Identification of key meta data to enable safe accurate and effective transferability of biological variation data.

Biological Variation Working Group, European Federation of Clinical Chemistry and Laboratory Medicine, http://efcclm.eu/science/wg-biological-variation, www.biologicalvariation.com .

***Bartlett William A :** Blood Sciences, Ninewells Hospital & Medical School, Scotland, UK DD1 9SY. bill.bartlett@nhs.net
***Braga Frederica:** Luigi Sacco Univeristy Hospital, Milano - Italy.
***Carobene Anna:** *Diagnostica e Ricerca, San Raffaele Spa, Milano - Italy.*
***Coşkun Abdurrahman:** Acibadem University, School of Medicine, Gülsuyu, Maltepe, Istanbul - Turkey.
***Prusa Richard:** Charles University and University Hospital Motol, Prague - Czech Republic.
***Fernandez-Calle Pilar:** Hospital Universitario La Paz, Madrid - Spain.
Røraas Thomas: Norwegian Quality Improvement of Primary Care Laboratories (NOKLUS), Haraldsplass, Hospital, Bergen, Norway
***Leimoni Irini:** Euromedic S.A. Athens - Greece.
***Sandberg Sverre:** Haukeland University Hospital, Bergen, Norway.
***Jonker Niels:** Certe, Wilhelmina Hospital, Assen, The Netherlands.

*** Biological Variation Working Group, EFCCLM**

Background

Biological variation data (BVD) are reference data with many applications in laboratory medicine. Appropriate transfer of BVD across populations and through time requires the user to have -knowledge of the characteristics of the population from which the data were derived -an understanding of how the data were derived and -an appreciation of the uncertainty that surrounds the reported estimates. As a consequence an estimate of within and between subject biological variations should be transmitted and adopted for use only if accompanied by a set of meta data that sufficiently characterises the BVD in those contexts. The Biological Variation Working Group (BVWG), set up by the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM), have undertaken work to identify a candidate minimum data set (MDS) to accompany published indices of within and between subject biological variations to enable this issue to be addressed

WWW.BIOLOGICALVARIATION.COM

Users of biological variation data (BV) require an understanding of the provenance and uncertainty around these data. Safe, accurate and effective application of BV data in clinical settings across the world requires that they are well characterised and accompanied by sufficient metadata to enable transferability into practice.

Survey of the literature indicates a high degree of heterogeneity in BV data. Publications by Braga *et al* (Clinica Chimica Acta 2010;411: 1606-1610), Carobene *et al* (CCLM, 2013;51:1997-2007) and Miller et al (Clin Chem 2009;55:24-38) relating to HBA_{1c}, hepatic enzymes and urinary albumin respectively highlight the problem In Carobene's review subject variability (CV_i) of 3 liver enzymes ranged from 3% to 58% while in Miller's review of urinary albumin excretion CV_i values ranged from 4% to 103%. Those publications not only highlight significant differences in the published estimates of BV, but also identify limitations in experimental design used to derive the data, inappropriate study lengths, and poorly described of statistical methods. This clearly identifies a need for standards for production, reporting and transmission of BV data to ensure generation of fit for purpose data and to enable correct contextual application of those data in clinical practice. The EFCCLM Biological Variation Working Group on Biological Variation (BVWG) are proposing that a minimum data set (MDS) to accompany published BV data is required to enable transmission of the BV data and to enable the transferability of the data across populations.

