Introduction:
This document ties together the four different files that makeup the GRASP example drawn from analysis of TLR-production of cytokines that is stimulated specifically from each of six different ligands per participant at one point in time, i.e., cross-sectional. Because the six ligands are clustered within participants, their associated outcome measurements are correlated. Specifically, we use an unstructured covariance structure that allows each participant to have his or her own specific correlation structure for their set of six ligands, thus accounting for the inherent variation of each participant. Data has been sanitized by removing identifying information and adding random noise.

Keyword Categories:
>   Clinical: toll-like receptor (TLR), cytokines, aging, immunology, ligands
>   Genetics: Not Applicable (N/A)
>   Statistical: multivariable, mixed models, correlation structure, cross-sectional
>   Software: SAS
>   Related: Not Applicable (N/A)

References:
1. van Duin D, Mohanty S, Thomas V, Ginter S, Montgomery RR, Fikrig E, Allore HG, Medzhitov R, Shaw AC. Age-Associated Defect in Human TLR-1/2 Function. *J Immunol*. 2007;178(2):970-5. PMID: 17202359
2. van Duin, Allore HG, Mohanty S, Ginter S, Newman FK, Belshe RB, Medzhitov R, Shaw AC Prevaccine determination of the expression of costimulatory b7 molecules in activated monocytes predicts influenza vaccine responses in young and older adults. *J. Infectious Disease*. 2007 Jun 1; 195(11):1590-7. PMID: 17471428
3. Verbeke, G., and G. Molenberghs. 1997. Linear mixed models in practice. In A SAS-Oriented Approach. G. Verbeke, and G. Molenberghs, editors. Springer, New York.
4. Laird, N.M., and J.H. Ware. 1982. Random-effects models for longitudinal data. *Biometrics* 38:963-974.
5. Schluchter, M.D., and J.D. Elashoff. 1990. Small-sample adjustments to tests with unbalanced repeated measures assuming several covariance structures. *Journal of Statistical Computation and Simulation* 37:69-87.

Component Files:
>   a.   PDF summary document: LigandCytokCorrSummaryAllore.pdf
>   b.   Related publications   See reference articles cited above
>   c.   SAS program: LigandCytokCorrProgramAllore.txt
>   d.   SAS data file: LigandCytokCorrData.txt
>   e.   PDF file showing SAS output: LigandCytokCorrOutputAllore.pdf

Optimal Use:
1. Read this Summary file completely   Component a listed above
2. Read the reference articles cited above   :   Component b listed above
3. Run the SAS program in concert with the data and inits files.   Components c and d above
4. Generate output that should appear like that shown in the PDF file: Component e listed above

Prerequisites:
To run the example you must have a working knowledge of SAS and preferably some familiarity with how Proc MIX handles mixed models.

Potential Applications:
Immunological responses of individuals are often measured at a variety of ligands (an entity such as an antibody that binds to a receptor). Accounting for the correlation induced by their measurement within the same individual provides a more rigorous accounting of variance and therefore refines statistical inference based on such measurements.

Any feedback on how to make this submission more useful is welcome. Log into the main GRASP page, i.e. http://grasp.med.yale.edu
and choose the "forum" link in the upper menu on the right to enter feedback on any GRASP submission. Please refer to the specific file names when commenting so we can appropriately steer your suggestions.