# Biomarker Reference Table

| CATEGORY/ SUBCATEGORY | REFERENCES | COMMENTS |
|---|---|---|
| GENERAL | | |
| ME/CFS-specific guidelines | Jason LA, Unger ER, Dimitrakoff JD, Fagin AP, Houghton M, Cook DB, et al. Minimum data elements for research reports on CFS. Brain Behav Immun. 2012 Mar;26(3):401-6. | Primarily focused on clinical and demographic data |
| Observational studies | von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. PLoS Med. 2007 Oct 16;4(10): e296. | Checklist of items that should be addressed in reports of observational studies<br>Guidelines for reporting observational studies (STROBE-The STRengthening the reporting of Observational Studies in Epidemiology) |
| Guidelines for biological and biomedical investigations | McShane LM. In Pursuit of Greater Reproducibility and Credibility of Early Clinical Biomarker Research. Clin Transl Sci. 2017 Mar;10(2):58-60.<br><br>Kettner C, Field D, Sansone SA, Taylor C, Aerts J, Binns N,et al . Meeting Report from the Second "Minimum Information for Biological and Biomedical Investigations" (MIBBI) workshop. Stand Genomic Sci. 2010 Dec 25;3(3):259-66.<br><br>Taylor CF, Field D, Sansone SA, Aerts J, Apweiler R, Ashburner M, et al. Promoting coherent minimum reporting guidelines for biological and biomedical investigations: the MIBBI project. Nat Biotechnol. 2008 Aug;26(8):889-96.<br><br>EQUATOR Network (Enhancing the Quality and Transparency of | A key initiative for identifying the minimum data required information with the aim of harmonizing data: Minimum Information for Biological and Biomedical Investigations (MIBBI): http://mibbi.org<br><br>McShane paper contains links to initiatives identifying minimum required information for the aim of harmonizing data |

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| | Health Research; http://www.equator-network.org/)<br>*Simera I, Altman DG, Moher D, Schulz KF, Hoey J. Guidelines for reporting health research: the EQUATOR network's survey of guideline authors. PLoS Med. 2008 Jun 24;5(6): e139.*<br><br>Becker, R., Jr. Analytical validation of in vitro diagnostic tests. In Design and Analysis of Clinical Trials for Predictive Medicine (eds. Matsui, S., Buyse, M., Simon, R.) 33-49 (Chapman & Hall/CRC, Boca Raton FL, 2015)<br><br>Jennings, L., Van Deerlin, V.M., Gulley, M.L. for the College of American Pathologists Molecular Pathology Resource Committee. Recommended principles and practices for validating clinical molecular pathology tests. *Arch Pathol Lab Med* **133**,743-755 (2009).<br><br>Linnet, K., Boyd, J.C. Selection and analytical evaluation of methods with statistical techniques. In *Tietz textbook of clinical chemistry and molecular diagnostics* 5th edn. (eds. Burtis, C.A., Ashwood, E.R., Bruns, D.E.) 7-47 (Elsevier Saunders, St Louis MO, 2012).<br><br>Pennello, G.A. Analytical and clinical evaluation of biomarkers assays: When are biomarkers ready for prime time? *Clinical Trials* **10**, 666–676 (2013).<br><br>Wallstrom G, Anderson KS, LaBaer J. Biomarker discovery for heterogeneous diseases. Cancer Epidemiol Biomarkers Prev. 2013 May;22(5):747-55. doi: 10.1158/1055-9965.EPI-12-1236. Epub 2013 Mar 5.<br><br>Gosho M, Nagashima K, Sato Y. Study Designs and Statistical Analyses for Biomarker Research. Sensors (Basel, Switzerland). | |

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| | 2012;12(7):8966-8986. doi:10.3390/s120708966.<br><br>Wallstrom G, Anderson KS, LaBaer J. Biomarker discovery for heterogeneous diseases. Cancer Epidemiol Biomarkers Prev. 2013 May;22(5):747-55. doi: 10.1158/1055-9965.EPI-12-1236. Epub 2013 Mar 5.<br><br>Power analysis tools for biomarker discovery with heterogeneous diseases | |
| Assessing / Reporting Biomarker Accuracy | Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig L, et al. STARD Group. STARD 2015: an updated list of essential items for reporting diagnostic accuracy studies. BMJ. 2015 Oct 28;351:h5527.<br><br>Cohen JF, Korevaar DA, Altman DG, Bruns DE, Gatsonis CA, Hooft L, et al. STARD 2015 guidelines for reporting diagnostic accuracy studies: explanation and elaboration. BMJ Open. 2016 Nov 14;6(11): e012799. | Biomarkers may serve many purposes: diagnosis, screening, staging, surveillance, prognosis, monitoring, treatment targeting, etc. Despite the title, this article's recommendations were intended for evaluating biomarkers in general and not only diagnostic biomarkers. |
| Sample quality (preanalytical variables and sample quality controls) | Moore HM, Kelly AB, Jewell SD, McShane LM, Clark DP, Greenspan R, et al. Biospecimen reporting for improved study quality (BRISQ). Cancer Cytopathol. 2011 Apr 25;119(2):92-101. | These recommendations are intended to apply to any study in which human biospecimens are used. Quick-reference BRISQSummary/Checklist. Documentation of factors that could influence the integrity, quality, and/or molecular composition of biospecimens.<br><br>Biological and environmental |