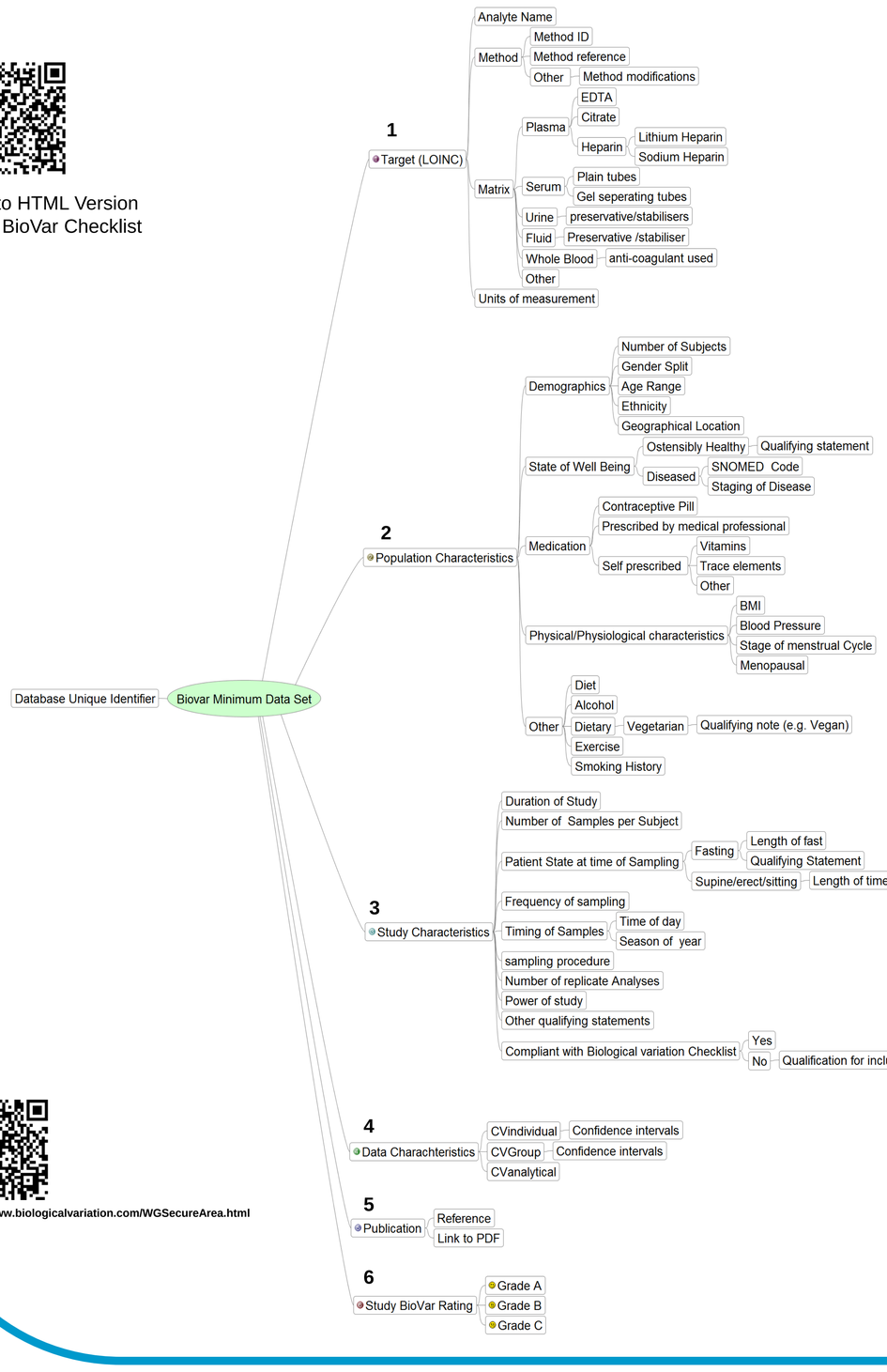
Six main data domains were identified by the BVWG to enable transferability of BV data safely, accurately and effectively (Fig. 1). The high level domains, 1 to 4, encompass a high degree of complexity and a practical difficulty arises in communication of the detail. In consequence domains 5 and 6 should form part of the MDS to enable users to link to source publications to ascertain fine detail and also enable sharing of expert opinion as to the quality of the data. The study rating (domain 6) is a concept that is being development, but may take into account a scoring systems assessing experimental design and study power. Roraas et al (Clin Chem 2012;58:1306-13) have identified an approach to delivering confidence intervals and power calculations for within-person biological variation. They looked at the effect of analytical imprecision, number of replicates, number of samples, and number of individuals on the estimates. Such a rating might easily be included in published database. There are parallels in this approach to the rating of medical evidence. Ideally only "A" rated data should be published in the future, but there will be a requirement to assess the existing literature accrued over the past 40 years into further categories . The BVWG checklist will provide a route to enable this (see QR Code in Fig. 1 or visit www.biologicalvaraition.com).

BV data are reference data and consequently the principles under-pinning the concept and theory of reference values that requires transmission of metadata to enable the valid application of reference data to a population apply. Consistent transmission of the BV data with required meta data will however prove challenging. The use of coding systems such as SNOMED, LOINC *etc* may enable the delivery of an MDS electronically. The use of approaches that include embedded links from laboratory documentation to *bona fide* reference sites may provide a solution. An alternative might be incorporation of data into QR codes (Fig2). These can be read on smart telephones and other electronic devices. They could be passed on *via* manufacturers kit inserts containing the full MDS or an agreed skeleton content that links to the more detailed data set.

This approach will enable definition of a data archetype that will enable forward transmission of BVD to enable their safe, accurate and effective adoption and application into contemporary practice.

Fig.1. Data domains defining minimum data set to enable transferability of biological variation data.

Link to HTML Version
Draft BioVar Checklist



http://www.biologicalvariation.com/WGSecureArea.html

Fig 2. QR Code: MDS For BV Creatinine

Conclusion

The working group believe that availability of a standardised minimum data set, as proposed above, will enable users to be more objective in the transfer of published BVD into their local and wider practice. This will prove challenging to deliver, and require mechanisms to facilitate the extraction of meta-data from publications for attachment to the BVD to enable forward transmission and transferability (e.g. incorporation into databases). This will require further development of the concept of a BVD data archetype incorporating internationally accepted coding systems (e.g. SNOMED, LOINC) and vocabularies.