be made.

### **Light Protection**

Specimens submitted for testing of light-sensitive analytes must be collected in containers that protect the specimen from light.

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## The cost of poor quality samples

Healthcare institutions are busy places. A 400-bed hospital can see hundreds of thousands of patients a year. Millions of blood tests will be taken, analysed and the results sent back for diagnosis and medical intervention.

The chance of error is small, often only 2 in every 1,000 tests, but the consequences can be enormous. And, with so many tests being processed, even a small chance of error means that thousands take place in every hospital, every year.

Frost & Sullivan, specialist analysts in market risk and growth consulting, were approached by Becton Dickinson in order to investigate the total direct and indirect impact of specimen quality on patient treatment and hospital costs in hospitals and laboratories. The objective was to develop metrics that would allow both hospitals and laboratories to ensure greater efficiency in the management of their organisations.

Healthcare institutions are under tremendous cost pressure and it is necessary to identify savings potential in a process-oriented and budget-spanning way. Laboratory diagnostics is a critical operational service centre in hospitals: 70 to 85% of the clinical decisions are based upon results from the laboratory<sup>1,2</sup>. Erroneous laboratory results can have severe consequences, from delaying the appropriate therapy, to unnecessary and additional clinical measures, to life threatening complications. Several studies have shown that the majority of errors occur in the pre-analytical phase of the laboratory diagnostics process, outside of the highly standardised and reliable laboratory procedures<sup>3,4,5</sup>.

Research has already been conducted into the causes of specimen rejection both in the pre-analytical and analytical phases of specimen collection but little information exists which quantifies the costs of such rejection on individual patients, or on the operating costs of health institutions.

There are two ways in which such analysis can be conducted: either through the quantification of every component of patient care, and the cost of each step and the time involved; or via a top-down approach where the overall macro-factors are analysed.

The former, bottom-up, approach would require measurement of every eventuality, as well as the interactions of all staff throughout the treatment process of a wide variety of scenarios. Since the total cost of running a hospital, and the total number of patients that a hospital can treat, are a function of its efficiency, the quantification of pre-analytical specimen rejection is all that is necessary to calculate the impact throughout the hospital treatment process. For this reason, a top-down approach was chosen as being more meaningful and cost-effective.

The model for measuring the cost of poor quality is derived from the impact of pre-analytical errors on the patients' length of stay. The top-down approach is perfect for this since it can be extremely difficult to track the impact of an individual error in unrelated areas of the hospital. An error which causes a healthy patient to be retested and discharged after an additional overnight stay can result in increased waiting lists in unrelated departments.

The model also allows a hospital to compare its results with those achieved at other hospitals.

In an evaluation and benchmarking study, the model was tested at hospitals in Germany, France and the UK. The total annual cost caused by pre-analytical errors differs widely between the different hospitals in the study as they differed in size, specialisation, strategy and approach. However, the model led to the conclusion that 0.2-0.3% of total hospital expenditure may be caused by pre-analytical errors (study result: mean of annual cost is €347,000). This magnitude reveals a tremendous potential for cost savings, even if human error cannot be completely eliminated.

BD now has a methodology to measure the cost related to pre-analytical errors. Combined with a concept for diagnosing areas for improvement, and the right tools to address these issues in a well-directed way, this approach has the potential for significant reduction of pre-analytical errors and their associated costs.

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## CASE STUDY

### Conversion to BD Vacutainer® Luer-Lok™ Access Device (LLAD) results in a 78% haemolysis reduction and improves healthcare worker safety

A case study was carried out in a 257 bed medical centre based in the US. Their focus on delivering high-quality patient care has driven performance improvement efforts at the institution. Specifically, one of these efforts sought to address the elevated rate of haemolysis in blood specimens received at the laboratory, particularly those collected from IV catheters on patients in the Emergency Department.

