BIGSdb Documentation

Release 1.9.0

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Gene-by-gene population annotation and analysis

BIGSdb is software designed to store and analyse sequence data for bacterial isolates. Any number of sequences can be linked to isolate records - these can be small contigs assembled from dideoxy sequencing through to whole genomes (complete or multiple contigs generated from parallel sequencing technologies such as 454 or Illumina).

BIGSdb extends the principle of MLST to genomic data, where large numbers of loci can be defined, with alleles assigned by reference to sequence definition databases (which can also be set up with BIGSdb). Loci can also be grouped into schemes so that types can be defined by combinations of allelic profiles, a concept analagous to MLST.

The software has been released under the GNU General Public Licence version 3. The latest version of this documentation can be found at http://bigsdb.readthedocs.org/.

CHAPTER 1

Concepts and terms

1.1 BIGSdb

BIGSdb is the software platform - not a specific database. There are many instances of BIGSdb databases, so referring to 'the BIGSdb' is meaningless.

1.2 Loci

Loci are regions of the genome that are identified by similarity to a known sequence. They can be defined by DNA or peptide sequence. They are often complete coding sequences (genes), but may represent gene fragments (such as used in MLST), antigenic peptide loops, or indeed any sequence feature.

In versions of BIGSdb prior to 1.8.0, an isolate record could only have one live *allele* designation for a locus (inactive/pending designations could be stored within the database but were unavailable for querying or analysis purposes). Since biology is rarely so clean, and some genomes may contain more than one copy of a gene, later versions of the software allow multiple allele designations for a locus, all of which can be queried and analysed.

Paralogous loci can be difficult to differentiate by sequence similarity alone. Because of this, loci can be further defined by context, where in silico PCR or hybridization reactions can be performed to *filter the genome* to specific regions based on sequence external to the locus.

1.3 Alleles

Alleles are instances of loci. Every unique sequence, either DNA or peptide depending on the locus, is defined as a new allele and these are defined in a sequence definition database, where they are given an allele identifier. These identifiers are usually integers, but can be text strings. Allele identifiers in text format can be constrained by length and formatting.

When a specific allele of a locus is identified within the sequence data of an isolate record, the allele designation, i.e. identifier, is associated with the isolate record. This efficiently stores the sequence variation found within an isolate. Two isolates with the same allele designation for a locus have identical sequences at that locus. Once the sequence variation within a genome has been reduced to a series of allele designations, genomes can be efficiently compared by identifying which loci vary between them.

It is important to note that allele identifiers are usually arbitrary and are allocated sequentially in the order of discovery. Alleles with adjacent identifiers may vary by a single nucleotide or by many.

1.4 Schemes

Schemes are collections of loci that may be associated with additional field values. At their simplest they just group loci together. Example uses of simple schemes include:

- Antibiotic resistance genes
- Genes involved in specific biochemical pathways
- Antigens
- Vaccine components
- Whole genome MLST (wgMLST)

When schemes are associated with additional fields, one of these fields must be the primary key, i.e. its value uniquely defines a particular combination of alleles at its member loci. The pre-eminent example of this is MLST - where a sequence type (ST) is the primary key that uniquely defines combinations of alleles that make up the MLST profiles. Additional fields can also then be included. The values for these need not be unique. In the MLST example, a field for clonal complex can be included, and the same value for this can be set for multiple STs.

1.5 Profiles

Profiles are instances of *schemes*. A profile consists of a set of *allele identifiers* for the *loci* that comprise the scheme. If the scheme has a primary key field, e.g. sequence type (ST) in MLST schemes, then the unique combination of alleles in a complete profile can be defined by the value of this field.

1.6 Sequence tags

Sequence tags record locus position within an isolate record's sequence bin. The process of creating these tags, is known as *tag-scanning*. A sequence tag consists of:

- sequence bin id - this identifies a particular contig
- locus name
- start position
- end position
- flag to indicate if sequence is reversed
- flag to indicate if sequence is complete and does not continue off the end of the contig

1.7 Sets

Sets provide a means to take a large database with multiple loci and/or schemes and present a subset of these as though it was a complete database. The loci and schemes chosen to belong to a set can be renamed when used with this set. The rationale for this is that in a database with disparate isolates and a large number of loci, the naming of these loci may have to be long to specify a species name. For example, you may have a database that contains multiple MLST schemes for different species, but since these schemes may use different fragments of the same genes they may have to be named something like 'Streptococcus_pneumoniae_MLST_aroE' to uniquely specify them. If we define a set for 'Streptococcus pneumoniae' we can then choose to only include S. pneumoniae loci and therefore shorten their names, e.g. to 'aroE'.

Additional metadata fields can also be associated with each set so it is possible to have a database containing genomes from multiple species and a generic set of metadata, then have additional specific metadata fields for particular species or genera. These additional fields only become visible and searchable when the specific set that they belong to has been selected.

CHAPTER 2

BIGSdb dependencies

2.1 Required packages

BIGSdb requires a number of software components to be installed:

2.1.1 Linux packages

- Apache2 web server with mod_perl2
- PostgreSQL database
- Perl
- BioPerl
- BLAST+
- EMBOSS
  - infoalign - use to extract alignment stats in Genome Comparator.
  - sixpack - used to translate sequences in multiple reading frames.
  - stretcher - used for sequence alignment in allele query.
- Ipcress - part of exonerate package - used to simulate PCR reactions which can be used to filter the genome to predicted amplification products.
- Xvfb - X virtual framebuffer - needed to support SplitsTree in command line mode as used in Genome Comparator.

2.1.2 Perl modules

These are included with most Linux distributions.

- DBI - Database Independent interface - module used to interact with databases.
- DBD-Pg - PostgreSQL database driver for DBI.
- XML::Parser::perlSAX - part of libxml-perl - Used to parse XML configuration files.
- Log::Log4perl - Configurable status and error logging
- Log::Dispatch::File - Object for logging to file
- Error - Exception handling

- Config::Tiny - Configuration file handling
- Bio::Biblio - this used to be part of BioPerl but will need to be installed separately if using BioPerl 1.6.920 or later
- IO::String
- Data::UUID - Globally unique identifer handling for preference storage
- List::MoreUtils
- Time::Duration [optional] - Used by Job Viewer to display elapsed time in rounded units
- Excel::Writer::XLSX - Used to export data in Excel format
- Parallel::ForkManager - Required for multi-threading autotagger and autodefiner scripts.

2.1.3 Optional packages

Installing these packages will enable extra functionality, but they are not required by the core BIGSdb package.

- ChartDirector - library used for generating charts. Used by some plugins.
- ImageMagick - mogrify used by some plugins.
- MAFFT - sequence alignment used by some plugins.
- Muscle - sequence alignment used by some plugins.
- Splitstree4 - used by GenomeComparator plugin.

CHAPTER 3

Installation and configuration of BIGSdb

3.1 Software installation

BIGSdb consists of two main Perl scripts, bigsdb.pl and bigscurate.pl, that run the query and curator's interfaces respectively. These need to be located somewhere within the web cgi-bin directories. In addition, there are a large number of library files, used by both these scripts, that are installed by default in /usr/local/lib/BIGSdb. Plugin scripts are stored within a 'Plugins' sub-directory of this library directory.

All databases on a system can use the same instance of the scripts, or alternatively any database can specify a particular path for each script, enabling these script directories to be protected by apache htaccess directives.

- *Software requirements*
- Download from SourceForge.net or GitHub.

1. Unpack the distribution package in a temporary directory:

   ```
   gunzip bigsdb_1.x.x.tar.gz
   tar xvf bigsdb_1.x.x.tar
   ```

2. Copy the bigsdb.pl and bigscurate.pl scripts to a subdirectory of your web server's cgi-bin directory. Make sure these are readable and executable by the web server daemon.
3. Copy the contents of the lib directory to /usr/local/lib/BIGSdb/. Make sure you include the Plugins and Offline directories which are subdirectories of the main lib directory.
4. Copy the contents of the javascript directory to a javascript directory within the web root tree, i.e. accessible from http://your_website/javascript/.
5. Copy the bigsdb.css stylesheet to the root directory of your website, i.e. accessible from http://your_website/bigsdb.css.
6. Copy the images directory to the root directory of your website, i.e. accessible from http://your_website/images.
7. Copy the contents of the conf directory to /etc/bigsdb/. Check the paths of helper applications and database names in the bigsdb.conf file and modify for your system.
8. Create a PostgreSQL database user called apache - this should not have any special priveleges. Use the createuser command to do this, e.g.

   ```
   createuser apache
   ```

   From the psql command line, set the apache user password:

   ```
   psql
   ALTER ROLE apache WITH PASSWORD 'remote';
   ```

9. Create PostgreSQL databases called bigsdb_auth, bigsdb_prefs and refs using the scripts in the sql directory. Create the database using the createdb command and set up the tables using the psql command, e.g.

   ```
   createdb bigsdb_auth
   psql -f auth.sql bigsdb_auth
   ```

10. Create a writable temporary directory in the root of the web site called tmp, i.e. accessible from http://your_website/tmp.

11. Create a log file, bigsdb.log, in /var/log owned by the web server daemon, e.g.

    ```
    touch /var/log/bigsdb.log
    chown www-data /var/log/bigsdb.log
    ```

    (substitute www-data for the web daemon user).

3.2 Configuring PostgreSQL

PostgreSQL can be configured in many ways and how you do this will depend on your site requirements.

The following security settings will allow the appropriate users 'apache' and 'bigsdb' to access databases without allowing all logged in users full access. Only the UNIX users 'postgres' and 'webmaster' can log in to the databases as the Postgres user 'postgres'.

You will need to edit the pg_hba.conf and pg_ident.conf files. These are found somewhere like /etc/postgresql/9.1/main/

pg_hba.conf

```
# Database administrative login by UNIX sockets
local   all         postgres                          ident map=mymap

# TYPE  DATABASE    USER        CIDR-ADDRESS          METHOD

# "local" is for Unix domain socket connections only
local   all         all                               ident map=mymap
# IPv4 local connections:
host    all         all         127.0.0.1/32          md5
# IPv6 local connections:
host    all         all         ::1/128               md5
```

pg_ident.conf

```
# MAPNAME     SYSTEM-USERNAME    PG-USERNAME

  mymap       postgres           postgres
  mymap       webmaster          postgres
  mymap       www-data           apache
  mymap       bigsdb             bigsdb
  mymap       bigsdb             apache
```

You may also need to change some settings in the postgresql.conf file. As an example, a configuration for a machine with 16GB RAM, allowing connections from a separate web server may have the following configuration changes made:

```
listen_addresses = '*'
max_connections = 200
shared_buffers = 1024Mb
work_mem = 8Mb
```

```
effective_cache_size = 8192Mb
stats_temp_directory = '/dev/shm'
```

Setting stats_temp_directory to /dev/shm makes use of a ramdisk usually available on Debian or Ubuntu systems for frequently updated working files. This reduces a lot of unneccessary disk access.

See Tuning Your PostgreSQL Server for more details.

Restart PostgreSQL after any changes, e.g.

```
/etc/init.d/postgresql restart
```

3.3 Site-specific configuration

Site-specific configuration files are located in /etc/bigsdb by default.

- `bigsdb.conf` - main configuration file
- `logging.conf` - error logging settings. See log4perl project website for advanced configuration details.

3.4 Setting up the offline job manager

To run plugins that require a long time to complete their analyses, an offline job manager has been developed. The plugin will save the parameters of a job to a job database and then provide a link to the job status page. An offline script, run frequently from CRON, will then process the job queue and update status and outputs via the job status page.

1. Create a 'bigsdb' UNIX user, e.g.:

   ```
   sudo useradd -s /bin/sh bigsdb
   ```

2. As the postgres user, create a 'bigsdb' user and create a bigsdb_jobs database using the jobs.sql SQL file, e.g.:

   ```
   createuser bigsdb [no need for special priveleges]
   createdb bigsdb_jobs
   psql -f jobs.sql bigsdb_jobs
   ```

   From the psql command line, set the bigsdb user password::

   ```
   psql
   ALTER ROLE bigsdb WITH PASSWORD 'bigsdb';
   ```

3. Set up the jobs parameters in the /etc/bigsdb/bigsdb.conf file, e.g.:

   ```
   jobs_db=bigsdb_jobs
   max_load=8
   ```

   The jobs script will not process a job if the server's load average (over the last minute) is higher than the max_load parameter. This should be set higher than the number of processor cores or you may find that jobs never run on a busy server. Setting it to double the number of cores is probably a good starting point.

4. Copy the job_logging.conf file to the /etc/bigsdb directory.

5. Set the script to run frequently (preferably every minute) from CRON. Note that CRON does not like '.' in executable filenames, so either rename the script to 'bigsjobs' or create a symlink and call that from CRON, e.g.:

```
copy bigsjobs.pl to /usr/local/bin
sudo ln -s /usr/local/bin/bigsjobs.pl /usr/local/bin/bigsjobs
```

You should install xvfb, which is a virtual X server that may be required for third party applications called from plugins. This is required, for example, for calling splitstree4 from the Genome Comparator plugin.

Add the following to /etc/crontab::

```
* * * * * bigsdb xvfb-run -a /usr/local/bin/bigsjobs
```

(set to run every minute from the 'bigsdb' user account).

If you'd like to run this more frequently, e.g. every 30 seconds, multiple entries can be added to CRON with an appropriate sleep prior to running, e.g.:

```
* * * * * bigsdb  xvfb-run -a /usr/local/bin/bigsjobs
* * * * * bigsdb  sleep 30;xvfb-run -a /usr/local/bin/bigsjobs
```

6. Create a log file, bigsdb_jobs.log, in /var/log owned by 'bigsdb', e.g.:

```
sudo touch /var/log/bigsdb_jobs.log
sudo chown bigsdb /var/log/bigsdb_jobs.log
```

3.5 Periodically delete temporary files

There are two temporary directories (one public, one private) which may accumulate temporary files over time. Some of these are deleted automatically when no longer required but some cannot be cleaned automatically since they are used to display results after clicking a link or to pass the database query between pages of results.

The easiest way to clean the temp directories is to run a cleaning script periodically, e.g. create a root-executable script in /etc/cron.hourly containing the following::

```
#!/bin/sh
#Remove temp BIGSdb files from secure tmp folder older than 1 week.
find /var/tmp/ -name '*BIGSdb_*' -type f -mmin +10080 -exec rm -f {} \; 2>/dev/null

#Remove .jnlp files from web tree older than 1 day
find /var/www/tmp/ -name '*.jnlp' -type f -mmin +1440 -exec rm -f {} \; 2>/dev/null

#Remove other tmp files from web tree older than 1 week
find /var/www/tmp/ -type f -mmin +10080 -exec rm -f {} \; 2>/dev/null
```

3.6 Log file rotation

Set the log file to auto rotate by adding a file called 'bigsdb' with the following contents to /etc/logrotate.d:

```
/var/log/bigsdb.log {
  weekly
  rotate 4
  compress
  copytruncate
  missingok
  notifempty
  create 640 root adm
}
```

```
/var/log/bigsdb_jobs.log {
  weekly
  rotate 4
  compress
  copytruncate
  missingok
  notifempty
  create 640 root adm
}
```

3.7 Upgrading BIGSdb

Major version changes, e.g. 1.7 -> 1.8, indicate that there has been a change to the underlying database structure for one or more of the database types. Scripts to upgrade the database are provided in sql/upgrade and are named by the database type and version number. For example, to upgrade an isolate database (bigsdb_isolates) from version 1.7 to 1.8, log in as the postgres user and type:

```
psql -f isolatedb_v1.8.sql bigsdb_isolates
```

Upgrades are sequential, so to upgrade from a version earlier than the last major version you would need to upgrade to the intermediate version first, e.g. to go from 1.6 -> 1.8, requires upgrading to 1.7 first.

Minor version changes, e.g. 1.8.0 -> 1.8.1, have no modifications to the database structures. There will be changes to the Perl library modules and possibly to the contents of the Javascript directory, images directory and CSS files. The version number is stored with the bigsdb.pl script, so this should also be updated so that BIGSdb correctly reports its version.

CHAPTER 4

Database setup

There are two types of BIGSdb database:

- sequence definition databases, containing
  - allele sequences and their identifiers
  - scheme data, e.g. MLST profile definitions
- isolate databases, containing
  - isolate provenance metadata
  - genome sequences
  - allele designations for loci defined in sequence definition databases.

These two databases are independent but linked. A single isolate database can communicate with multiple sequence definition databases and vice versa. Different access restrictions can be placed on different databases.

Databases are described in XML files telling BIGSdb everything it needs to know about them. Isolate databases can have any fields defined for the isolate table, allowing customisation of metadata - these fields are described in the XML file (config.xml) and must match the fields defined in the database itself.