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| | Ellervik C, Vaught J. Preanalytical variables affecting the integrity of human biospecimens in biobanking. Clin Chem. 2015 Jul;61(7):914-34. | variability affecting downstream analysis measured in blood, urine and saliva. Special focus on blood, saliva, and urine as well as the DNA, RNA, and proteins derived from these biospecimens. |
| | Betsou F, Lehmann S, Ashton G, Barnes M, Benson EE, Coppola D, et al. International Society for Biological and Environmental Repositories (ISBER) Working Group on Biospecimen Science. Standard preanalytical coding for biospecimens: defining the sample PREanalytical code. Cancer Epidemiol Biomarkers Prev. 2010 Apr;19(4):1004-11. | SPREC code- Sample PREanalytical Code. Expected to facilitate and consolidate international multicenter biomarker identification research and biospecimen research in the clinical Biobank environment.<br><br>QC tools for samples used in proteomics, metabolomics, transcriptomics, or targeted analytical applications. |
| | Betsou F, Barnes R, Burke T, Coppola D, Desouza Y, Eliason J, et al. [International Society for Biological and Environmental Repositories (ISBER) Working Group on Biospecimen Science]. Human biospecimen research: experimental protocol and quality control tools. Cancer Epidemiol Biomarkers Prev. 2009 Apr;18(4):1017-25. | QC tools for molecular and cellular derivatives.<br>ISBER web site:<br>http://www.isber.org |
| | Feng H, Zhang X, Zhang C. mRIN for direct assessment of genome-wide and gene-specific mRNA integrity from large-scale RNA-sequencing data. Nat Commun. 2015 Aug 3;6:7816 | |
| Data analysis and data quality | DeLuca DS, Levin JZ, Sivachenko A, Fennell T, Nazaire MD, Williams | |

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| controls | C, Reich M, Winckler W, Getz G. RNA-SeQC: RNA-seq metrics for quality control and process optimization. Bioinformatics. 2012 Jun 1;28(11):1530-2.<br><br>Gosho M, Nagashima K, Sato Y. Study Designs and Statistical Analyses for Biomarker Research. Sensors (Basel, Switzerland). 2012;12(7):8966-8986. doi:10.3390/s120708966. | |
| Data management/ reporting/ sharing | McQuilton P, Gonzalez-Beltran A, Rocca-Serra P, Thurston M, Lister A, Maguire E, Sansone SA. BioSharing: curated and crowd-sourced metadata standards, databases and data policies in the life sciences. Database (Oxford). 2016 May 17;2016.<br><br>Perez-Arriaga MO, Wilson S, Williams KP, Schoeniger J, Waymire RL, Powell AJ. Omics Metadata Management Software (OMMS). Bioinformation. 2015 Apr 30;11(4):165-72.<br><br>Wolstencroft K, Owen S, Krebs O, Nguyen Q, Stanford NJ, Golebiewski M, et al. SEEK: a systems biology data and model management platform. BMC Syst Biol. 2015 Jul 11;9:33.<br><br>Haug K, Salek RM, Steinbeck C. Global open data management in metabolomics. Curr Opin Chem Biol. 2017 Feb;36:58-63.<br><br>Navarange M, Game L, Fowler D, Wadekar V, Banks H, Cooley N, Rahman F, et al. MiMiR: a comprehensive solution for storage, annotation and exchange of microarray data. BMC Bioinformatics. 2005 Nov 9;6:268.<br><br>Ara T, Enomoto M, Arita M, Ikeda C, Kera K, Yamada M, et al. Metabolonote: a wiki-based database for managing hierarchical | |

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| | metadata of metabolome analyses. Front Bioeng Biotechnol. 2015 Apr 7;3:38.<br><br>Schumacher A, Rujan T, Hoefkens J. A collaborative approach to develop a multi-omics data analytics platform for translational research. Appl Transl Genom. 2014 Sep 16;3(4):105-8. | |
| **BIOMARKER SUBGROUP-SPECIFIC** | | |
| Microbiome/ Microorganisms | Doris Vandeputte, Raul Y. Tito, Rianne Vanleeuwen, Gwen Falony and Jeroen Raes. Practical considerations for large-scale gut microbiome studies.2017, FEMS Microbiol. Revs. 41: S154-S164. | • Sample collection, transport and storage<br>• Nucleic acid extraction methods<br>• Any amplification (details)<br>• Next-Generation Sequencing (NGS) protocol [Whole Genome Shotgun Sequencing (WGSS), rRNA]<br>• NGS platforms<br>• Sequence analysis & pipelines |
| Proteome/Proteins | Martínez-Bartolomé S, Binz PA, Albar JP. The Minimal Information about a Proteomics Experiment (MIAPE) from the Proteomics Standards Initiative. Methods Mol Biol. 2014;1072:765-80. | Proteomic studies should report:<br>● Biological material that was extracted, how it was collected and stored<br>● Extraction procedure—reagents, pH, detergent concentration, resultant protein concentration and how protein concentration |