#### The Challenges

Blood collections are performed for various laboratory tests from outpatients, nursing floors, and the Emergency Department (ED); many specimens collected from the ED are from IV catheters. As such, a high rate of hemolysis has been documented, particularly from specimens collected in the ED. Following an assessment by a BD Care Consultant, the following observations were made:

- High number of haemolysed specimens (153), particularly from the ED. This was 83% of the total haemolysed specimens (184) received in the laboratory per month—an average of 5.1 haemolysed specimens per day.
- High rate of haemolysis in the ED as compared to other hospital units (e.g., ICU, Cath Lab, Outpatient).
- Non-standardised practices for collection of blood specimens from IV catheters:
  - Collection with a syringe and transfer of blood from the syringe with a straight or blunt needle.
  - Variable use of an extension set.
  - Collection via BD Vacutainer® Luer Adapter, BD Vacutainer® One-Use Holder and/or Saf-T Holder® Device (Smiths Medical).
- Potential for exposure to blood and/or needlestick injury when transferring the specimen from syringe to tube using a sharp needle.
- Reporting of results with caution statements about specimen quality due to the presence of haemolysis.
- Lack of data for rejected specimens and no method for recording; patients are simply re-drawn and treated as a new draw; non-capture of waste of time and products.
- Blood leakage encountered with current blood collection system (Saf-T Holder® Device) (increased blood exposure to healthcare workers).
- Non-adherence to an order of draw or to tube filling recommendations.

#### The Solution

Subsequent observation of current blood collection practices identified problem areas; the BD Care Consultant collaborated with the staff at the Medical Centre to address these areas, specifically, the issue of increased haemolysis. The Medical Centre then implemented the following:

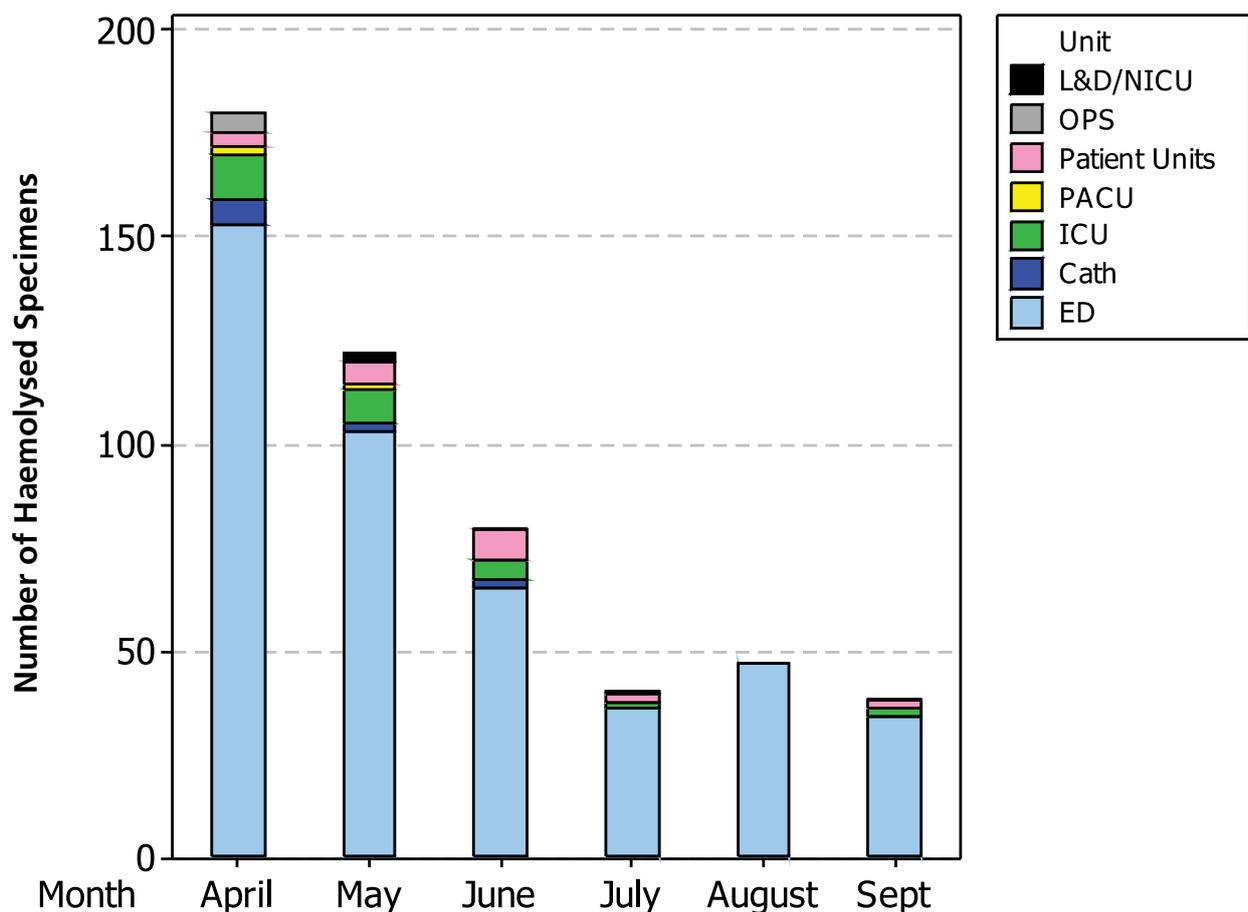
- Converted to BD Vacutainer® Luer-Lok™ Access Device (LLAD) for blood collection from an IV catheter, facilitating direct draw of specimen from the catheter to the evacuated tube. The one-piece transfer device of the LLAD provides a secure connection that enables sufficient blood flow and the best quality sample. It also minimises the potential for blood exposure.
- Adhered to CLSI recommended blood collection best practices (e.g. allowing alcohol to dry before venipuncture, reducing tourniquet time).
- Developed a color wall chart to distinguish order of draw and tube filling requirements as per CLSI guidelines.
- When a syringe collection was warranted, the use of a BD Vacutainer® Blood Transfer Device was recommended. This practice will help in the prevention of accidental needlestick injuries during transfer of the specimen from the syringe to the evacuated tubes, as well as better management of blood to additive ratio in the evacuated tubes.
- Conducted training with the staff to review specimen quality recommendations and improve current practices.

