Design of blood collection devices (cards) – items for consideration

(prepared by Kate Hall, January, 2016)

Introduction

A dried blood spot (DBS) collection device or card is an approved in vitro diagnostic (IVD) medical device (eg, US Food and Drug Administration Class II) comprising a specified collection medium, usually an untreated cellulose based paper often described as filter paper, on which printed circles indicate the area to be filled with whole blood. For example, a specimen of approximately 75 µL of whole blood, haematocrit of 50-55%, will fill a 12–13 mm diameter and 30 - 50 µL whole blood a 10 mm diameter circle printed on the device.

Blood collection devices (cards) may be designed and redesigned for a variety of reasons which can include:

- commencing newborn screening for the first time
- improving ease of form completion
- commencing a new or additional screening test
- requiring additional demographics and/or specimen detail for result interpretation
- commencing new screening strategies or policies for current screening related to a specific demographic
- introducing laboratory automation which may require specific card features
- introducing digital blood collection devices (cards) image storage
- introducing long term blood collection devices (cards) /collection matrix storage
- introducing tracking of each baby's blood collection devices (cards) journey (specimen tracking)
- commencing formalised collection of consent or decline for newborn screening

Cellulose based absorbent paper

The fundamental part of any blood collection device (card) is the collection paper which absorbs drops of blood. It is strongly recommended that the blood absorption characteristics of the collection medium used for card manufacture are specified and that batch to batch variability is checked for compliance versus the specification. The only international standard currently available for specification and evaluation of collection paper blood absorption uniformity, lot by lot, and after card construction is CLSI NBS01-A6. Papers which have been able to satisfy this specification include

Perkin Elmer 226
Whatman 903 from GE Healthcare Life Sciences
Munktell TFN Neonatal Screening from Ahlstrom (in house testing by manufacturer)

Collection paper from other manufacturers may be able to comply.

The Centers for Disease Control, CDC, will test absorbent papers utilising the NBS01-A6 testing protocol for lot to lot blood absorption consistency both before and after blood collection device (card) construction. Approval certificates for each lot of paper should be sought from card manufacturers prior to purchasing cards. The blood absorption an blood spread data for cards pulled for quality assurance post manufacture should be requested. Calibration and quality assurance materials must also be made from collection paper with the same properties for valid test results.

Card construction

The absorbent paper is likely to be the most expensive part of the card if CLSI NBS01-A6 compliant due to the validation of blood absorption characteristics which needs to take place. It may therefore be advisable to reduce the size of this as much as possible to keep costs down by confining printed circles to a thin strip attached to a card. The demographic detail form may be attached along one edge of the absorbent paper, a 2-part card.

For simplicity the whole blood collection device (card) may alternatively be formed entirely from the cellulose based absorbent paper, a 1-part card, and demographic information recorded on it in suitably viscous ink eg ballpoint pen. However, print resolution may be severely compromised by printing onto filter paper, bars of barcodes bleeding into neighboring bars for example. For increased print quality at reduced costs especially

where barcodes are required, 2-part cards as described above are optimal. Another option, when the whole card is formed of absorbent paper, is for the manufacturers to staple a sheet/request form for demographic details along the edge opposite the target circles. The sheet should not cover the bloodspot collection area.

Several copy-through demographic/request forms may be useful for some purposes such as the card submitter retaining a detachable copy of what was sent to the laboratory in their records. These forms may also be attached by the card manufacturer either by stapling as described above or gluing to a back sheet along the edge opposite to the guide circles. If birth labels are then to be applied rather than handwriting demographics great care should be taken to ensure each sheet has a matching label affixed.

Printed circles on the absorbent paper to guide the size of blood drop required should be dotted or dashed and not compress the paper lines so that there is no or minimal damming effect on the flow of the blood droplet. If printed (dashed or dotted) circles are required on *both* sides of the absorbent paper, it may be important to specify to the printer that the circles are aligned and particular caution exercised to avoid or minimise compression of the paper.

Automation

Hands free automated punchers and processors require a card frame around the printed target circles, a cassette, as the absorbent paper alone is insufficiently stiff to be handled mechanically.

Demographics to request

Enough written and pre-printed information should be collected onto the blood collection devices (cards) to be able to

1. identify the infant robustly
2. record consent, opting in or out according to the country or jurisdiction of testing's policies and requirements. Examples include consent for specific tests, provision of specific test results eg carrier results, card storage post analysis.
3. track the specimen through the whole process
4. interpret test results correctly

Robust identification of the infant

Ideally, if provided at birth, a unique identification number for the infant should be recorded on the blood collection device (card). Labels may be produced by the birth facility containing the identification number in a barcoded format to apply to the card and to avoid transcription errors. Using the baby's unique identification number it may be possible to access and link to birth details recorded digitally elsewhere via the birth facility in some countries eg UK.

