GE Healthcare

Whatman™ Neonatal Screening Cards-Capabilities

Whatman

Dear Customer

I am delighted to present this new brochure to you, outlining our extensive capabilities for supporting the global newborn screening community. Our goal is to work closely with your international community to better understand your specific needs, and to provide products and technologies that meet and exceed the stringent requirements of the crucially important newborn screening tests worldwide.

Whatman is recognized for its expertise in separations technology and for developing new and innovative products and services for the scientific community. The Whatman 903™ Specimen Collection Paper is a key strategic product for Whatman, and I would like to express my commitment to continue the supply of this product to the highest possible standards of quality and reproducibility. Our ultimate aim is that this will, in turn, support the efficient and effective screening of newborn babies worldwide.

The Whatman 903 Specimen Collection Paper is available in a range of pre-printed formats or can be custom printed for this very specific application. This paper can also be supplied in an unprinted format for customers wishing to develop their own devices.

Field based sample collection often requires the use of multiple products such as gloves, sterile wipes and a lancet in addition to the sample collection card itself. In partnership with our customers, we can develop and manufacture customised ready-to-use kits, ensuring that all the tools for optimal sample collection are available on site, clean, safe and ready for use.

All products are manufactured to the highest possible standards and are controlled by the internationally recognized quality management standards ISO 9001:2000 and ISO 13485:2003 as well as complying with the applicable regulatory requirements.

Our sales team is at your service to answer any of your requests. Please feel free to contact them through our customer service line that you will find at the end of this brochure.

Yours sincerely

Richard Dool
General Manager, Consumables

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Whatman 903

In 1962 Dr. Robert Guthrie first published procedures for screening newborns for Phenylketonuria (PKU). The Whatman 903 specimen collection device has played an important role in this screening, assisting in the widespread testing of PKU. This has resulted in the early detection and intervention for tens of thousand babies in the US. Today screening for anywhere between three to twenty or more analytes, including congenital hypothyroidism, galactosaemia, branched-chain ketonuria, maple sugar urine disorder and sickle-cell anaemia is possible with our 903 collection paper. More recently, with the advent of tandem mass spectrometry technology, many programs are adding less frequently occurring disorders to their panel of analytes, including MCAD, cystic fibrosis and a range of amino acid disorders. In 1998, Whatman 903 became the international standard for body fluid sample collection, transport, analysis and archiving.

Purity, consistency, and excellent absorption characteristics is important for neonatal blood collection papers. The paper must be free from impurities that may interfere with the quality or composition of the sample. It must also be validated in compliance with the requirements of the CLSI LA4-A5 consensus standard. The Whatman 903 cards meet these specifications and are listed as a FDA Class II Medical Device and are sold as a 'CE' marked 'In-Vitro Diagnostic' in Europe in compliance with 98/79/EC.

Whatman 903 Quality Control

The Whatman 903 paper, which is an FDA-registered 'In-vitro' Class II medical device in the USA, is used in virtually all US and international newborn screening programs. All 903 manufacturing is in accordance with Good Manufacturing Practices (GMP). Novel equipment ensures uniformity and adherence to specified parameter ranges. Since the stability of the collected sample can be affected by the composition of the paper, Whatman carefully controls the manufacturing process to ensure homogeneous composition, uniform thickness, flow-rate, absorbency and purity.

The Whatman 903 paper is manufactured from 100% pure cotton linters with no wet-strength additives. Since it is a medical device in the US, Whatman 903 paper has to be manufactured under controls compliant with the FDA Quality System Regulations. In addition, serum uptake analysis is conducted for each lot of 903 paper by an independent testing laboratory and by the Centers for Disease Control Newborn Screening Quality Assurance Program. Only when all test results confirm that a batch of 903 paper meets the aforementioned specifications can that lot be released and used for specimen collection.