4.1 Creating databases

There are templates available for the sequence definition and isolate databases. These are SQL scripts found in the sql directory.

To create a database, you will need to log in as the postgres user and use these templates. For example to create a new sequence definition database called bigsdb_test_seqdef, navigate to the sql directory and log in as the postgres user, e.g.:

```
sudo su postgres
```

then

```
createdb bigsdb_test_seqdef
psql -f seqdef.sql bigsdb_test_seqdef
```

Create an isolate database the same way::

```
createdb bigsdb_test_isolates
psql -f isolatedb.sql bigsdb_test_isolates
```

The standard fields in the isolate table are limited to essential fields required by the system. To add new fields, you need to log in to the database and alter this table. For example, to add fields for country and year, first log in to the newly created isolate database as the postgres user::

```
psql bigsdb_test_isolates
```

and alter the isolate table::

```
ALTER TABLE isolates ADD country text;
ALTER TABLE isolates ADD year int;
```

Remember that any fields added to the table need to be described in the config.xml file for this database.

4.2 Database-specific configuration

Each BIGSdb database on a system has its own configuration directory, by default in /etc/bigsdb/dbases. The database has a short configuration name used to specify it in a web query and this matches the name of the configuration sub-directory, e.g. http://pubmlst.org/cgi-bin/bigsdb/bigsdb.pl?db=pubmlst_neisseria_isolates is the URL of the front page of the PubMLST Neisseria isolate database whose configuration settings are stored in /etc/bigsdb/dbases/pubmlst_neisseria_isolates. This database sub-directory contains a number of files (hyperlinks lead to the files used on the Neisseria database):

- `config.xml` - the database configuration file. Fields defined here correspond to fields in the isolate table of the database.
- banner.html - optional file containing text that will appear as a banner within the database index pages. HTML markup can be used within this text.
- header.html - HTML markup that is inserted at the top of all pages. This can be used to set up site-specific menubars and logos.
- footer.html - HTML markup that is inserted at the bottom of all pages.
- curate_header.html - HTML markup that is inserted at the top of all curator's interface pages.
- curate_footer.html - HTML markup that is inserted at the bottom of all curator's interface pages.

4.3 XML configuration attributes used in config.xml

The following lists describes the attributes used in the config.xml file that is used to describe databases.

4.3.1 Isolate database XML attributes

Please note that database structure described by the field and sample elements must match the physical structure of the database isolate and sample tables respectively.:

`<db>`

Top level element. Contains child elements: system, field and sample.:

`<system>`

- db
  - name of database on system

  - required
- dbtype
  - type of database: either 'isolates' or 'sequences'
  - required
- description
  - Description of database used throughout interface
  - required
- authentication
  - method of authentication: either 'builtin' or 'apache'. See user authentication.
  - required
- webroot
  - URL of web root, which can be relative or absolute. The bigsdb.css stylesheet file should be located in this directory. Default '/'.
  - optional
- view
  - database view containing isolate data, default 'isolates'
  - optional
- script_path_includes
  - partial path of the bigsdb.pl script used to access the database. See user authentication.
  - optional
- curate_path_includes
  - partial path of the bigscurate.pl script used to curate the database. See user authentication.
  - optional
- noshow
  - comma-separated list of fields not to use in breakdown statistic plugins
  - optional
- fieldgroup1 - fieldgroup10
  - allows multiple fields to be queried as a group. Value should be the name of the group followed by a colon (:) followed by a comma-separated list of fields to group, e.g. identifiers:id,strain,other_name
  - optional
- maindisplay_aliases
  - default setting for whether isolates aliases are displayed in main results tables: either 'yes' or 'no', default 'no'. This setting can be overridden by individual user preferences.
  - optional
- read_access
  - describes who can view data: either 'public' for everybody, 'authenticated_users' for anybody who has been able to log in, or 'acl' (access control list) for fine-grained access control to individual isolate records. Default 'public'.

  - optional
- write_access
  - describes who can curate isolate records: either 'acl' (access control list) for fine-grained access control to individual isolate records, or leave empty for anybody with curator permission to alter isolate records.
  - optional
- locus_superscript_prefix
  - superscript the first letter of a locus name if it is immediately following by an underscore, e.g. f_abcZ would be displayed as fabcZ within the interface: must be either 'yes' or 'no', default 'no'. This can be used to designate gene fragments (or any other meaning you like).
  - optional
- hide_unused_schemes
  - sets whether a scheme is shown in a main results table if none of the isolates on that page have any data for the specific scheme: either 'yes' or 'no', default 'no'.
  - optional
- use_temp_scheme_table
  - sets whether entire schemes are imported in to the isolate database in to an indexed table rather than querying the seqdef scheme view for isolate results tables. Under some circumstances this can be considerably quicker than querying the seqdef scheme view (a few ms compared to >10s if the seqdef database contains multiple schemes with an uneven distribution of a large number of profiles so that the Postgres query planner picks a sequential rather than index scan). This scheme table can also be generated periodically using the update_scheme_cache.pl script to create a persistent cache. This is particularly useful for large schemes (>10000 profiles) but data will only be as fresh as the cache so ensure that the update script is run periodically.
  - optional
- labelfield
  - field that is used to describe record in isolate info page, default 'isolate'
  - optional
- tblastx_tagging
  - sets whether tagging can be performed using TBLASTX: either 'yes' or 'no', default 'no'.
  - optional
- host
  - host name/IP address of machine hosting isolate database, default 'localhost'
  - optional
- port
  - port number that the isolate host is listening on, default '5432'
  - optional
- user
  - username for access to isolates database, default 'apache'
  - optional
- password

  - password for access to isolates database, default 'remote'
  - optional
- privacy
  - displays E-mail address for sender in isolate information page if set to 'no'. Default 'yes'.
  - optional
- annotation
  - semi-colon separated list of accession numbers with descriptions (separated by a |), eg. 'AL157959|Z2491;AM421808|FAM18;NC_002946|FA 1090;NC_011035|NCCP11945;NC_014752|020-06'. Currently used only by Genome Comparator plugin
  - optional
- sets
  - use sets: either 'yes' or 'no', default 'no'.
  - optional
- set_id
  - Force the use of a specific set when accessing database via this XML configuration: Value is the name of the set.
  - optional
- only_sets
  - when defined, don't allow option to view the 'whole database' - only list sets that have been defined: either 'yes' or 'no', default 'no'.
  - optional
- views
  - comma-separated list of views of the isolate table defined in the database. This is used to set a view for a set.
  - optional
- all_plugins
  - enable all appropriate plugins for database: either 'yes' or 'no', default 'no'.
  - optional
- job_priority
  - Isolate databases only: Integer with default job priority for offline jobs (default:5) (Version v1.7+)
  - optional
- dbase_job_quota
  - isolate databases only:Integer with number of offline jobs that can be queued or currently running for this database (Version 1.7+)
  - optional
- default_seqdef_config
  - isolate databases only: Name of the default seqdef database configuration used with this database. Used to automatically fill in details when adding new loci. (Version 1.7+)

  - optional
- default_seqdef_dbase
  - isolate databases only: Name of the default seqdef database used with this database. Used to automatically fill in details when adding new loci. (Version 1.7+)
  - optional
- default_seqdef_script
  - isolate databases only: URL of BIGSdb script running the seqdef database (default: '/cgi-bin/bigsdb/bigsdb.pl'). (Version 1.7+)
  - optional
- default_access
  - the default access to the database configuration, either 'allow' or 'deny'. If 'allow', then specific users can be denied access by creating a file called 'users.deny' containing usernames (one per line) in the configuration directory. If 'deny' then specific users can be allowed by creating a file called 'users.allow' containing usernames (one per line) in the configuration directory. (Version 1.7+)
  - optional
- no_publication_filter
  - isolate databases only: Switches off display of publication filter in isolate query form by default: either 'yes' or 'no', default 'no'. (Version 1.8+)
  - optional
- seqbin_size_threshold
  - Sets the size values in Mbp to enable for the *seqbin filter*.
  - Example: seqbin_size_threshold="0.5,1,2,4".
  - optional

```
<field>
```

Element content: Field name + optional list <optlist> of allowed values, e.g.:

```
<field type="text" required="no" length="40" maindisplay="no"
   web="http://somewebsite.com/cgi-bin/script.pl?id=[?]" optlist="yes">epidemiology
  <optlist>
   <option>carrier</option>
   <option>healthy contact</option>
   <option>sporadic case</option>
   <option>endemic</option>
   <option>epidemic</option>
   <option>pandemic</option>
  </optlist>
</field>
```

- type
  - data type: int, text, float or date
  - required
- min
  - minimum value for integer types.(introduced in v1.7)
  - optional

- max
  - maximum value for integer types. Special values such as CURRENT_YEAR can be used. (introduced in v1.7)
  - optional
- required
  - is data required for this field? 'yes' or 'no', default 'yes'
  - optional
- maindisplay
  - is field displayed in main table after database search? 'yes' or 'no', default 'yes'. This setting can be overridden by individual user preferences.
  - optional
- length
  - length of field, default 12
  - optional
- optlist
  - does this field have a list of allowed values? default 'no'. Surround each option with an <option> tag
  - optional
- dropdown
  - select if you want this field to have its own dropdown filter box on the query page. If the field has an option list it will use the values in it, otherwise all values defined in the database will be included: 'yes' or 'no', default 'no'. This setting can be overridden by individual user preferences.
  - optional
- comments
  - comments about the field
  - optional
- web
  - URL that will be used to hyperlink field values. If [?] is included in the URL, this will be substituted for the actual field value.
  - optional
- regex
  - regular expression used to constrain field values, e.g. regex="^[A-Z].*$" forces the first letter of the value to be capitalized.
  - optional

Special values

The following special variables can be used in place of an actual value:

- CURRENT_YEAR: the 4 digit value of the current year

`<sample>`

Element content: Sample field name + optional list <optlist> of allowed values. Attributes are essentially the same as isolate field attributes, but refer to the samples table rather than the isolates table.

The sample table, if defined, must include isolate_id and sample_id fields, which must also be described in the XML file. These must be set as integer fields.

4.3.2 Sequence definition database XML attributes

`<db>`

Top level element. Contains child elements: system, field and sample.

`<system>`

- db
  - name of database on system
  - required
- dbtype
  - type of database: either 'isolates' or 'sequences'
  - required
- description
  - description of database used throughout interface
  - required
- authentication
  - method of authentication: either 'builtin' or 'apache'. See user authentication.
  - required
- webroot
  - URL of web root, which can be relative or absolute. The bigsdb.css stylesheet file should be located in this directory. Default '/'
  - optional
- script_path_includes
  - partial path of the bigsdb.pl script used to access the database. See user authentication.
  - optional
- curate_path_includes
  - partial path of the bigscurate.pl script used to curate the database. See user authentication.
  - optional
- read_access
  - describes who can view data: either 'public' for everybody, or 'authenticated_users' for anybody who has been able to log in. Default 'public'.
  - optional

- disable_seq_downloads
  - prevent users or curators from downloading all alleles for a locus (admins always can). 'yes' or 'no', default 'no'.
  - optional
- materialized_views
  - enable materialized views: either 'yes' or 'no', default 'no'.
- allele_flags
  - enable flags to be set for alleles: either 'yes' or 'no', default 'no'.
- allele_comments
  - enable comments on allele sequences: either 'yes' or 'no', default 'no'.
  - this is not enabled by default to discourage the practice of adding isolate information to allele definitions (this sort of information belongs in an isolate database).
- sets
  - use sets: either 'yes' or 'no', default 'no'.
  - optional
- set_id
  - force the use of a specific set when accessing database via this XML configuration: Value is the name of the set.
  - optional

4.4 User authentication

You can choose whether to allow Apache to handle your authentication or use built-in authentication.

4.4.1 Apache authentication

Using apache to provide your authentication allows a flexible range of methods and back-ends (see the Apache authentication HowTo for a start, or any number of tutorials on the web).

At its simplest, use a .htaccess file in the directory containing the bigscurate.pl (and bigsdb.pl for restriction of read-access) script or by equivalent protection of the directory in the main Apache server configuration. It is important to note however that, by default, any BIGSdb database can be accessed by any instance of the BIGSdb script (including one which may not be protected by a .htaccess file, allowing public access). To ensure that only a particular instance (protected by a specific htaccess directive) can access the database, the following attributes can be set in the system tag of the database XML description file:

- script_path_includes: the BIGSdb script path must contain the value set.
- curate_path_includes: the BIGSdb curation script path must contain the value set.

For public databases, the 'script_path_includes' attribute need not be set.

To use apache authentication you need to set the authentication attribute in the system tag of the database XML configuration to 'apache'.

4.4.2 Built-in authentication

BIGSdb has its own built-in authentication, using a separate database to store password and session hashes. The advantages of using this over many forms of apache authentication are:

- Users are able to update their own passwords.
- Passwords are not transmitted over the Internet in plain text.

When a user logs in, the server provides a random one-time session variable and the user is prompted to enter their username and password. The password is encrypted within the browser using a Javscript one-way hash algorithm, and this is combined with the session variable and hashed again. This hash is passed to the server. The server compares this hash with its own calculated hash of the stored encrypted password and session variable that it originally sent to the browser. Implementation is based on perl-md5-login.

To use built-in authentication you need to set the authentication attribute in the system tag of the database XML configuration to 'builtin'.

4.5 Setting up the admin user

The first admin user needs to be manually added to the users table of the database. Connect to the database using psql and add the following (changing details to suit the user).:

```
INSERT INTO users (id, user_name, surname, first_name, email, affiliation, status, date_entered,
datestamp, curator) VALUES (1, 'keith', 'Jolley', 'Keith', 'keith.jolley@zoo.ox.ac.uk',
'University of Oxford, UK', 'admin', 'now', 'now', 1);
```

If you are using built-in authentication, set the password for this user using the *add_user.pl* script. This encrypts the password to a hash and stores this within the authentication database. Other users can be added by the admin user from the curation interface accessible from http://your_website/cgi-bin/private/bigscurate.pl?db=test_db (or wherever you have located your bigscurate.pl script).

4.6 Updating PubMed citations

Publications listed in PubMed can be associated with individual isolate records, profiles, loci and sequences. Full citations for these are stored within a local reference database, enabling these to be displayed within isolate records and searching by publication and author. This local database is populated by a script that looks in BIGSdb databases for PubMed records not locally stored and then requests the full citation record from the PubMed database.

The script is called getrefs.pl and can be found in the scripts/maintenance directory. This script needs to know which BIGSdb databases and tables it needs to search for PubMed ids. These are listed in a configuration file (usually called getrefs.conf) which contains two columns - the first is the name of the database, the second is a comma-separated list of tables to search, e.g.

```
pubmlst_bigsdb_neisseria_isolates          refs
pubmlst_bigsdb_neisseria_seqdef            profile_refs,sequence_refs,locus_refs
```

The script can be called as follows:

```
getrefs.pl getrefs.conf
```

This should be run periodically from a CRON job, e.g. every hour.

CHAPTER 5

Administrator's guide

Please note that links displayed within the curation interface will vary depending on database contents and the permissions of the curator.

5.1 Types of user

There are three types of user in BIGSdb:

- User - can view data but never modify it. Users should be created for every submitter of data so that records can be tracked, even if they do not actually use the database. Individual isolate records may not be available to every user if access control lists (ACLs) are configured for the database.
- Curator - can modify data but does not have full control of the database. *Individual permissions* can be set for each curator, so their roles can be controlled. A curator with no specific permissions set has no more power than a standard user.
- Admin - has full control of the database, including setting permissions for curators and setting user passwords if built-in authentication is in use.