*Surname (and forename if known) are important in identification but *may not be robust* where some surnames are very common

*Indication of rank for multiple births is essential eg 2/3 can be used to represent the second born of triplets

*Birth weight assists with identification for multiple births and for those babies with the same name born by chance on the same day

*Mother's name, date of birth plus her own unique id number if available are extremely important

*Address for the baby is helpful for identification and essential for follow up of abnormal results. An opportunity to add a temporary address is very valuable for this purpose as babies do not always return immediately to the family home on discharge from the birthing facility

Tracking the specimen through the whole process

Card - recording by blood collector

Some options are possible here and include printing a unique, non-repeating, serial number on the card at manufacture. Additionally adhesive labels can be put on the cards in manufacturing containing the card's unique number alongside that actually printed on the card. The label can then be removed and adhered to baby's records. The blood collector should thus note the card serial number in the baby's records or notes either manually or by use of the label on the card. Note that barcodes are difficult to print onto the absorbent paper.

Card - recording by laboratory

The card should be printed with a unique, not repeating for at least a few years, card serial number. This serial number may be barcoded for subsequent accurate reading into the laboratory computer with a barcode reader thereby avoiding transcription errors. In addition, removable adhesive labels containing the identical barcode or unique number can be put on the cards in manufacture alongside that printed on the card. The label can be removed and adhered to patient records. The card serial number can be recorded in the testing

laboratory against the screening test results and can be tied to or linked with the baby's unique identifier and/or name and date of birth. Otherwise the card may be tracked through the laboratory by addition of a second unique, not repeating for at least a few years, specimen identification number applied on receipt in the laboratory and recording this against the baby's name, date of birth and additional demographics as required in the laboratory.

Baby- recording by laboratory

Layout of device

Provision of squares or blocks into which to write demographic data can help in encouraging legibility. Fixed demographics such as date of birth, time of birth, mother's demographics, ethnicity, gender, billing information could be kept together on one side of the form so that a birth label produced by the birthing facility can be affixed. Variable demographics could then be positioned on a separate part of the form eg date and time of blood collection, date and time of last transfusion- for manual completion on the appropriate day of life and at the time. This can assist data entry personnel to more quickly enter onto computer.
If the details on the form are to be optically character read the form layout will need to accommodate this. Blocks should be lined up and can be checked by viewing the card from its edge.

Requesting information that is difficult to obtain or not routinely used is a waste of resources. Furthermore, it is recommended not to ask for information that is not to be used or monitored for legal protection. If there is an information block present, it is assumed that you are using it and, should there be a lawsuit, you may be asked to explain why you did not take a certain action given the information on the form. In addition, information requested should be evidence based and relate to methods of testing currently in use eg feeding information for galactosaemia screening and drug or antibiotic use if there is known interference with the method of analysis.

Forms which highlight infant, mother, physician and submitter information read more clearly

Optically character reading

If the details on the card are to be optically character read in to the screening laboratory computer then the ink colour on the form should contrast with the colour of pen marking generally being used in the birthing facility. Thus red ink printed on the form is preferable as it is usefully colourless to computer systems that might use machine readable forms.

Interpretation of test results

For many bloodspot screening tests analyte concentration cutoffs relate to the age in days of the baby, thus date of birth and date of specimen are essential. Similarly some test results require knowledge of gestation/birth weight for interpretation (e.g. congenital adrenal hyperplasia). A simple way of recording gestation can be by relating to 40 weeks as the accepted typical full term gestation. A pre-term baby of 29 weeks gestation can be recorded simply as 29 (weeks) for example.

Some test results may require knowledge of gender (e.g., Duchenne muscular dystrophy). The majority of test results are likely to be affected by transfusions either by dilution of the baby's blood or provision of donor's instead of the baby's red cells for haemoglobin and red cell enzyme screening. The date and time of the most recent transfusion and time of blood collection may be relevant demographics to confirm whether the transfusion was before or after spot collection. Distinguishing between red cell and plasma transfusions may be helpful.

Some test interpretations are assisted by knowledge of ethnicity or racial ancestry if accurately recorded. For example a suspected sickle cell disease screening test result is unlikely in a baby of Chinese ancestry. Ethnicity or racial ancestry may be coded country wide for ease of gaining valuable information and experience. There is no internationally agreed coding for ethnicity.

Note

No matter how well a bloodspot collection card is constructed and quality checked pre and post manufacture, the validity of analytical test results depends critically on the volume and homogeneity of blood applied.

References

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