Whatman 903 Properties

Parameter	Range	Parameter	Range
Basis weight (g/m^2)	170 – 188	Blood spot diameter (mm/100 µl)	15 – 17
Serum uptake intact red blood cells (µl 1/8" disc)	1.37 – 1.71	Blood absorption time (seconds/100 ml)	5-30

Neonatal Screening Cards – Regulatory requirements

Classified as a Class II Medical Device the Whatman Neonatal Screening Cards are manufactured and quality released in compliance with the FDA Quality System Regulation 21 CFR Part 820.QSR. As such, Whatman manufacturing sites may be inspected by the Food and Drug Administration. In April 2007 Whatman was audited by the Center for Devices and Radiological Health. During this process Whatman was able to confirm that the Neonatal Cards are manufactured in compliance with Good Manufacturing Practices (GMP).

As an 'In-Vitro Diagnostic' Device in both the US and EU, Whatman applies the IVD mark to 903 neonatal blood collection cards. This identifies that Whatman has applied and demonstrated all applicable requirements of the FDA and European 'IVD' Directive with regard to sample collection devices.

The FDA and European 'IVD' Directive requires that medical devices benefit patients and users by being both safe and effective, and does this by setting out 'Essential Requirements' to ensure that the device does not compromise the health or safety of the patient or user in use. Whatman is responsible for ensuring that the product is both safe and effective under these guidelines in addition to meeting regulatory requirements such as the International Quality Standard for Medical Devices, ISO 13485:2003 and the Directive 98/79/EC.

Manufacturing of quality cards

Printing of paper for newborn screening is a very critical production step that is strictly defined in the CLSI standard. Inappropriate printing technologies may have a negative impact on the characteristics of the paper resulting in false test results. Whatman 903 paper is printed and provided as a controlled package that includes detailed demographic information about the newborn.

Whatman Quality Control tests a number of cards from each printed job to evaluate blood absorption time and circle size. Only if all test results are within agreed parameters can the card production be released and dispatched to the customer.

Custom printing – Capabilities and advantages

Transportation and storage of Neonatal Screening Cards

Whatman 903 Neonatal Blood Collection Cards provide a safe and efficient method for easy sample collection, identification and transport.

Newborn data is documented on the demographic portion of the form which is attached to the Whatman 903 sample area. This product design reduces the likelihood of sample misidentification.

Transportation of newborn samples collected and dried on Whatman 903 cards can be safely mailed in non-specialized packaging for shipment to a central laboratory for processing. This significantly eliminates the high costs of overnight delivery on dry ice. Air transport is also not a concern as dried blood samples bound to the paper are classified in the lowest risk category by the International Air Transportation Association (IATA).

Blood samples dried on Whatman 903 cards for protein analysis should be stored at –20°C in a sealed bag with a desiccant pouch to eliminate the possibility of degradation over extended periods of time (CLSI LA4-A5).

Whatman 903 Cards – Advantages

Regardless of where the procedure is conducted, information about the sample must be recorded and cataloged at the time of collection.

Whatman custom printed forms are designed with this function in mind. Individually designed collection matrices are available and can be used as a single part card or incorporated into multi part specimen collection cards.

To avoid any potential risk of sample misidentification, Neonatal Screening Cards need to clearly show newborn details in the demographic section of the form. The minimum information which should be present on the card as documented in CLSI LA4-A5:

- Infant´s name (surname/family) (first (forename) if available)
- Mother´s last name (surname/family) (optional: include mother´s maiden name) and first name (forename)
- Sex
- Birth date (optional: include time of birth; gestational age)
- Date of specimen collection (optional: include time of collection)
- Infant´s age (if this can be extrapolated from other data fields it is optional)
- Patient identification number (eg: medical record number, optional: include address and phone number)
- Birth weight
- Submitter identification & address or submitter code, if linked to address (optional: include birth facility)
- Physician´s (healthcare provider) name & telephone number
- Name of newborn screening
- Program and laboratory address
- Unique nonrepeating Serial Number
- Expiration date of specimen collection device
- Appropriate number of preprinted circles should be available with preprinted broken- or dotted- line circles on one side of the filter paper section (with optional printing of circles on both sides). (In the United States, the preprinted circle 12 mm to 13 internal diameter is filled to the printed line by 75 µl of blood while 100 µl fills slightly beyond the print).
- Manufacturer and lot number of filter paper indicated on the filter paper section, and manufacturer or printer listed on the patient information section of the form (optional: bar codes may be imprinted on the specimen collection device [see Section 7.2.2] and bar codes should contain a check sum digit). To avoid confusion, neither the manufacturer's nor the printer's address should be placed on the collection device.