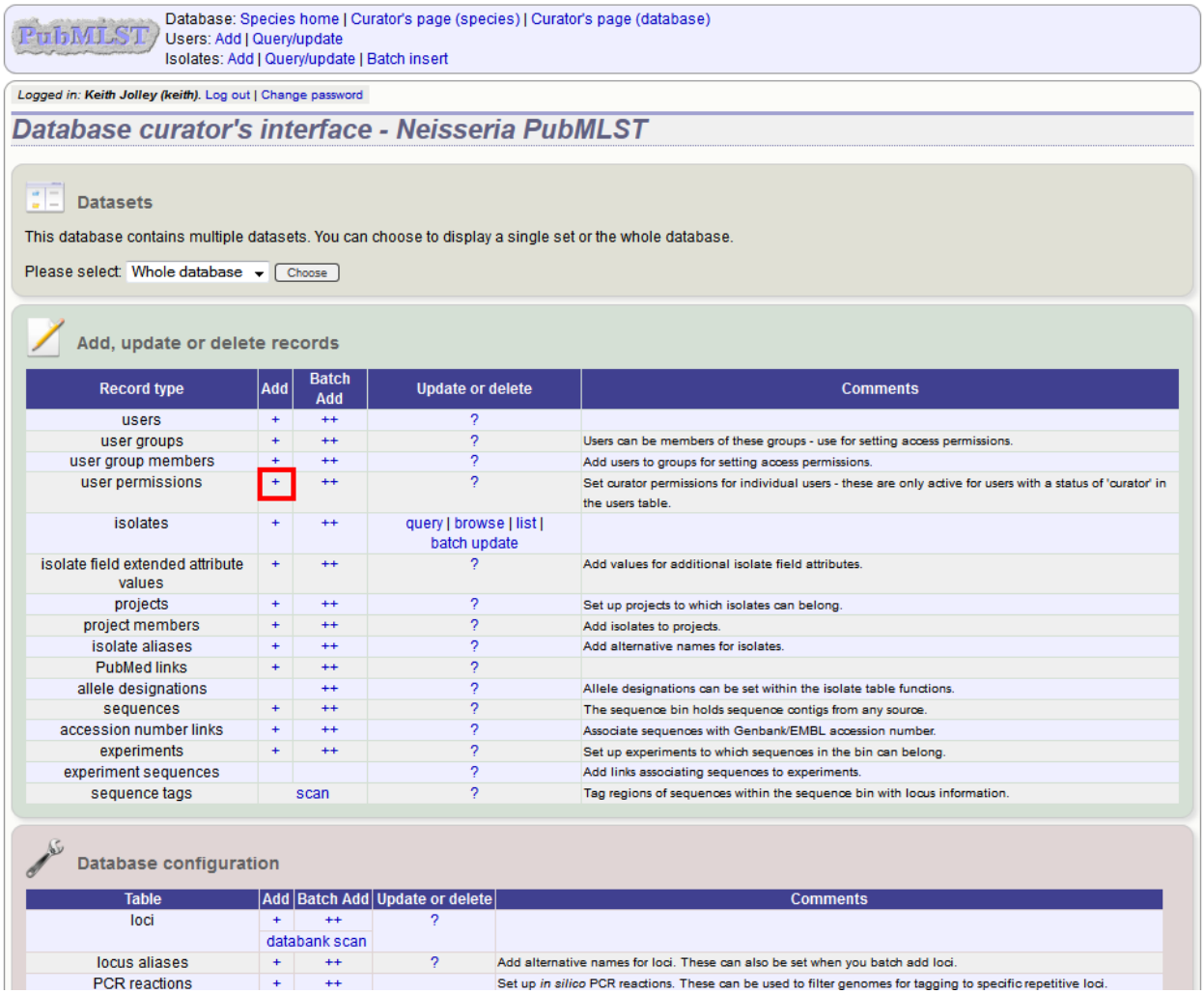
5.2 Curator permissions

Individual permissions can be set for each curator:

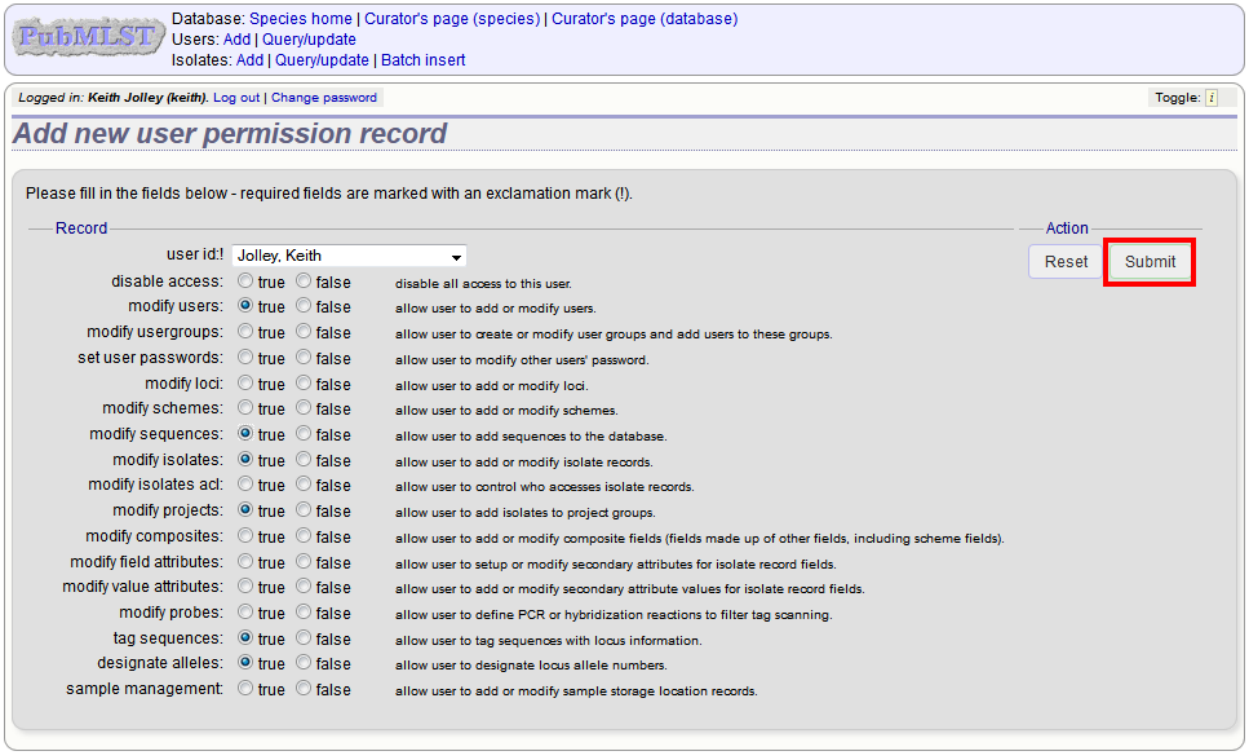
- disable_access - if set to true, this user is completely barred from access.
- modify_users - allowed to add or modify user records. They can change the status of users, but can not revoke admin priveleges from an account. They can also not raise the status of a user to admin level.
- modify_usergroups - allowed to add or modify user groups and add users to these groups.
- set_user_passwords - allowed to modify other users' passwords (if built-in authentication is in use).
- modify_loci - allowed to add or modify loci.
- modify_schemes - allowed to add or modify schemes.
- modify_sequences - allowed to add sequences to the sequence bin (for isolate databases) or new allele definitions (for sequence definition databases).
- modify_isolates - allowed to add or modify isolate records.
- modify_isolates_acl - allowed to control who accesses isolate records (provided they themselves have access to a particular isolate).

- modify_projects - allowed to create projects, modify their descriptions and add or remove isolate records to these.
- modify_composites - allowed to add or modify composite fields (fields made up of other fields, including scheme fields defined in external databases). Composite fields involve defining regular expressions that are evaluated by Perl - this can be dangerous so this permission should be granted with discretion.
- modify_field_attributes - allow user to create or modify secondary field attributes (lookup tables) for isolate record fields.
- modify_value_attributes - allow user to add or modify secondary field values for isolate record fields.
- modify_probes - allow user to define PCR or hybridization reactions to filter tag scanning.
- tag_sequences - allowed to tag sequences with locus information.
- designate_alleles - allowed to manually designate allele numbers for isolate records.
- modify_profiles - allowed to add or modify scheme profiles (only used in a sequence definitions database).

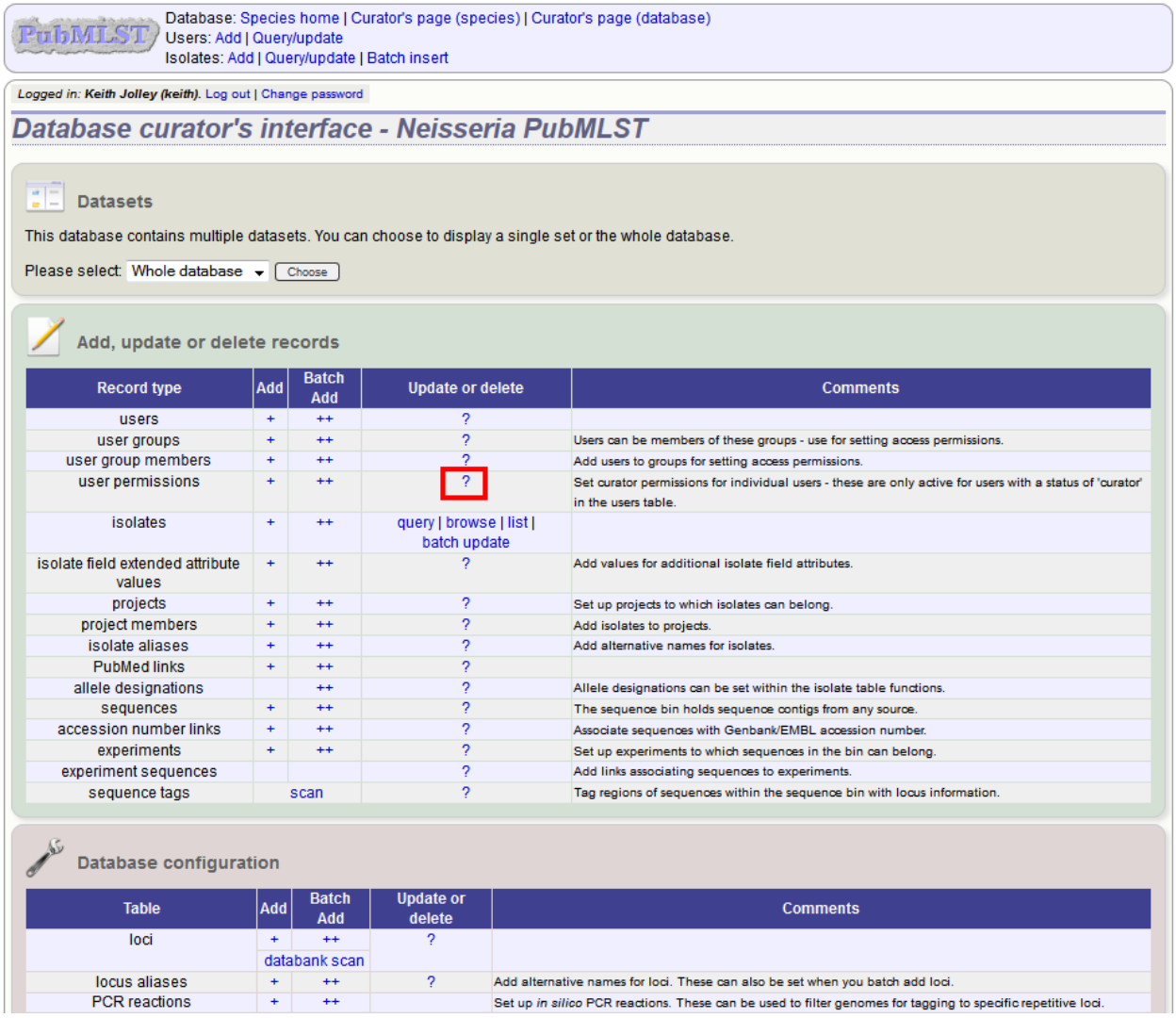
Permissions can be set by clicking the '+' button next to 'user permissions' on the curator's interface:



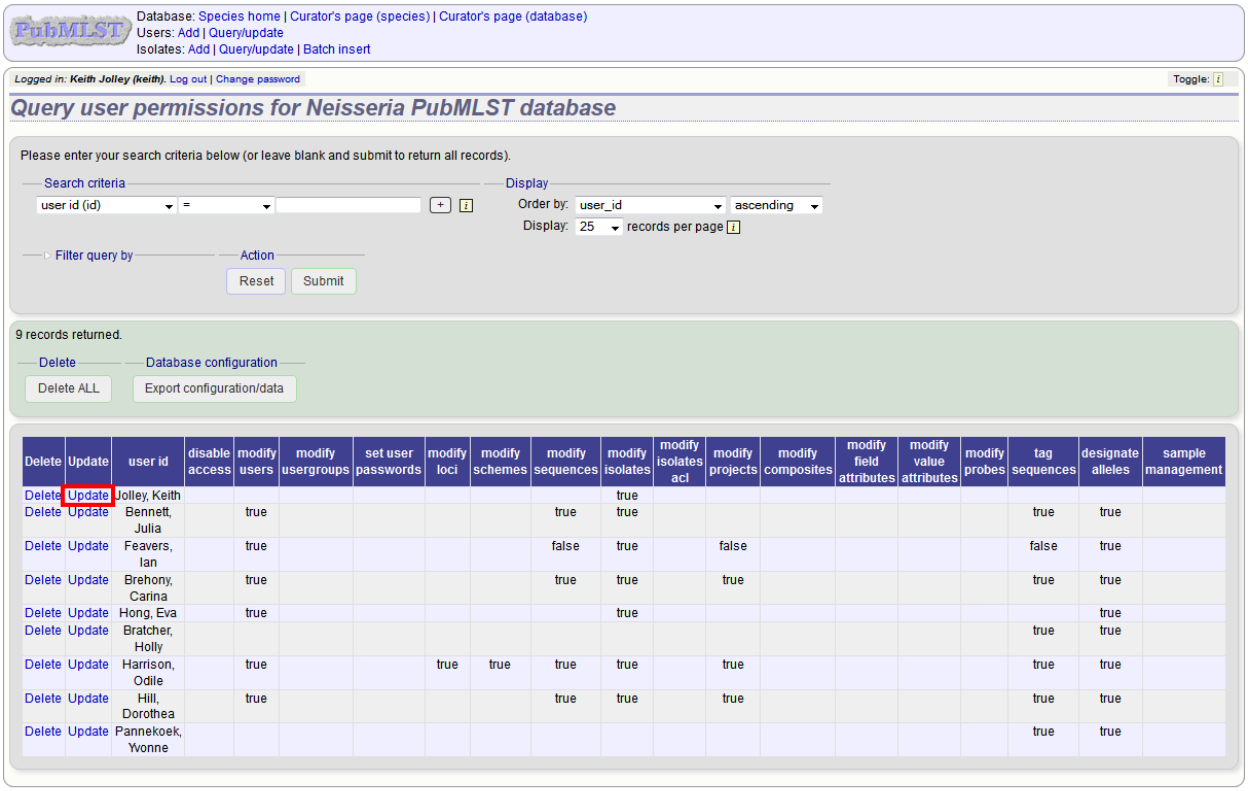
Set specific permissions and then click 'Submit'.



If permissions have already been set for a user, click the 'Update or delete' link on the curator's page instead.



then search for the user by entering specific criteria, or simply press 'Submit' to display all users. Update a specific user by clicking on the 'Update' link next to their name.