## Results

The laboratory experienced significant qualitative and quantitative progress following conversion to the LLAD and in-service training for the staff:

- Significant reduction in haemolysis demonstrated over a 6-month period (from a total of 184 haemolysed specimens in the first month to 38 in the sixth month) (see Table)
- Substantial decrease in hemolysis in specimens from the ED (from 153 in the first month to 34 in the sixth month; a 78% decrease in incidence of haemolysis) (see Table)
- Standardised blood collection practices for specimens from IV catheters
- Better specimen quality = improved accuracy of test results and overall patient care
- Improved healthcare worker safety by minimising exposure to blood and/or potential needlestick injury
- Enhanced staff morale and communication between departments (e.g. Emergency department, nursing floors, laboratory)

**Table. Number of Haemolysed Specimens Per Month**



Following the introduction of BD Vacutainer® Luer-Lok™ Access Device (LLAD), the number of haemolysed specimens received in the laboratory substantially decreased. Although the ED continues to have the highest incidence of haemolysis, the rate of haemolysis decreased by 78% after the introduction of LLAD.

# Needlestick Injury

One risk that can be prevented

Needlesticks are:

**“One of the most serious health and safety threats in European workplaces... Estimated to cause one million injuries each year.”**

*New EU Directive 2010\**



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Injuries caused by needles, sharp instruments and other objects are often considered to be an occupational hazard within the healthcare sector. In fact, every year, over 40,000 NHS workers suffer needlestick and sharps injuries<sup>1</sup>, exposing them to high-risk, blood-borne viruses such as Hepatitis B, Hepatitis C and HIV.

BD has developed a methodical, step-by-step approach to every aspect of the implementation of safety engineered devices into hospitals and other healthcare environments. With a comprehensive range of safety devices and support material, BD has the experience and knowhow to significantly reduce needlestick and sharps-related risks in your environment.

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