Whatman offers an extensive range of devices to fit your application needs. By combining our knowledge of the minimum regulatory information required together with your specific requirements, we can develop a customized card that meets your needs and complies with the IVD regulations.

Custom printing – Capabilities

Two part card

Writing directly onto the 903 paper is not feasible as it absorbs ink from the pen and words may appear illegible. It also increases the risk of sample contamination. The A two part card consists of the 903 sample area glued to a demographic card available in either black or OCR (optical character recognition) red.

The two part card can also include additional features such as a barcode and can be printed in multiple colors.

Product benefits:
- Use of barcode system
- Card can be printed with several colors
- Easier writing on the demogophic section
- OCR scannable format

Multi part card

The multi part card consists of three parts or more and can be printed in black or OCR. Similar to the two part card, the 903 sample area is attached to the demographic card and can have one or two top carbon layers for trans-fering information.

Additional features of the multi-part card include a wrap-around cover, which protects the 903 blood collection paper, one barcode, unique identification numbering and is available in a variety of ink colors.

Product benefits:
- Carbonless top layers for the production of several copies
- Protection of the sample area by wrap-around cover

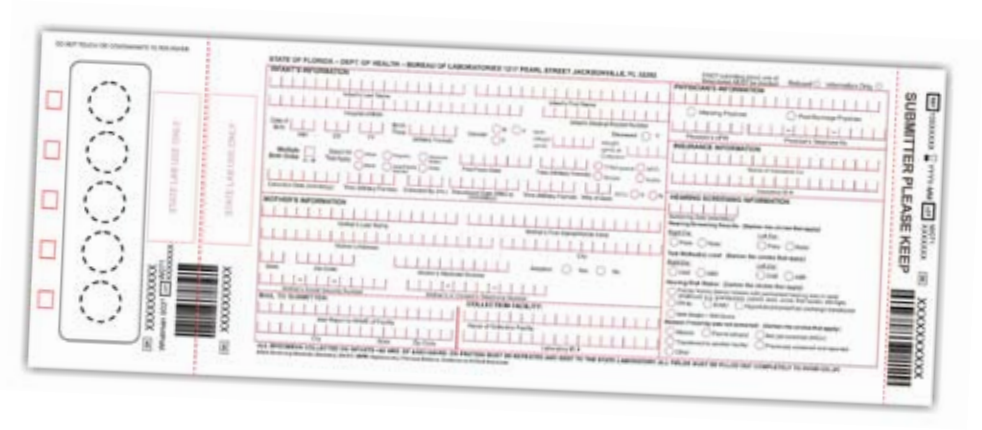
Cassette card

Custom cassette formats are ideally suited for automated processing. The 903 sample area is integrated into a cardboard frame, which is glued with the demographic part.

The cardboard frame gives stability to the 903 sample area, which is required when samples are handled by robotic instruments.

The cassette card is available with barcode information for traceability and OCR scannable demographic sections. Of course your individual logo can be printed in multiple colors.

Product benefits:
- Cardboard cassette frame around the sample area for automated handling



Whatman 903 Capabilities – Summary

Capabitities

	903 single part card	903 two part card	903 multi part card	903 cassette card
CDC recommended paper for neonatal screening		✓	✓	✓
Product meets US and EU for neonatal screening		✓	✓	✓
Product manufactured under Good Manufacturing Practices (GMP)	✓	✓	✓	✓
Sequential card	✓	✓	✓	✓
Available in more than one printing color		✓	✓	✓
OCR scannable formal		✓	✓	✓
Barcodes adapted to your barcode system		✓	✓	✓
Wrap-around cover for protection of sample area			✓	✓
Additional carbon layers for duplicating information			✓	✓
Cassette frame for automation				✓

Custom Kits – Capabilities

Customized kits
Field based sample collection often requires the use of multiple products such as gloves, sterile wipes and a lancet in addition to the sample collection card itself. Whatman can develop and manufacture customized ready-to-use kits for specific end user applications, ensuring that all the tools for optimal sample collection are there on site and ready for use.