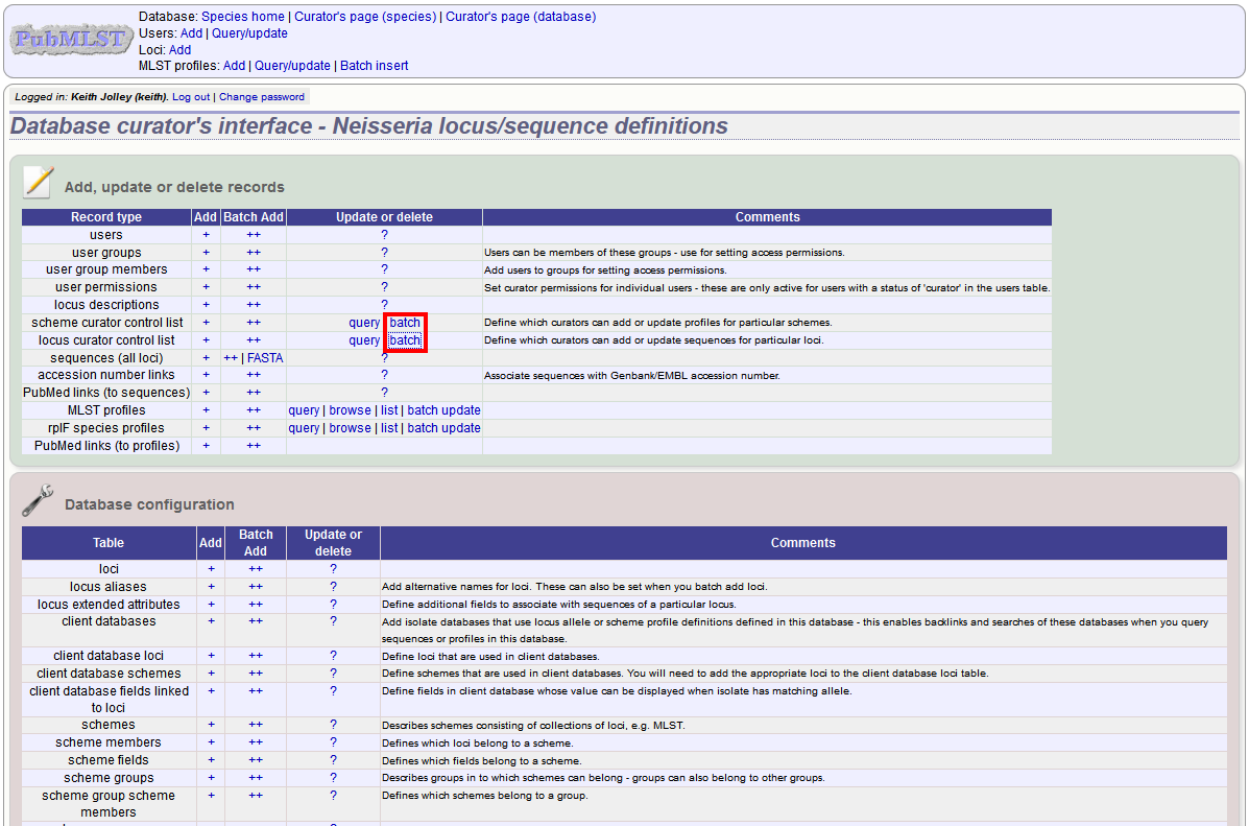


Delete	Update	user id	disable access	modify users	modify usergroups	set user passwords	modify loci	modify schemes	modify sequences	modify isolates	modify isolates acl	modify projects	modify composites	modify field attributes	modify value attributes	modify probes	tag sequences	designate alleles	sample management
Delete	Update	Jolley, Keith								true									
Delete	Update	Bennett, Julia		true					true	true							true	true	
Delete	Update	Feavers, Ian		true					false	true		false					false	true	
Delete	Update	Brehony, Carina		true					true	true		true					true	true	
Delete	Update	Hong, Eva		true						true								true	
Delete	Update	Bratcher, Holly															true	true	
Delete	Update	Harrison, Odile		true			true	true	true	true		true					true	true	
Delete	Update	Hill, Dorothea		true					true	true		true					true	true	
Delete	Update	Pannekoek, Yvonne															true	true	

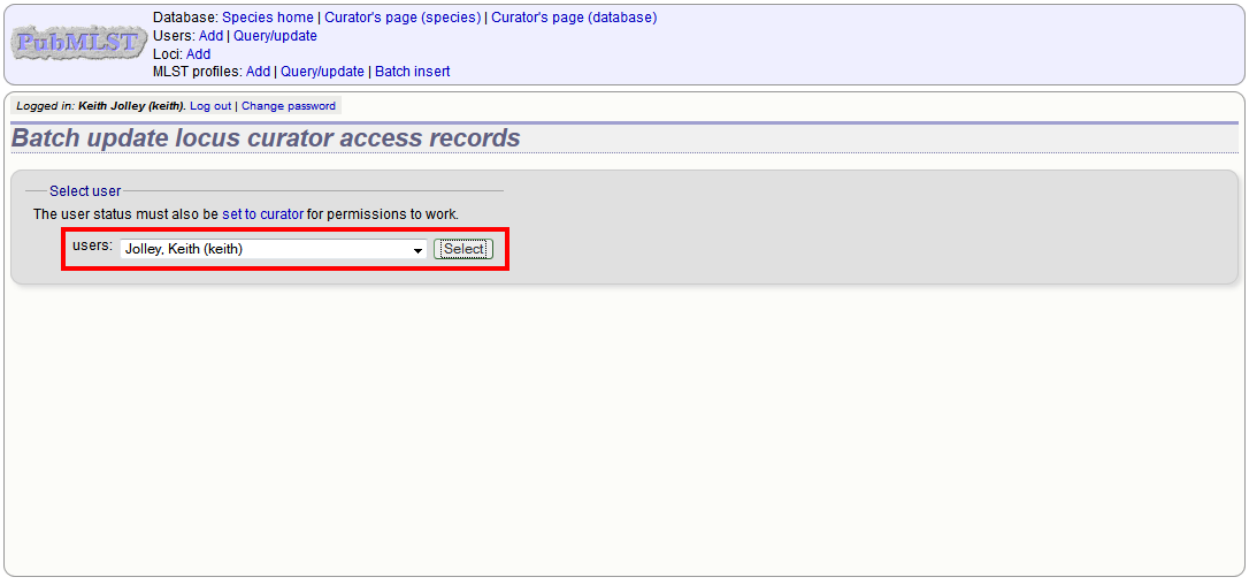
5.3 Locus and scheme permissions (sequence definition database)

To be allowed to define alleles or scheme profiles, curators must be granted specific permission for each locus and scheme by adding their user id number to the 'locus curator' and 'scheme curator' lists.

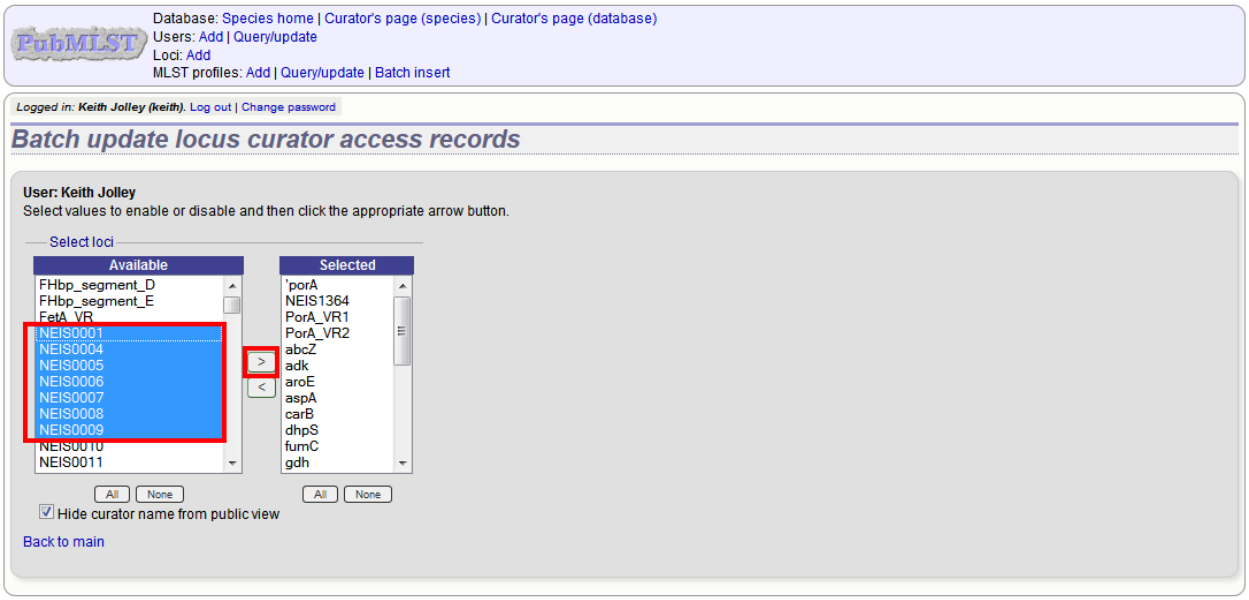
The easiest way to modify these lists is to use the batch update link next to 'locus curator control list' and 'scheme curator control list':



Select the curator from the list:



Then select loci/schemes that the user is allowed to curate in the left hand 'Available' list, and click the right button to move these to the 'Selected' list:



If you uncheck the 'Hide curator name from public view' checkbox, the curator name and E-mail address will appear alongside loci in the download table on the website.

5.4 Controlling access

5.4.1 Access control lists

If access control lists are in use (set the read_access attribute to 'acl' in the system tag of the database XML configuration file), viewing and modifying of individual isolates can be restricted to particular users or usergroups.

> **Warning:** Please note that access control lists are likely to be deprecated in future releases. This is in favour of creating a new class of user that would be allowed to curate their own data only.

New isolate records are automatically set with the following access control:

- All users: read, not write (all users are members of 'All users' group).
- Curator who added data: read and write.

All access controls can be modified by an admin or curator with appropriate permission. This can be done for individual isolate records or in batch mode following an isolate search in the curation interface.

5.4.2 Restricting particular configurations to specific user accounts

Suppose you only wanted specific users to access a database configuration.

In the config.xml, add the following directive:

```
default_access="deny"
```

This tells BIGSdb to deny access to anybody unless their account name appears within a file called users.allow within the config directory. The users.allow file should contain one username per line.

Alternatively, you can deny access to specific users, while allowing every other authenticated user. In config.xml, add the following directive:

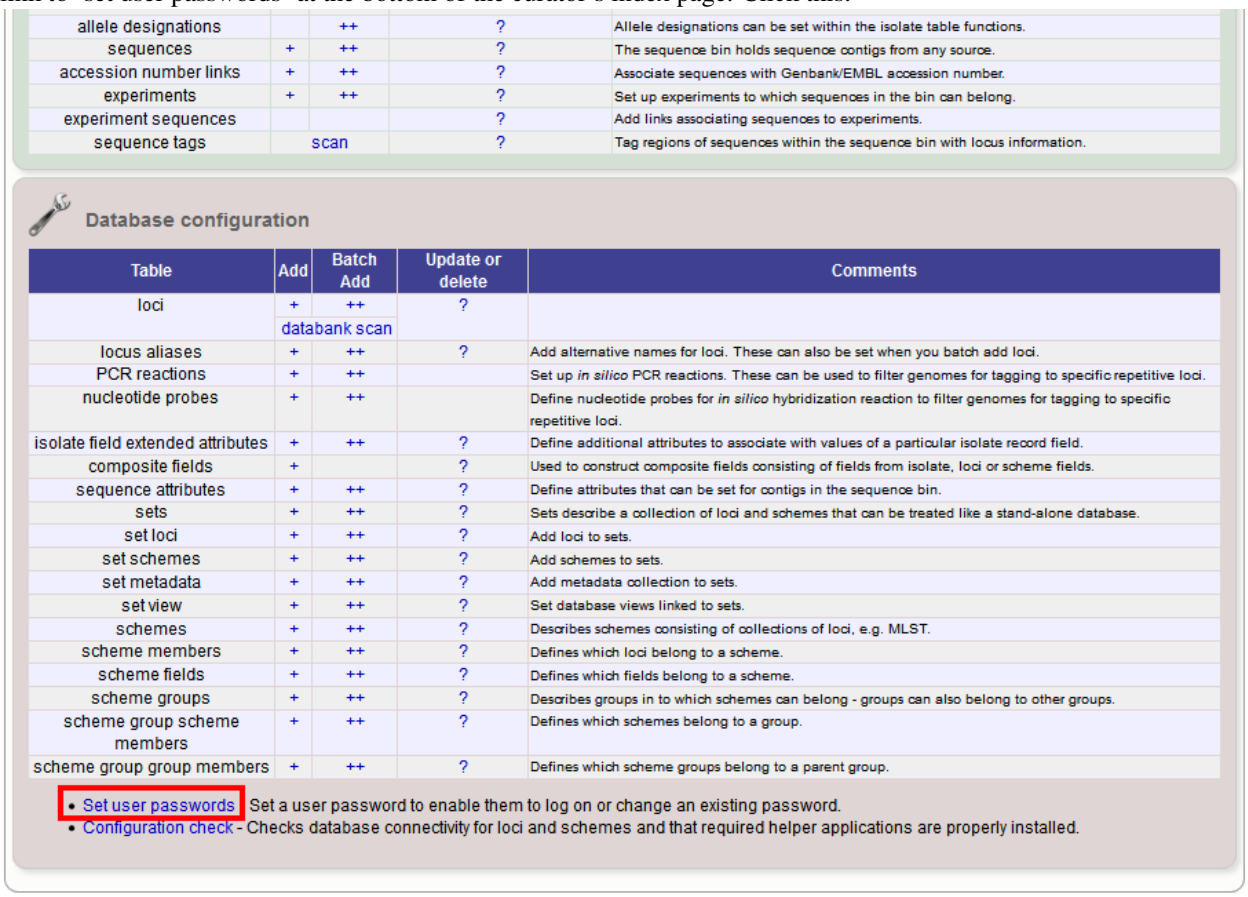
```
default_access="allow"
```

This tells BIGSdb to allow access to anybody unless their account name appears within a file called users.deny within the config directory. The users.deny file should contain one username per line.

5.5 Setting user passwords

Please note that these instructions only apply if using the built-in BIGSdb authentication system.

If you are an administrator or a curator with specific permission to change other users' passwords, you should see a link to 'set user passwords' at the bottom of the curator's index page. Click this.



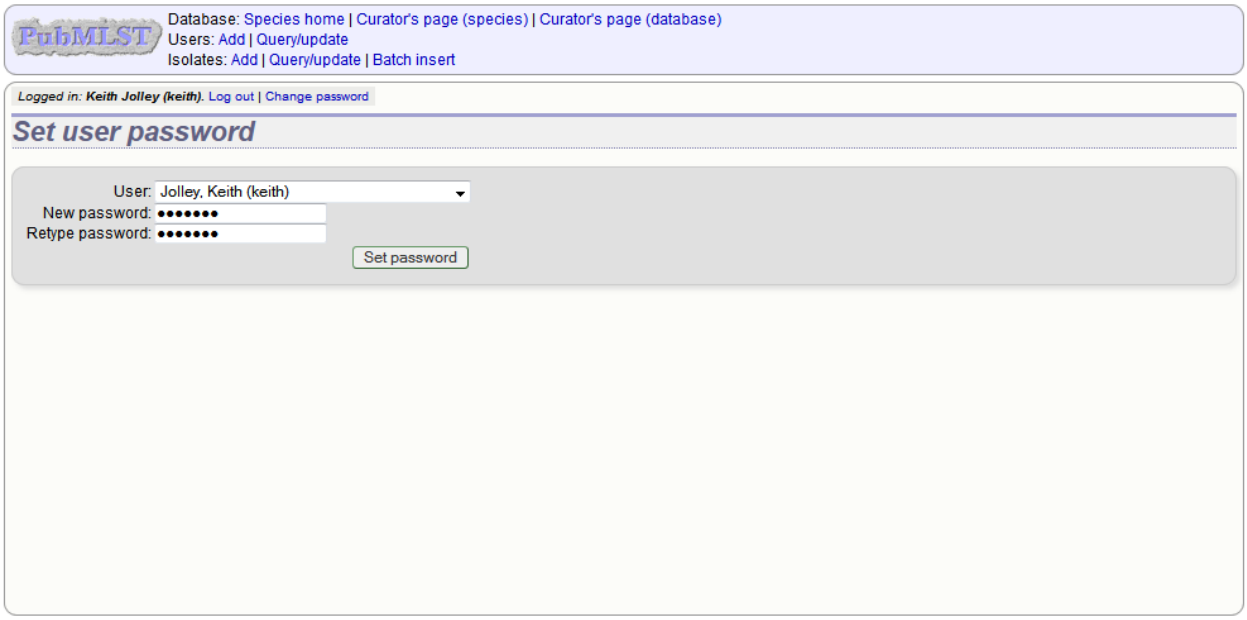
allele designations		++	?	Allele designations can be set within the isolate table functions.
sequences	+	++	?	The sequence bin holds sequence contigs from any source.
accession number links	+	++	?	Associate sequences with Genbank/EMBL accession number.
experiments	+	++	?	Set up experiments to which sequences in the bin can belong.
experiment sequences			?	Add links associating sequences to experiments.
sequence tags	scan		?	Tag regions of sequences within the sequence bin with locus information.

Database configuration

Table	Add	Batch Add	Update or delete	Comments
loci	+	++	?	
	databank scan			
locus aliases	+	++	?	Add alternative names for loci. These can also be set when you batch add loci.
PCR reactions	+	++		Set up *in silico* PCR reactions. These can be used to filter genomes for tagging to specific repetitive loci.
nucleotide probes	+	++		Define nucleotide probes for *in silico* hybridization reaction to filter genomes for tagging to specific repetitive loci.
isolate field extended attributes	+	++	?	Define additional attributes to associate with values of a particular isolate record field.
composite fields	+		?	Used to construct composite fields consisting of fields from isolate, loci or scheme fields.
sequence attributes	+	++	?	Define attributes that can be set for contigs in the sequence bin.
sets	+	++	?	Sets describe a collection of loci and schemes that can be treated like a stand-alone database.
set loci	+	++	?	Add loci to sets.
set schemes	+	++	?	Add schemes to sets.
set metadata	+	++	?	Add metadata collection to sets.
set view	+	++	?	Set database views linked to sets.
schemes	+	++	?	Describes schemes consisting of collections of loci, e.g. MLST.
scheme members	+	++	?	Defines which loci belong to a scheme.
scheme fields	+	++	?	Defines which fields belong to a scheme.
scheme groups	+	++	?	Describes groups in to which schemes can belong - groups can also belong to other groups.
scheme group scheme members	+	++	?	Defines which schemes belong to a group.
scheme group group members	+	++	?	Defines which scheme groups belong to a parent group.

- Set user passwords Set a user password to enable them to log on or change an existing password.
- Configuration check - Checks database connectivity for loci and schemes and that required helper applications are properly installed.