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| | | was determined<br>● How digestion and cleanup was carried out<br>● What quality control is performed on the mass spectrometry (MS) system<br>● Brand and model of mass spec system<br>● Separation column used<br>● How long a gradient was used<br>● Pooling strategy of samples |
| Metabolome/ Metabolism | The Metabolomics Standards Initiative (MSI) http://www.metabolomics-msi.org/<br>CIMR http://msi-workgroups.sourceforge.net<br><br>Haug K, Salek RM, Steinbeck C. Global open data management in metabolomics. Curr Opin Chem Biol. 2017 Feb;36:58-63. | Metabolomic studies should report:<br><br>● Biological material that was extracted, how it was collected, stored, and prepared for analysis.<br>● Extraction procedure—solvent, instrumentation (e.g. magnetic/mechanical stirrer, sonication, temperature, duration)<br>● Whether and what type of cleanup was carried out, e.g. filtration, centrifugation, concentration or complete evaporation and re-uptake in a different solvent<br>● How samples are stored – temperature, duration |

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| | | • What quality control is performed on the MS system, e.g. standards used<br>• Brand and model of MS system, ionization mode, brand and model of high performance liquid chromatography (HPLC) system<br>• Separation column used<br>• Solvent gradient parameters<br>• Targeted or non-targeted analysis<br>• Relative quantitation or absolute quantitation (using stable isotope labelled internal standards)<br>• MS/MS validation using multiple fragment ions for quantitation plus qualifier fragment ions when needed. |
| Genome/Epigenome | Huang J, Mirel D, Pugh E, Xing C, Robinson PN, Pertsemlidis A, Ding L, Kozlitina J, Maher J, Rios J, Story M, Marthandan N, Scheuermann RH. Minimum Information about a Genotyping Experiment (MIGEN). Stand Genomic Sci. 2011 Nov 30;5(2):224-9.<br><br>Little J, Higgins JP, Ioannidis JP, Moher D, Gagnon F, von Elm E, et al. STrengthening the REporting of Genetic Association Studies. STrengthening the REporting of Genetic Association Studies (STREGA): an extension of the STROBE statement. PLoS Med. 2009 | Genome/Epigenome studies should at least report:<br><br>• Source of DNA (cells, tissue, etc. and how was prepared)<br>• How DNA was prepared and stored<br>• DNA quality parameters |

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| | Feb 3;6(2): e22. | • Method and platform (type and vendor) used to obtain expression levels<br>• How bioinformatic analysis was performed<br><br>STREGA Reporting Recommendations, Extended from STROBE Statement and Rationale for Inclusion of Topics in the STREGA Recommendations |
| Gene expression/Transcriptome | **RT-qPCR**<br>*Huggett JF, Foy CA, Benes V, Emslie K, Garson JA, Haynes R, et al. The digital MIQE guidelines: Minimum Information for Publication of Quantitative Digital PCR Experiments. Clin Chem. 2013 Jun;59(6):892-902.*<br><br>*Bustin SA, Benes V, Garson JA, Hellemans J, Huggett J, Kubista M, et al. The MIQE guidelines: minimum information for publication of quantitative real-time PCR experiments. Clin Chem. 2009 Apr;55(4):611-22.*<br><br>**Microarrays**<br>*Brazma A. Minimum Information About a Microarray Experiment (MIAME)--successes, failures, challenges. ScientificWorldJournal. 2009 May 29;9:420-3.*<br><br>**HTP nucleotide sequencing experiments**<br>MINSEQE (MINimum information about a high-throughput | The following information should be provided if RNA-level gene expression analysis is done:<br>• Source of RNA (cells, tissue, etc. and how prepared)<br>• How RNA was prepared and stored<br>• RNA quality parameters<br>• Method and platform (type and vendor) used to obtain expression levels<br>• How bioinformatic analysis was performed<br><br>Technology for gene expression analysis is developing rapidly. Cost considerations are significant and some investigators will be limited to |

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| | Nucleotide SeQuencing Experiment) http://www.fged.org/projects/minseqe/ | certain platforms. Current ones:<br><br>Biased (targeted): qRT-PCR, microarrays, differential display, Nanostring, etc.<br><br>Unbiased: high-throughput sequencing strategies (various vendors such as Illumina) |