Sequential numbering
Cards can be provided with sequential numbering. This means that each of your cards will have a different number which is essential for tracking and identification purposes.

Barcodes
Cards can be provided with barcoding on the demographic portion in any format that can print alphanumeric characters (letters, digits and some special symbols). Data integrity is enhanced by the use of modulus check digit characters.

Barcodes can be printed across a perforation where the card would be separated in the laboratory. This ensures traceability of all sections of the card. Shown on the left is a depiction of the Florida card shown on P10. We can also print removable adhesive barcodes for your cards that can be adhered to accompanying paperwork.

Color coding
Custom printed cards can be color coded to simplify form distribution after sample collection.

OCR-scannable format
Whatman can use special inks for printing forms that are invisible to optical character recognition (OCR) scanners, ensuring that scanners will detect only the variable demographic information (i.e. written information input by the sampler).

Wrap-around covers
Wrap-around covers are attached to the 903 card and can be “wrapped around” the 903 sample collection part of the card to protect the sampling area. This wrap-around cover is available in different materials: 28-pound paper, translucent glassine or clear moisture-proof barrier. This protects the sample and can eliminate the need for additional glassine envelopes.

Custom packaging
A specified coding system can be printed on every package, carton and shipping box. Outside cartons can be labeled to reflect the sequential numbering of the forms enclosed.

Hearing section
It is possible to add a section to a card for hearing test results. This puts all the screening results together in a database under a single control number.

Parent information sheets/pamphlets
Parent information sheets that are part of the neonatal collection device and include the device numbers can be provided as the first part of a multiple-part form. Alternatively, detailed parent information pamphlets can be glued to the form.

Transfer or mailing envelopes
Whatman can provide custom envelopes for mailing of samples to the central laboratory, for sending a screening form home with the parent for follow-up sampling, or sending samples to separate laboratories for non-standard screening tests, i.e. for DNA testing or supplemental screening. These envelopes are frequently color-coded.

Case Studies

Case studies: How 903 cards meet the requirements of different international screening programs

Safe and secure handling

Linda Malan:

"The standardization and quality assurance of the one part card is most important to us as it ensures safe and accredited handling."

Safe and quality tested handling

Linda Malan is manager of the newborn screening laboratory at North-West University in Potchefstroom, North West Province of South Africa. As the South African Government does not yet support routine newborn screening, the laboratory is in the final stages of a pilot project as well as rendering a service based on requests. The disorders tested for currently are congenital hypothyroidism, cystic fibrosis, classical galactosemia, and several amino acid disorders, organic acidurias and fatty acid oxidation disorders. The laboratory analyses 100 to 200 samples from newborns per week and also performs monitoring of PKU patients. Since neonatal screening started in 1999 the laboratory has processed about 80.000 samples in total. Before introduction of the Whatman one part card Malan's group had used 903 paper in A4 size, which was cut and attached to their requisition card. With the one part card the process is considerably streamlined, as the 903 paper itself does not have to be handled by the laboratory staff anymore. The group can also design individual cards for each pediatrician so samples sent in can be immediately and safely identified. The one part cards are standardized and quality controlled after printing of the cards. Whatman Quality Control tests 903 paper for blood absorbency and circle size throughout the manufacturing run and ensures that each lot of 903 paper meets CLSI specifications. Another advantage for the laboratory is the fact that the card is manufactured and tested according to FDA standards. This is an important feature, as the group is undergoing the process of accreditation, for which an established quality evaluation of the cards needs to be demonstrated.

Safe data storage

Dr. rer. nat. Cornelia Mueller:

"The Two Part Card is of high value as it enables us to store the blood sample and the demographic data in different places, thus ensuring absolute data protection."