Select the appropriate user from the drop-down list box and enter the new password twice where prompted.



Click 'Set password' and the password will be updated.

5.6 Setting the first user password

To set the first administrator's password for a new database, use the add_user.pl script found in the scripts/maintenance directory:

```
add_user.pl [-a] -d <dbase> -n <username> -p <password>
```

The first user account needs to be added to the database *manually*.

5.7 Enabling plugins

Some plugins can be enabled/disabled for specific databases. If you look in the get_attributes function of the specific plugin file and see a value for system_flag, this value can be used in the system tag of the database configuration XML file to enable the plugin.

For example, the get_attributes function of the BURST plugin looks like:

```
sub get_attributes {
       my %att = (
               name        => 'BURST',
               author      => 'Keith Jolley',
               affiliation => 'University of Oxford, UK',
               email       => 'keith.jolley@zoo.ox.ac.uk',
               description => 'Perform BURST cluster analysis on query results query results',
               category    => 'Cluster',
               buttontext  => 'BURST',
               menutext    => 'BURST',
               module      => 'BURST',
               version     => '1.0.0',
               dbtype      => 'isolates,sequences',
```

```
                section     => 'postquery',
                order       => 10,
                system_flag => 'BURST',
                input       => 'query',
                requires    => 'mogrify',
                min         => 2,
                max         => 1000
        );
        return \%att;
}
```

The 'system_flag' attribute is set to 'BURST', so this plugin can be enabled for a database by adding:

```
BURST="yes"
```

to the system tag of the database XML file. If the system_flag value is not defined then the plugin is always enabled if it is installed on the system.

5.8 Temporarily disabling database updates

There may be instances where it is necessary to temporarily disable database updates. This may be during periods of server or database maintenance, for instance when running on a backup database server.

Updates can be disabled on a global or database-specific level.

5.8.1 Global

In the /etc/bigsdb/bigsdb.conf file, add the following line:

```
disable_updates=yes
```

An optional message can also be displayed by adding a disable_update_message value, e.g.

```
disable_update_message=The server is currently undergoing maintenance.
```

5.8.2 Database-specific

The same attributes described above for use in the bigsdb.conf file can also be used within the system tag of the database config.xml file, e.g.

```
<system
  db="bigsdb_neisseria"
  dbtype="isolates"
  ...
  disable_updates="yes"
  disable_update_message="The server is currently undergoing maintenance."
```

5.9 Host mapping

During periods of server maintenance, it may be necessary to map a database host to an alternative server. This would allow a backup database server to be used while the primary database server is unavailable. In this scenario, you would probably also want to disable updates.

Host mapping can be achieved by editing the /etc/bigsdb/host_mapping.conf file. Each host mapping is placed on a single line, with the current server followed by any amount of whitespace and then the new mapped host, e.g.

```
#Existing_host      Mapped_host
 server1            server2
 localhost          server2
```

[Lines beginning with a hash are comments and are ignored.]

This configuration would use server2 instead of server 1 or localhost wherever they are defined in the database configuration (either host attribute in the database config.xml file, or within the loci or schemes tables).

5.10 Improving performance

5.10.1 Use mod_perl

The single biggest improvement to speed can be obtained by running BIGSdb under mod_perl. There's very little point trying anything else until you have mod_perl set up and running - this can improve start-up performance a hundred-fold since the script isn't compiled on each page access but persists in memory.

5.10.2 Cache scheme definitions within an isolate database

If you have a large number of allelic profiles defined for a scheme, you can cache these definitions within an isolate database to speed up querying of isolates by scheme criteria (e.g. by ST for a MLST scheme).

To do this use the update_scheme_caches.pl script found in the scripts/maintenance directory, e.g. to cache all schemes in the pubmlst_bigsdb_neisseria_isolates database

```
update_scheme_caches.pl -d pubmlst_bigsdb_neisseria_isolates
```

This script creates indexed tables within the isolate database called temp_scheme_X and temp_isolates_scheme_fields_1 (where X is the scheme_id). If these table aren't present, they are created as temporary tables every time a query is performed that requires a join against scheme definition data. This requires importing all profile definitions from the definitions database and determining scheme field values for all isolates. This may sound like it would be slow but caching only has a noticeable effect once you have >5000 profiles.

Note that you will need to run this script periodically as a CRON job to refresh the cache.

If queries are taking longer than 5 seconds to perform and a cache is not in place, you will see a warning message in bigsdb.log suggesting that the caches be set up. Unless you see this warning regularly, you probably don't need to do this.

5.10.3 Use materialized views for scheme definitions

Because of the way BIGSdb allows any number of profile schemes to be set up, the data are stored in a normalised manner in multiple tables. A database view, e.g. scheme_1, is created that joins these tables so that they can be queried as you would a single table. A view, however, is only a pre-selected query rather than a physical table and you can not index columns on it to optimise query performance.

A materialized view is a real table that is created from the view and refreshed every time the data in the underlying view changes. Because it is a real table, the database doesn't need to perform these joins every time it is queried and indexes can be set up on it, both of which greatly speeds up querying.

To use materialized views within a seqdef database set the following attribute in the system tag of the XML description file:

```
materialized_views="yes"
```

You will then need to run the 'configuration repair' function at the bottom of the administrator's main curation page for each scheme. This rebuilds the view and creates a materialized view called mv_scheme_X. This materialized view is updated automatically whenever profile data are added or altered via the web interface.

If you want an isolate database to benefit from this materialized view, make sure you put 'mv_scheme_X' (where X is the scheme id) in the dbase_table field (rather than 'scheme_X') when setting up the scheme in the isolate database configuration.

Please note that if you make changes to your profile data by means other than the web interface then the materialized view will not be updated. You can update it by running the following SQL command:

```
SELECT refresh_matview('mv_scheme_X');
```

The materialized view is used, for example, for looking up a ST from a profile and vice-versa. Significant speed improvements will only be realised if you have lots of profiles (>5000) and you are doing lots of lookups, e.g. displaying more than the default 25 records per page.

5.11 Dataset partitioning

5.11.1 Sets

Sets provide a means to partition the database in to manageable units that can appear as smaller databases to an end user. Sets can include constrained groups of isolates, loci, and schemes from the complete database and also include additional metadata fields only applicable to that set.

See also:

Sets (concept)

5.11.2 Configuration of sets

First sets need to be enabled in the XML configuration file (config.xml) of the database. Add the following attribute to the system tag:

```
sets="yes"
```

With this attribute, the curation interface now has options to add sets, and then add loci or schemes to these sets.

sequences	+	++	?	The sequence bin holds sequence contigs from any source.
accession number links	+	++		Associate sequences with Genbank/EMBL accession number.
experiments	+	++	?	Set up experiments to which sequences in the bin can belong.
experiment sequences			?	Add links associating sequences to experiments.
sequence tags		scan	?	Tag regions of sequences within the sequence bin with locus information.

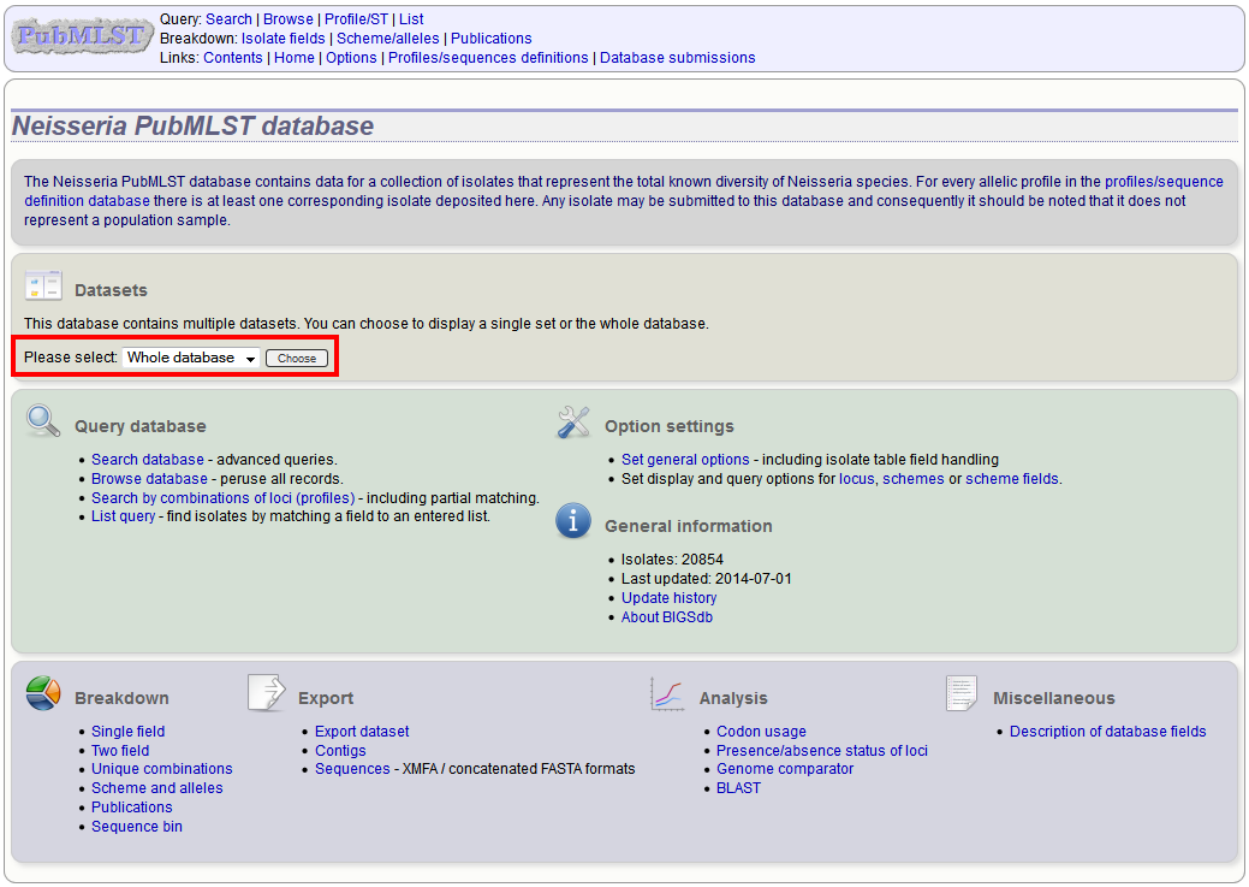
Database configuration

Table	Add	Batch Add	Update or delete	Comments
loci	+	++	?	
		databank scan		
locus aliases	+	++	?	Add alternative names for loci. These can also be set when you batch add loci.
PCR reactions	+	++		Set up *in silico* PCR reactions. These can be used to filter genomes for tagging to specific repetitive loci.
nucleotide probes	+	++		Define nucleotide probes for *in silico* hybridization reaction to filter genomes for tagging to specific repetitive loci.
isolate field extended attributes	+	++	?	Define additional attributes to associate with values of a particular isolate record field.
composite fields	+			Used to construct composite fields consisting of fields from isolate, loci or scheme fields.
sequence attributes	+	++		Define attributes that can be set for contigs in the sequence bin.
sets	+	++	?	Sets describe a collection of loci and schemes that can be treated like a stand-alone database.
set loci	+	++	?	Add loci to sets.
set schemes	+	++	?	Add schemes to sets.
set view	+	++	?	Set database views linked to sets.
schemes	+	++	?	Describes schemes consisting of collections of loci, e.g. MLST.
scheme members	+	++	?	Defines which loci belong to a scheme.
scheme fields	+	++	?	Defines which fields belong to a scheme.
scheme groups	+	++	?	Describes groups in to which schemes can belong - groups can also belong to other groups.
scheme group scheme members	+	++	?	Defines which schemes belong to a group.
scheme group group members	+	++	?	Defines which scheme groups belong to a parent group.

- Set user passwords - Set a user password to enable them to log on or change an existing password.
- Configuration check - Checks database connectivity for loci and schemes and that required helper applications are properly installed.

The name of a locus or scheme to use within a set can be defined in the set_name field when adding loci or schemes to a set. Common names can also be set for loci - equivalent to the common name used within the loci table.

Now when a user goes to the contents page of the database they will be presented with a dropdown menu of datasets and can choose either the 'whole database' or a specific set. This selection is remembered between sessions.



Alternatively, a specific set can be selected within the XML config file so that only a specific set is available when accessed via that configuration. In that case, the user would be unaware that the database contains anything other than the loci and schemes available within the set.

To specify this, add the following attributute to the system tag:

```
set_id="1"
```

where the value is the name of the set.

Note: If the set_id attribute is set, database configuration settings in the curator's interface are disabled. This is because when the configuration is constrained to a set, only loci and schemes already added to the set are visible, so functionality to edit schemes/loci would become very confusing. To modify these settings, you either need to access the interface from a different configuration, i.e. an alternative config.xml with the set_id attribute not set, or temporarily remove the set_id directive from the current config.xml while making configuration changes.

5.11.3 Set metadata

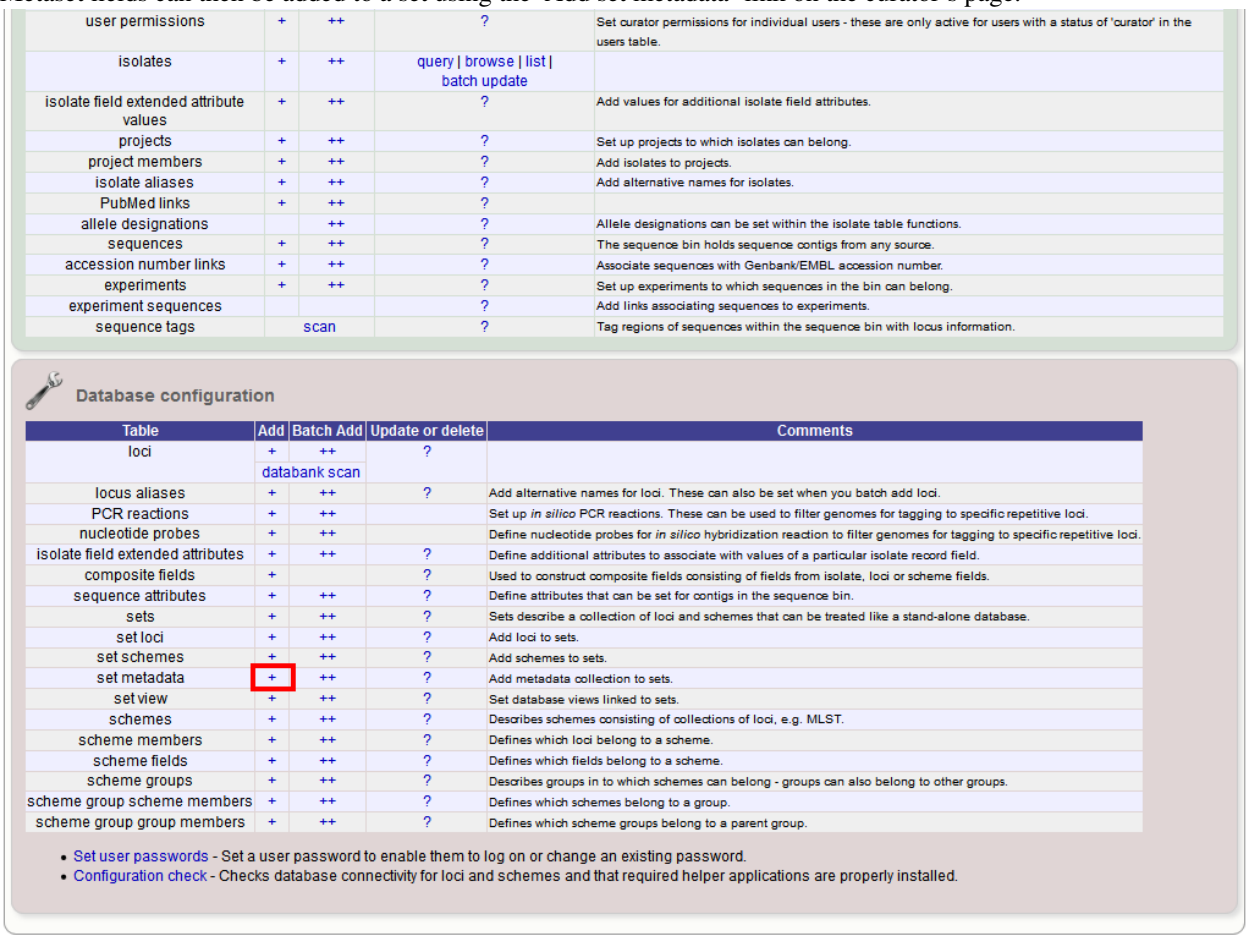
Additional metadata fields can be set within the XML configuration file. They are specified as belonging to a metaset by prefixing the field name with 'meta_NAME:' where NAME is the name of the metaset, e.g.

```
<field type="text" required="no" length="30" maindisplay="no"
    optlist="yes">meta_1:clinical_outcome
  <optlist>
    <option>no sequeleae</option>
```

```
    <option>hearing loss</option>
    <option>amputation</option>
    <option>death</option>
  </optlist>
</field>
```

Metaset fields can be defined just like any other *provenance field* and their position in the output is determined by their position in the XML file.

