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## ***Guidelines for Preparing Manuscripts Describing Research in Clinical Proteomics***

The purpose of these guidelines is to provide sufficient information from which the reviewers/readers can evaluate, interpret, compare, and, reproduce the reported study. They contain both mandatory and recommended information. The former are underlined and marked with asterisks (\*).

### **Ethics Approvals**

- \* It is required to provide a statement of institutional Ethics/Animal Committee (IRB/ACUC) approval for use of human/animal biological materials for the research purpose reported in this study including details of informed consent, if appropriate, for clinical or biomarker trial participation and/or primary cell line development. In addition, the mechanisms that were employed to protect human subject confidentiality, such as procedures for identification/de-identification and coding of biospecimens should be stated.

### **Study Goals and Design**

A comprehensive description of the study design should be provided, including the overall goal(s) of the study, with specific attention to the following qualifications:

- \* The stage/phase of the study, e.g. discovery, verification or validation, and state clearly the stage/phase that a candidate (biomarker, target, analyte) is at, e.g., exploratory/discovery; preclinical validation; etc.).
- \* the flow of subjects/samples through the study, including the initial number of cases, the number included in each stage of the analysis (a diagram is recommended for more complex/larger studies) and reasons for subject dropout.
- Samples from other diseases or disorders mimicking or similar to the disease of interest should be included as controls whenever a “differential-diagnostic disease-specific” biomarker is defined.
- The time period of the sample collection and/or study execution.
- The power, alpha and beta error, etc, used in the determination of cohort size(s).

### **Subject Source and Description**

\* The source and classification of subjects (or materials obtained there from) should be described with respect to as many of the following parameters as are known:

- Prospective or retrospective accrual.
- Stratification.
- Matching (gender, age, disease, etc).
- Randomization of subject assignments, such as treatment, intervention, etc.
- \* The source of biospecimens (e.g. centralized biobank, internal biobank, clinical trial collection, surgery etc) should be described.
- \* Inclusion/exclusion criteria for the study and reference cohorts should be given.



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- \* For all patients from whom samples were derived, a definition of disease or condition (including treatments if known) is required and should include:
  - a disease description, such as subtype, stage, grade, histology and clinical score (if applicable), and, if known, how these were determined.
  - disease type using standard medical terminology (include ICD codes where known), e.g. juvenile diabetes v. noninsulin-dependent diabetes.
  - any known potential confounders relative to the time of sampling, such as intra- or pre-operative status, administered drugs/anesthetics etc.
- \* Intrinsic factors, demographic and clinical characteristics for study and reference (control) subjects, including age, gender, disease stage, and co-morbidities, etc, should be provided.
- Trial treatment(s) or other intervention(s), if appropriate, should be described.
- Extrinsic factors, interventions, and lifestyle factors that may affect results, such as, smoking history, etc, should be listed, if known.
- If appropriate, follow up and duration, including median and range, should be given.

### **Biospecimen Qualification**

#### Tissue

If known/applicable, the following should be provided:

- the average time to tissue acquisition and processing (time to initial stabilization step), and range of times.
- \* the type of processing, e.g. formalin, ethanol, embedding medium, method of freezing, lysis solution etc. the average storage temperature, and mean and range of duration of storage.
- \* the post-cutting fixation for frozen tissue. \*the methods of enrichment for relevant component(s) of biospecimen if applicable (e.g. micro dissection, fractionation).
- \* any information regarding shipping of biospecimens to central repository, e.g., time, temperature
- \* any histologic review of biospecimens used in the reported experiments.
- If immunohistochemical staining, or other testing was done on tissue, it should be indicated if the pathology review was blinded and if agreement between reviewing pathologists was obtained. Note: Supporting histology (digitalized or original slides) may be requested by the reviewers and/or editors.

#### Biofluids

- \* For blood and biological fluid biospecimens, published standard operating procedures, if used, should be referenced; if not the following information should be provided:
  - \* the method of collection. [In the case of urine samples, the collection mode should be stated: 24-h, first morning, second morning or random urine early stream or midstream.]
  - \* the tube type (and size, if known) used for collection and storage.



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- \* the use of additives such as anti-coagulants, preservatives, and protease inhibitors, if used.
- \* the processing conditions including the time interval between collection and separation, \*centrifugation conditions, temperature of processing, time interval between processing and freezing.
- \* the storage temperature and length of storage
- \* the number of freeze thaw cycles. any variations in collection and processing across biospecimen set(s).

**Primary cell lines**

- \* For primary cell lines, generation and use, the following information should be provided:
  - Clinical details regarding subject and biospecimen of origin, the conditions/protocols of cell line generation and characterization including passage number and number of clones analyzed.

**Statistical Considerations**

The statistical analysis strategy should be described in detail, when applicable. This should include:

- the central hypothesis that is being tested.
- model building and validation.
- a clear definition of the statistical algorithm used.
- the rationale used to choose cut-off thresholds and other model parameters.
- the independence of exploratory (training) and confirmative (test) analysis.

The following details about the statistical analysis should be provided:

- the feature selection and multiple hypotheses testing strategy.
- the number of candidates (e.g., markers, targets, analytes) tested.
- the details of any subgroup analysis performed.
- any missing values and how these were handled, if applicable. ○ \*point estimates, p-values and/or confidence intervals.
- In the statistical presentation, a discussion of confounding factors and the methods employed to minimize their impact should be included.

**Technical Considerations**

\* The performance characteristics (technical and process including fractionation, digestion etc.) of the analytical process/assay(s) used (e.g., mass spectrometry, protein, antibody, nucleic acid arrays, immuno-chemistry, 2Dgel electrophoresis, or other measurement technology) should be described. For both the technical and processing steps (fractionation, digestion, etc.) noise assessment, reproducibility, normalization (e.g. array to array and protein to protein), measurement variation, specificity, limits of detection and quantization should be described.



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**Note:** the guidelines for protein identification analyses (found elsewhere in the Instructions to Authors) for articles submitted to MCP are fully applicable to papers dealing with clinical proteomics and should also be consulted if this type of information is included. As with these contributions, the journal strongly encourages the deposition of raw data in a suitably accessible database for such information collected for articles dealing with clinical proteomics and will provide hyperlinks to it. Authors are also strongly encouraged to identify markers wherever possible, particularly for validation studies

- The quality control and quality assurance methods employed should be described including how the analysis of samples was conducted, e.g. replicate number, whether randomized etc.
- Any software packages and bioinformatics tools used for model building, pathway analysis or data visualization should be described. Journal policy requires that all software employed is available to the general public.
- Authors are encouraged to place raw data in publicly accessible database storage sites. The journal will provide hyperlinks to this information.
- If applicable or known, any other studies (preferably by literature reference) that have used the same or a subset of the