Ensuring high data storage safety

Dr. Cornelia Mueller is head of the newborn screening laboratory (Director of newborn screening programme: Prof. Ch. Fusch) since 2000 and is associated with the children's hospital at the University of Greifswald, Germany. Since the beginning more than 4 million samples have been analyzed. Dr. Mueller is responsible for fast and quality oriented performance of all laboratory tests, laboratory organization and contact with customers (hospitals, resident doctors). Up to 130 newborn samples are analyzed per day, plus follow up samples of patients suffering from PKU and other diseases. Screening is performed following the guidelines of the German Federal Chamber of Medicine which iincludes screening for endocrine, metabolic and fatty acid oxidation disorders using tandem mass spectrometry. 99.8 % of all newborns are included in the program.

In the beginning, the laboratory used a One Part Card. This, however, did neither offer enough space for entering the necessary data, nor was there a possibility of separating the sample from demographic data. Since 2002 the laboratory has been using the Whatman Two Part Card. On the paper part the child's and mother's demographic data such as name, date of birth and weight can be entered while the filter part holds the blood sample. The filter is mounted on the card to ensure that the card can be printed by a computer printer. For archiving, the paper and the filter parts can be easily separated. Safe distinction of each card is ensured by means of barcodes on both parts, which will be stored for ten years at separate, secure places to ensure data safety and protection. The two parts of the card can only be reconnected with the parents' consent.

Use of Multi Part Neonatal Card in UK

Kate Hall:

"Not only screening laboratories but also the health service staff who collect the blood spots really appreciate the flexibility of using the same card for their individual documentation requirements."

More process flexibility

The UK Newborn Screening Laboratories Network, UKNSLN, decided to switch to the American CLSI specifications for their standard multipart newborn screening test cards. Whatman 903 paper complies fully with these standards and is the collection paper used in all UK cards. Consistency of paper quality is very important especially in tests for cystic fibrosis or other disorders, where there is less discrimination between normal and abnormal test results than for PKU or sickle cell disease screening. This makes excellent paper uniformity a prerequisite for reliable results.

The West Midlands Newborn Screening Center is part of the Pediatric Clinical Chemistry Department at Birmingham Children's Hospital NHS Trust (BCH) and provides a service for newborn screening for the West Midlands. The laboratory processes approximately 250 blood spot cards per day, with tests for five disorders for every baby. The 903 standard multi part card's major advantage for Birmingham and many UK screening laboratories is that separate sheets can be torn off individually and used for records by the various parties involved, i.e. the midwife collecting the blood spots, the laboratory performing the test, reporting results and finally archiving records. A sheet can also be used to request further samples or information. Barcodes are printed on the top sheet, enabling electronic registration of the card's unique serial number and process automation.

Kate Hall is Section Head of the West Midlands Newborn Screening Center at BCH and Secretary/Treasurer to the UKNSLN, for which she has acted as a consultant for the design of the standard multi part blood spot card.

Use of cassette card in Belgium

Dr. Francois Eyskens:

"The clear differentiation on the cassette cards between the frame where all the registration is placed and the filter paper where the blood is collected has clearly improved process workflows, speed and quality."

High throughput neonatal mass screening

The Metabolic Laboratory of the Provincial Center for Metabolic Disorders (PCMA) in Antwerp is a Belgian Government institution involved in the investigation and diagnosis of metabolic diseases. The laboratory performs neonatal mass screenings on 33,000 probes of newbornsper year. Selective screening is done on body fluids sent in by hospitals and independent specialists whenever a metabolic disorder is suspected, resulting in a sample amount of approx. 1,500 probes per year. Currently, the PCMA is preparing a shift from a manual to a fully automated workflow using Whatman 903 cassette cards, which are already designed to run on a new automation platform. All cassette cards are barcode labelled for clear identification and documented workflows. The charts are integrated into the laboratory's LIM system for data tracking.

Since 2006, when the PCMA switched to the cassette card, in which the 903 sample area is integrated into a cardboard frame, it has already been delivering significant advantages over the one part cards previously used.

Thanks to the cardboard frame the staff does not have to touch the paper itself anymore. This protects the sample area on the paper from being contaminated. The laboratory appreciates the fact that the cassette cards, which are archived for seven years at the PCMA, can be folded so that the frame completely covers the 903 sample paper, ensuring that the sample will not be exposed to other samples during storage.

Dr. Francois Eyskens, General Director of the PCMA, Antwerp, Belgium.

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