Metaset fields can then be added to a set using the 'Add set metadata' link on the curator's page.



user permissions	+	++	?	Set curator permissions for individual users - these are only active for users with a status of 'curator' in the users table.
isolates	+	++	query | browse | list | batch update	
isolate field extended attribute values	+	++	?	Add values for additional isolate field attributes.
projects	+	++	?	Set up projects to which isolates can belong.
project members	+	++	?	Add isolates to projects.
isolate aliases	+	++	?	Add alternative names for isolates.
PubMed links	+	++	?	
allele designations		++	?	Allele designations can be set within the isolate table functions.
sequences	+	++	?	The sequence bin holds sequence contigs from any source.
accession number links	+	++	?	Associate sequences with Genbank/EMBL accession number.
experiments	+	++	?	Set up experiments to which sequences in the bin can belong.
experiment sequences			?	Add links associating sequences to experiments.
sequence tags		scan	?	Tag regions of sequences within the sequence bin with locus information.

Database configuration

Table	Add	Batch Add	Update or delete	Comments
loci	+	++	?	
		databank scan		
locus aliases	+	++	?	Add alternative names for loci. These can also be set when you batch add loci.
PCR reactions	+	++		Set up *in silico* PCR reactions. These can be used to filter genomes for tagging to specific repetitive loci.
nucleotide probes	+	++		Define nucleotide probes for *in silico* hybridization reaction to filter genomes for tagging to specific repetitive loci.
isolate field extended attributes	+	++	?	Define additional attributes to associate with values of a particular isolate record field.
composite fields	+		?	Used to construct composite fields consisting of fields from isolate, loci or scheme fields.
sequence attributes	+	++	?	Define attributes that can be set for contigs in the sequence bin.
sets	+	++	?	Sets describe a collection of loci and schemes that can be treated like a stand-alone database.
set loci	+	++	?	Add loci to sets.
set schemes	+	++	?	Add schemes to sets.
set metadata	+	++	?	Add metadata collection to sets.
set view	+	++	?	Set database views linked to sets.
schemes	+	++	?	Describes schemes consisting of collections of loci, e.g. MLST.
scheme members	+	++	?	Defines which loci belong to a scheme.
scheme fields	+	++	?	Defines which fields belong to a scheme.
scheme groups	+	++	?	Describes groups in to which schemes can belong - groups can also belong to other groups.
scheme group scheme members	+	++	?	Defines which schemes belong to a group.
scheme group group members	+	++	?	Defines which scheme groups belong to a parent group.

- Set user passwords - Set a user password to enable them to log on or change an existing password.
- Configuration check - Checks database connectivity for loci and schemes and that required helper applications are properly installed.

A new database table needs to be added for each metaset. This should contain all the fields defined for a metaset. The table should also contain an isolate_id field to act as the foreign key linking to the isolate table, e.g. the SQL would look something like the following:

```
CREATE TABLE meta_1 (
isolate_id integer NOT NULL,
town text,
clinical_outcome text,
PRIMARY KEY (isolate_id),
CONSTRAINT m1_isolate_id FOREIGN KEY (isolate_id) REFERENCES isolates
ON DELETE CASCADE
ON UPDATE CASCADE
);

GRANT SELECT,UPDATE,INSERT,DELETE ON meta_1 TO apache;
```

The above creates the database table for a metaset called '1', defining new text fields for 'town' and 'clinical_outcome'.

5.11.4 Set views

Finally the isolate record table can be partitoned using database views and these views associated with a set. Create views using something like the following:

```
CREATE VIEW spneumoniae AS SELECT * FROM isolates WHERE species = 'Streptococcus pneumoniae';
GRANT SELECT ON spneumoniae TO apache;
```

Add the available views to the XML file as a comma separated list in the system tag 'views' attribute:

```
<system
 .....
 sets="yes"
 views="spneumoniae,saureus"
>
</system>
```

Set the view to the set by using the 'Add set view' link on the curator's page.

5.11.5 Using only defined sets

The only_sets attribute can be set to 'yes' to disable the option for 'Whole database' so that only sets can be viewed, e.g.

```
<system
 .....
 sets="yes"
 only_sets="yes"
>
</system>
```

5.12 Adding new loci

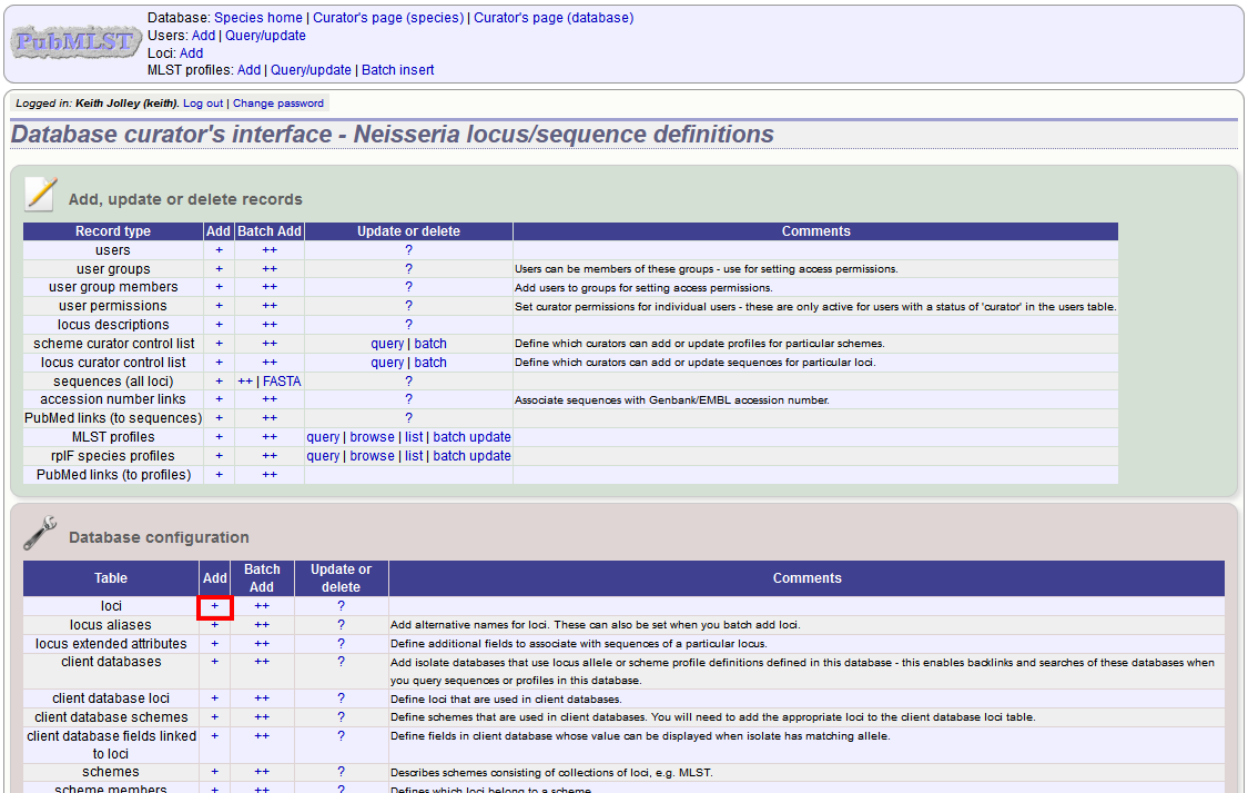
See also:

Loci (concept)

5.12.1 Sequence definition databases

Single locus

Click the add (+) loci link on the curator's interface contents page.



Fill in the web form with appropriate values. Required fields have an exclamation mark (!) next to them:

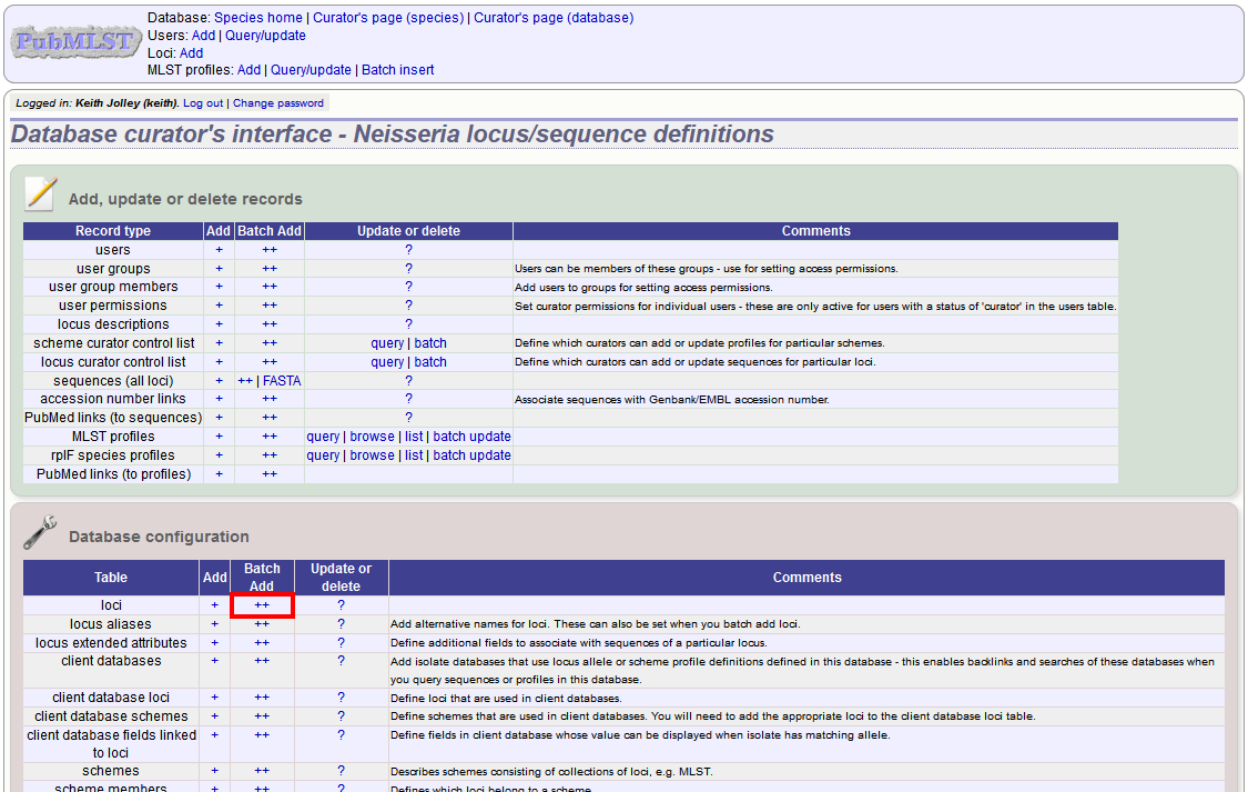
- id - The name of the locus.
  - Allowed: any value starting with a letter or underscore.
- data_type - Describes whether the locus is defined by nucleotide or peptide sequence.
  - Allowed: DNA/peptide.
- allele_id_format - The format for allele identifiers.
  - Allowed: integer/text.
- length_varies - Sets whether alleles can vary in length.
  - Allowed: true/false.
- coding_sequence - Sets whether the locus codes for a protein.
  - Allowed: true/false.
- formatted_name - Name with HTML formatting (optional).
  - This allows you to add formatting such as bold, italic, underline and superscripting to locus names as they appear in the web interface.
  - Allowed: valid HTML.
- common_name - The common name for the locus (optional).
  - Allowed: any value.
- formatted_common_name - Common name with HTML formatting (optional).
  - Allowed: valid HTML.

- allele_id_regex - Regular expression to enforce allele id naming (optional).
  - ^: the beginning of the string
  - $:the end of the string
  - d: digit
  - D: non-digit
  - s: white space character
  - S: non white space character
  - w: alpha-numeric plus '_'
  - .: any character
  - *: 0 or more of previous character
  - +: 1 or more of previous character
  - e.g. ^Fd-d+$ states that an allele name must begin with a F followed by a single digit, then a dash, then one or more digits, e.g. F1-12
- length - Standard length of locus (required if length_varies is set to false.
  - Allowed: any integer.
- min_length - Minimum length of locus (optional).
  - Allowed: any integer.
- max_length - Maximum length of locus (optional).
  - Allowed: any integer (larger than the minimum length).
- orf - Open reading frame of locus (optional).
  - 1-3 are the forward reading frame, 4-6 are the reverse reading frames.
  - Allowed: 1-6.
- genome_position - The start position of the locus on a reference genome (optional).
  - Allowed: any integer.
- match_longest - Specifies whether in a sequence query to only return the longest match (optional).
  - This is useful for some loci that can have some sequences shorter than others, e.g. peptide loci defining antigenic loops. This can lead to instances of one sequence being longer than another but otherwise being identical. In these cases, usually the longer sequence is the one that should be matched.
  - Allowed: true/false.
- full_name - Full name of the locus (optional).
  - Allowed: any value.
- product - Name of gene product (optional).
  - Allowed: Any value.
- description - Description of the locus (optional).
  - Allowed: any value.
- aliases - Alternative names for the locus (optional).
  - Enter each alias on a separate line in the text box.

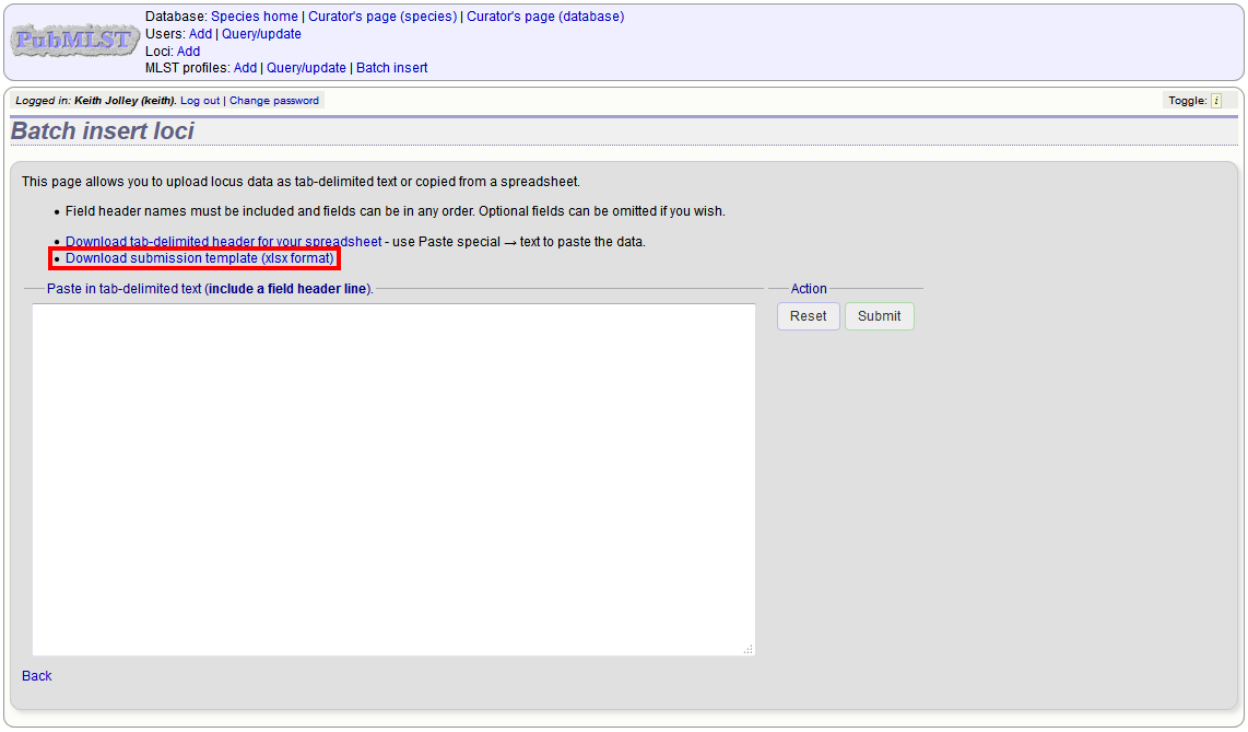
  - Allowed: any value.
- pubmed_ids - PubMed ids of publications describing the locus (optional).
  - Enter each PubMed id on a separate line in the text box.
  - Allowed: any integer.
- links - Hyperlinks pointing to additional resources to display in the locus description (optional).
  - Enter each link on a separate line in the format with the URL first, followed by a | then the description (URL|description).

