RECOMMENDED SYSTEM STATUS

REVIEWER REPORT

System: Locus Reference Genomic Sequence Format
Application No: RS005
Proposer: Raymond Dalgleish
Date Proposed: 2013-06-06
Reviewer Report Date: 2013-12-12

BACKGROUND

Recommended System Status is an accreditation process designed to encourage the adoption of HVP Standards and Guidelines and to provide guidance around what systems, procedures and tools are of use to the wider community. The decision to award Recommended System status is made by the International Scientific Advisory Committee of the Human Variome Project. A key component of their assessment process for is the comments and recommendations obtained during peer review by members of the wider human genetics and genomics community.

Applications for Recommended System Status that have made it to the peer-review stage have already been determined to comply with all published HVP Standards and Guidelines by the International Scientific Advisory Committee based on advice provided by the ICO. The peer review stage seeks to provide the International Scientific Advisory Committee with guidance from members of the genomics community on the usability and reliability of the system.

Reviewers are asked to provide an opinion on:

- the compatibility of the system with other Recommended Systems, if any;
- the usability and relevance of the system;
- the reliability and robustness of the system;
- the availability of system documentation and training materials; and
- the extent to which the system is currently being utilised.

REVIEWER 1: JOHN-PAUL PLAZZER

A standardised reference sequence format for genes. LRG is designed to standardize reference sequences for potentially all genes or genomic regions (driven by community demand for specific sequences). It is supported by NCBI and EBI, and therefore has international credence. LRG resolves issues with previous reference sequences, particularly ambiguities associated with multiple versions of gene sequences. It uses XML for storing and transfer of LRG records, and provides programmatic access to information relating to LRGs. The LRG website and data is freely accessible, user-friendly, well supported, and updated regularly.

Recommendation: Approve the application

John-Paul Plazzer
Database Curator
International Society for Gastrointestinal Hereditary Tumours

Competing or Conflicts of Interest: None Declared

REVIEWER 2: DR ARLEEN D. AUERBACH

I have obtained LRG ID numbers for all 16 genes that I curate for the Fanconi Anemia Mutation Database.

We have added links to the respective LRG webpage from each FA gene homepage. We found that we had rapid response to our request for LRG ID numbers, and are very happy with our experience with the system. Since the start of curating the FA databases, both the genes and variants have undergone multiple changes in nomenclature. The gene names were finally standardized after the third change in nomenclature. The nomenclature for has also changed over the years, each time the reference sequence undergoes a change. Since the purpose of the LRG system is to provide a stable reference sequence, it will be great not to have new nomenclature for variants every time the reference sequence changes.

The LRG schema has also been updated recently. Here is a summary I received in October by email of updates to the schema (see below). I think it is a good sign that the designers of the LRG system continue to work on improvements. My database manager also thinks "The update presents a good collection of information."

I would therefore recommend adoption of the LRG system as a recommended system by the HVP.

Schema Updates

All LRG records have been updated to a new XML schema (schema 1.8). The new records are available on the LRG website and on the FTP site (ftp://ftp.ebi.ac.uk/pub/databases/lrgex/).

The main changes to the schema are:

The inclusion of a fixed LRG-specific exon numbering system based on the transcript(s) included in the fixed section. Each distinct exon is numbered consecutively 5' to 3'; the numbering is then applied to individual transcripts.

The creation of a new "Community" annotation set in the updatable section. It includes additional, relevant information provided directly to LRG project curators by collaborators such as Locus Specific Database (LSDB) curators, members of the diagnostic community, clinicians, and researchers.

Alternate or legacy exon and amino acid numbering systems widely used by the community have been moved from the NCBI updatable section to the new community annotation set to reflect the fact that this data is provided directly to LRG project curators by members of the community.

Inclusion of the HGNC ID as the main identifier in the fixed section since the HGNC symbol and the LRG gene name can update and are not fixed.

Display Updates

Improvements to the view have also been made, notably the inclusion of a summary box at the top right corner of each LRG's webpage. It lists key information such as identifiers, genomic and transcript sequence sources, and the number of transcripts included in the fixed section.

In addition, the updatable section of each LRG now contains the most up to date information available from NCBI and Ensembl (Ensembl release 73). The next update will be in early 2014 with information from the GRCh38 assembly.

Recommendation: Approve the application

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Competing or Conflicts of Interest: None Declared

The Human Variome Project International Scientific Advisory Committee resolved to award Recommended System Status to the Locus Reference Genomic Sequence Format at their December 2013 meeting. It was decided at this meeting that, given the positive nature of the two reports received from reviewers that a recommendation from a third reviewer was not necessary.