Batch adding

Click the batch add (++) loci link on the curator's interface contents page.



Click the link to download a header line for an Excel spreadsheet:



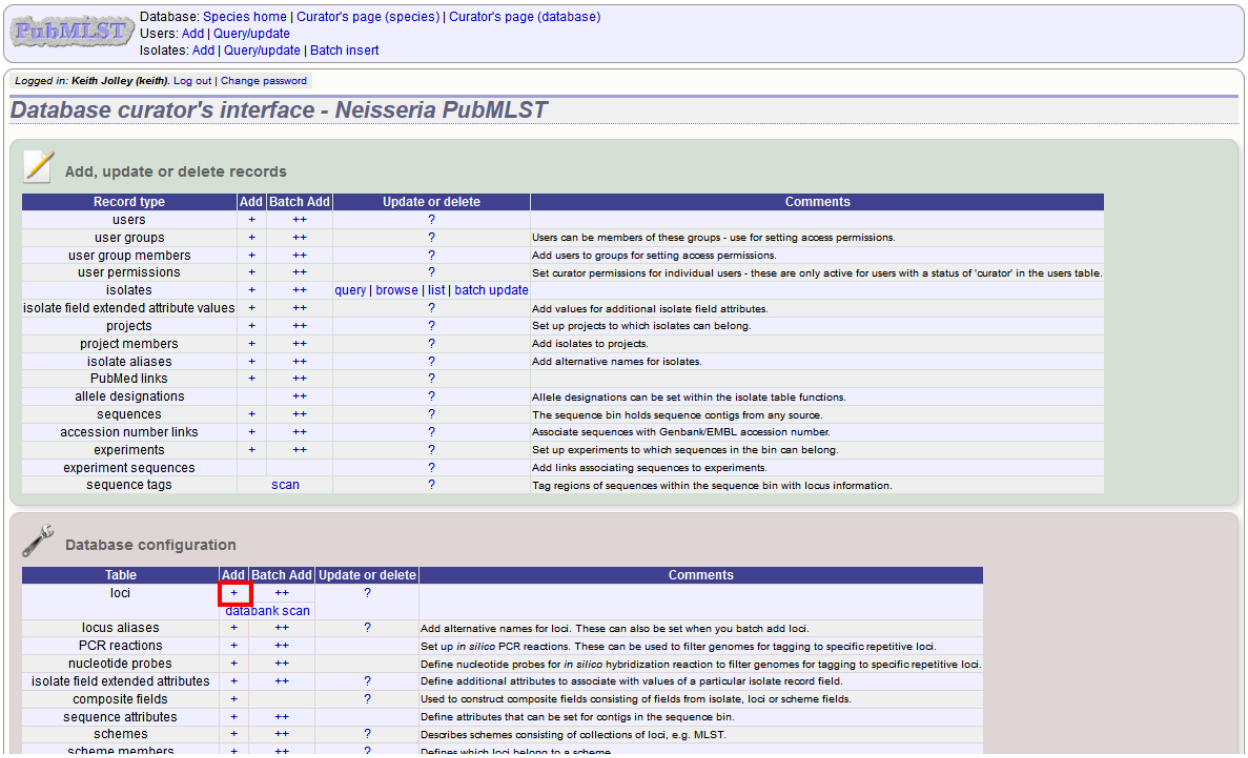
Fill in the spreadsheet using the fields described for *adding single loci*.

Fill in the spreadsheet fields using the table above as a guide, then paste the completed table into the web form and press 'Submit query'.

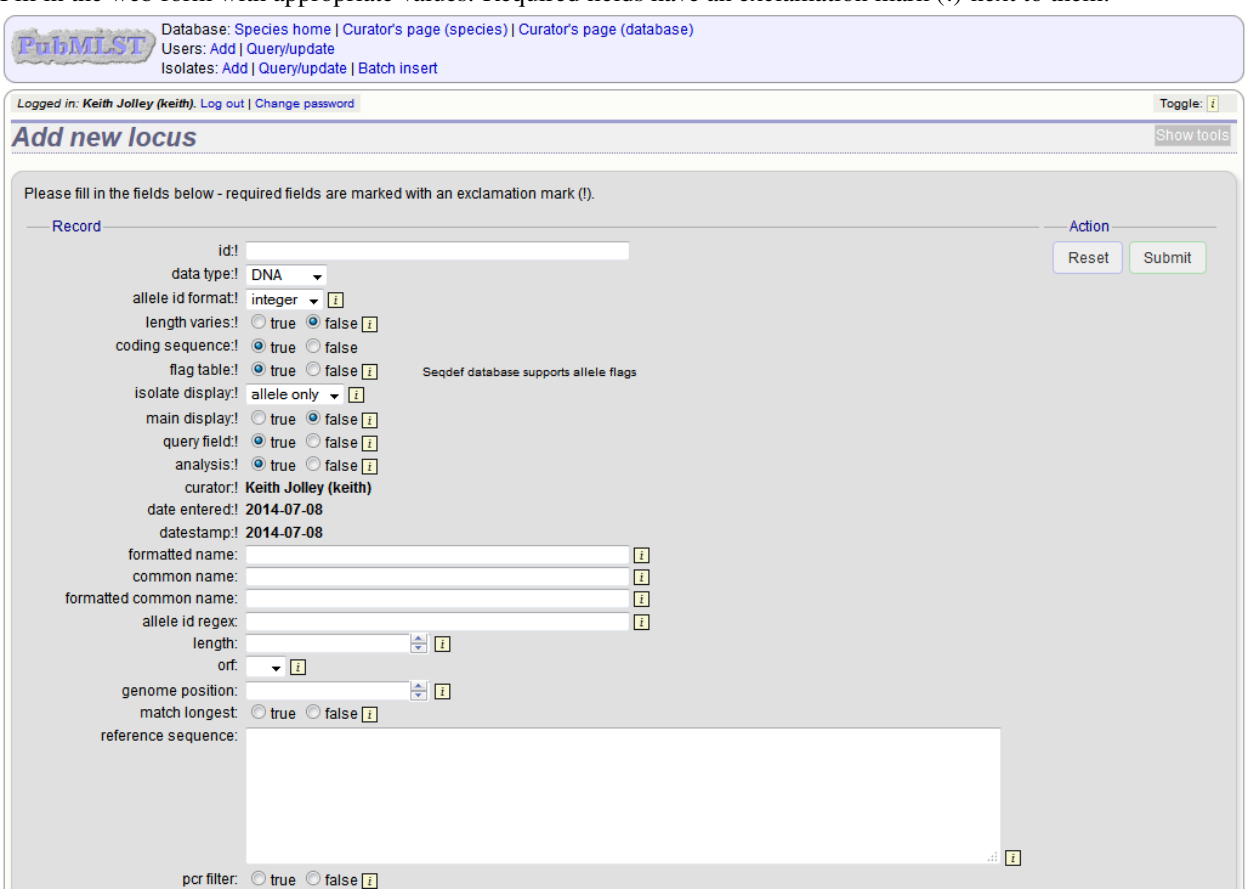
5.12.2 Isolate databases

Single locus

Click the add (+) loci link on the curator's interface contents page.



Fill in the web form with appropriate values. Required fields have an exclamation mark (!) next to them:



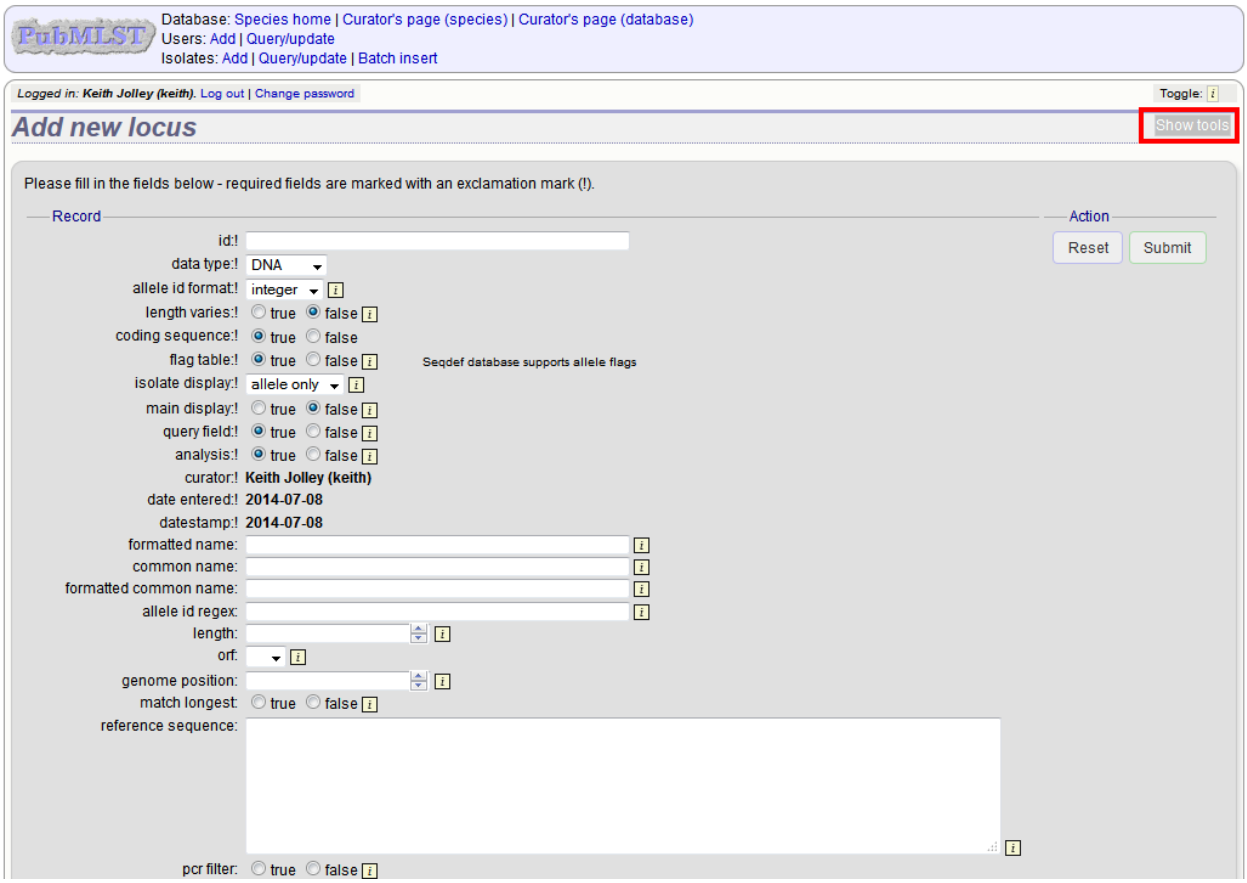
- id - The name of the locus
  - Allowed: any value starting with a letter or underscore.
- data_type - Describes whether the locus is defined by nucleotide or peptide sequence.
  - Allowed: DNA/peptide.
- allele_id_format - The format for allele identifiers.
  - Allowed: integer/text.
- length_varies - Sets whether alleles can vary in length.
  - Allowed: true/false.
- coding_sequence - Sets whether the locus codes for a protein.
  - Allowed: true/false.
- flag_table - Set to true to specify that the sequence definition database contains an allele flag table (which is the case for BIGSdb version 1.4 onwards).
  - Allowed: true/false.
- isolate_display - Sets how alleles for this locus are displayed in a detailed isolate record - this can be overridden by user preference.
  - Allowed: allele only/sequence/hide.
- main_display - Sets whether or not alleles for this locus are displayed in a main results table by default - this can be overridden by user preference.
  - Allowed: true/false.
- query_field - Sets whether or not alleles for this locus can be used in queries by default - this can be overridden by user preference.
  - Allowed: true/false.
- analysis - Sets whether or not alleles for this locus can be used in analysis functions by default - this can be overridden by user preference.
  - Allowed: true/false.
- formatted_name - Name with HTML formatting (optional).
  - This allows you to add formatting such as bold, italic, underline and superscripting to locus names as they appear in the web interface.
  - Allowed: valid HTML.
- common_name - The common name for the locus (optional).
  - Allowed: any value.
- formatted_common_name - Common name with HTML formatting (optional).
  - Allowed: valid HTML.
- allele_id_regex - Regular expression to enforce allele id naming.
  - ^: the beginning of the string
  - $:the end of the string
  - d: digit
  - D: non-digit

  - s: white space character
  - S: non white space character
  - w: alpha-numeric plus '_'
  - .: any character
  - *: 0 or more of previous character
  - +: 1 or more of previous character
  - e.g. ^Fd-d+$ states that an allele name must begin with a F followed by a single digit, then a dash, then one or more digits, e.g. F1-12
- length - Standard length of locus (required if length_varies is set to false).
  - Allowed: any integer.
- orf - Open reading frame of locus (optional). 1-3 are the forward reading frame, 4-6 are the reverse reading frames.
  - Allowed: 1-6.
- genome_position - The start position of the locus on a reference genome.
  - Allowed: any integer.
- match_longest - Only select the longest exact match when tagging/querying.
  - This is useful for some loci that can have some sequences shorter than others, e.g. peptide loci defining antigenic loops. This can lead to instances of one sequence being longer than another but otherwise being identical. In these cases, usually the longer sequence is the one that should be matched.
  - Allowed: true/false.
- reference_sequence - Sequence used by the automated sequence comparison algorithms to identify sequences matching this locus. **This is only used if a sequence definition database has not been set up for this locus.**
- pcr_filter - Set to true if this locus is further defined by genome filtering using in silico PCR.
  - Allowed: true/false.
- probe_filter - Set to true if this locus is further defined by genome filtering using in silico hybdridization.
  - Allowed: true/false.
- dbase_name - Name of database (system name).
  - Allowed: any text.
- dbase_host - Resolved name of IP address of database host - leave blank if running on the same machine as the isolate database.
  - Allowed: network address, e.g. 129.67.26.52 or zoo-oban.zoo.ox.ac.uk
- dbase_port - Network port on which the sequence definition database server is listening - leave blank unless using a non-standard port (5432).
  - Allowed: integer.
- dbase_user - Name of user with permission to access the sequence definition database - depending on the database configuration you may be able to leave this blank.
  - Allowed: any text (no spaces).
- dbase_password - Password of database user - again depending on the database configuration you may be able to leave this blank.

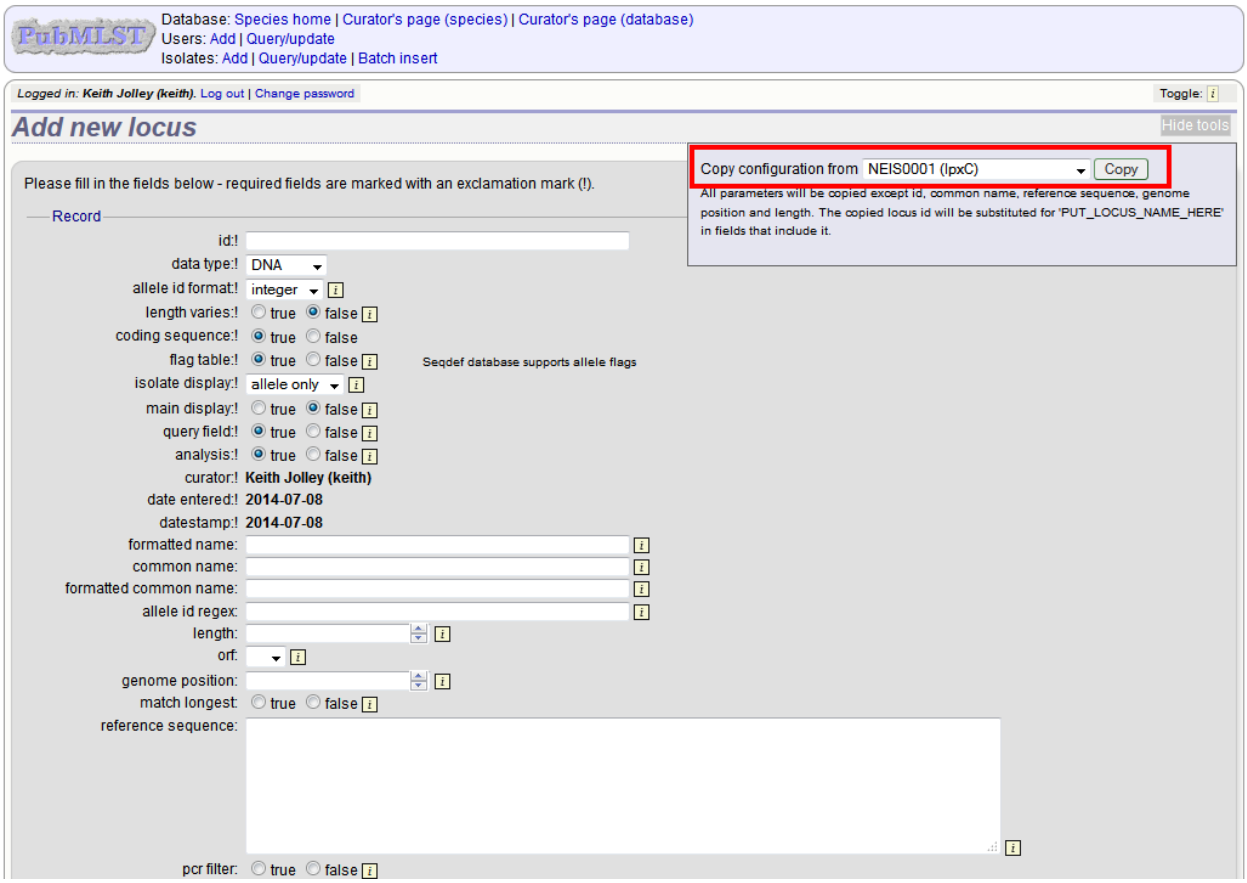
  - Allowed: any text (no spaces).
- dbase_table - Table in the sequence definition database that contains allele sequences for this locus. If the definition database uses BIGSdb this will be 'sequences'.
  - Allowed: any text (no spaces).
- dbase_id_field - Primary field in sequence database that defines allele. If the definition database uses BIGSdb this will be 'allele_id'.
  - Allowed: any text (no spaces).
- dbase_id2_field - Secondary field in sequence database that defines alleles. If dbase_id_field uniquely defines alleles for this locus then this should be left blank. If the definition database uses BIGSdb this will be 'locus'.
  - Allowed: any text (no spaces).
- dbase_id2_value - Secondary field value in sequence database that defines alleles. If dbase_id_field uniquely defines alleles for this locus then this should be left blank. If the definition database uses BIGSdb this will be the name of the locus used in the id field
  - Allowed: any text (no spaces).
- dbase_seq_field - Field in sequence database containing allele sequence. If the definition database uses BIGSdb this will be 'sequence'.
  - Allowed: any text (no spaces).
- description_url - The URL used to hyperlink to locus information in the isolate information page. This can either be a relative (e.g. /cgi-bin/...) or an absolute (containing http://) URL.
  - Allowed: any valid URL.
- url - The URL used to hyperlink to information about the allele. This can either be a relative or absolute URL. If [?] (including the square brackets) is included then this will be substituted for the allele value in the resultant URL. To link to the appropiate allele info page on a corresponding seqdef database you would need something like /cgi-bin/bigsdb/bigsdb.pl?db=pubmlst_neisseria_seqdef&page=alleleInfo&locus=abcZ&allele_id=[?].
  - Allowed: any valid URL.

Using existing locus definition as a template

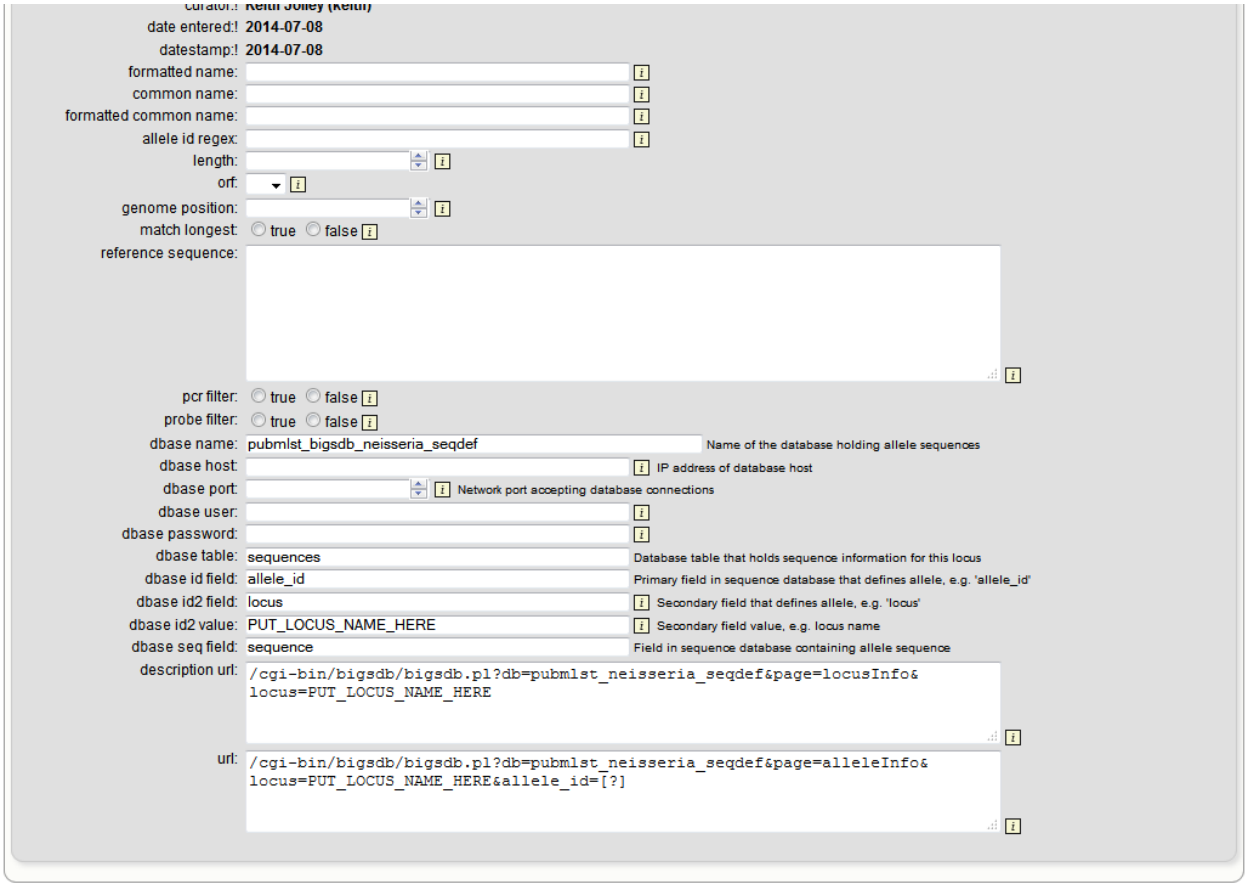
When defining a new locus in the isolate database, it is possible to use an existing locus record as a template. To do this, click the 'Show tools' link in the top-right of the screen:



This displays a drop-down box containing existing loci. Select the locus that you wish to use as a template, and click 'Copy'.



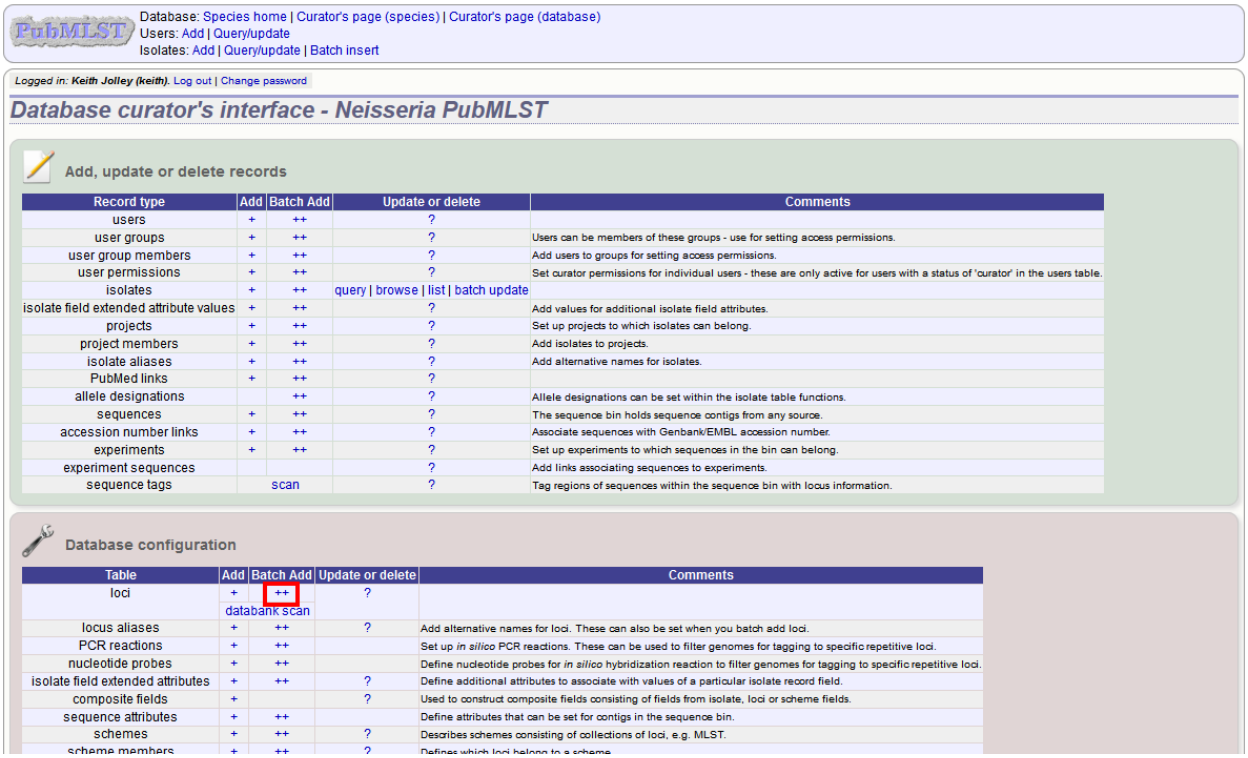
The configuration will be copied over to the web form, with the exception of name fields. Some fields will require you to change the value 'PUT_LOCUS_NAME_HERE' with the value you enter in the id field. These are usually the dbase_id2_value, description_url and url fields:



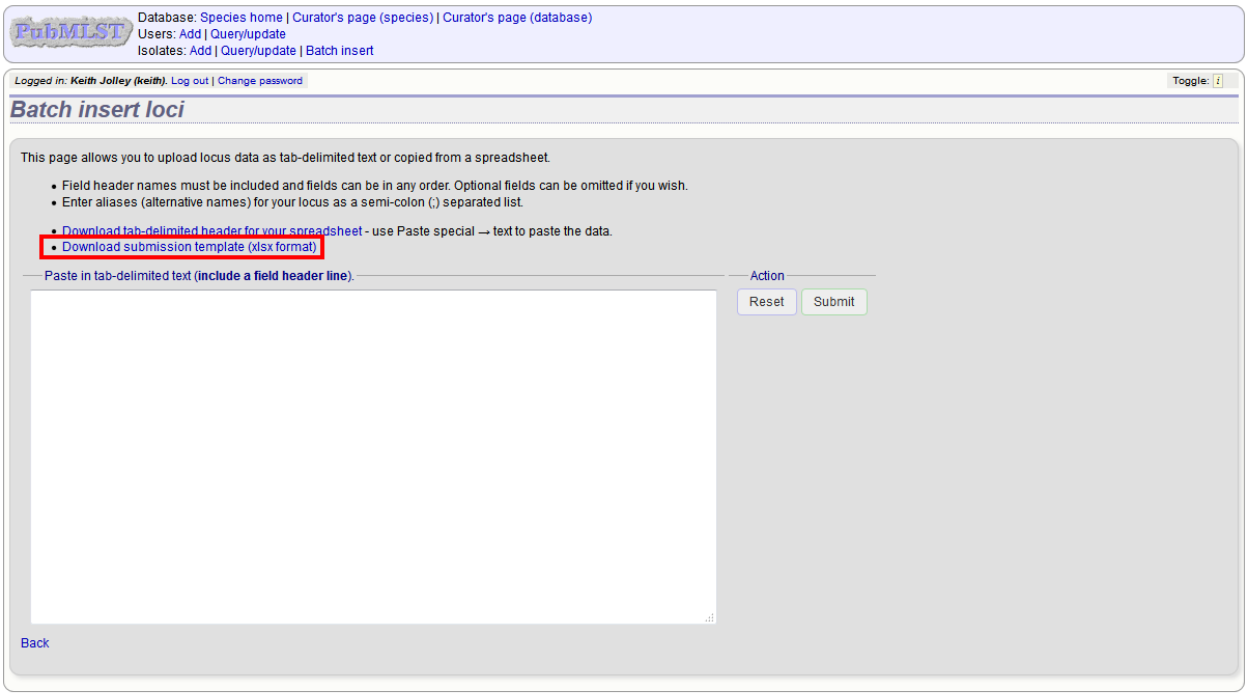
Complete the form and click 'Submit'.

Batch adding

Click the batch add (++) loci link on the curator's interface contents page.



Click the link to download an Excel template:

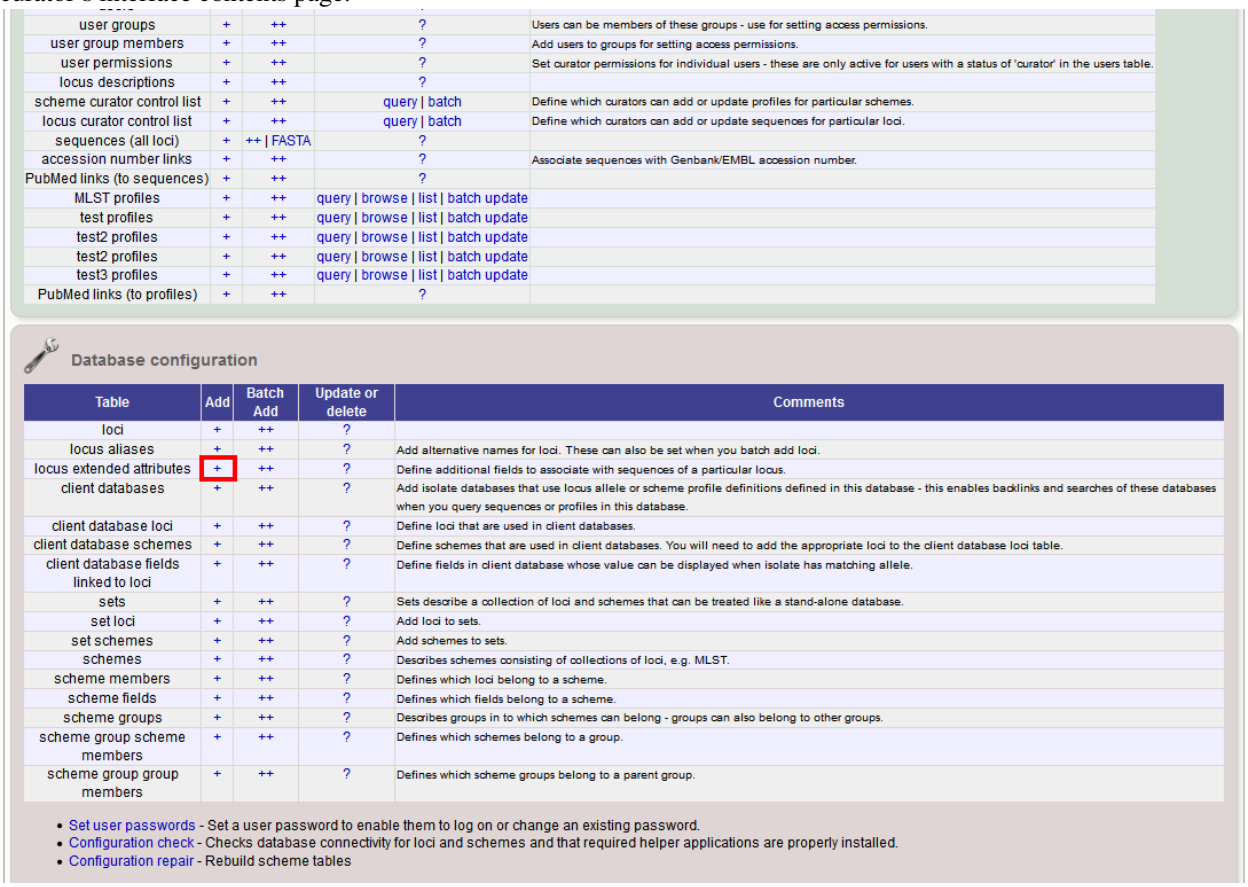


Fill in the spreadsheet fields using the *table above as a guide*, then paste the completed table into the web form and press 'Submit query'.

5.13 Defining locus extended attributes

You may want to add additional metadata for the allele definitions of some loci. Since these are likely to be specific to each locus, they cannot be defined generically within the standard locus definition. We can, instead, define extended attributes. Examples of these include higher order grouping of antigen sequences, antibody reactivities, identification of important mutations, or cross-referencing of alternative nomenclatures.

To add extended attributes for a locus, click add (+) locus extended attributes in the sequence definition database curator's interface contents page.



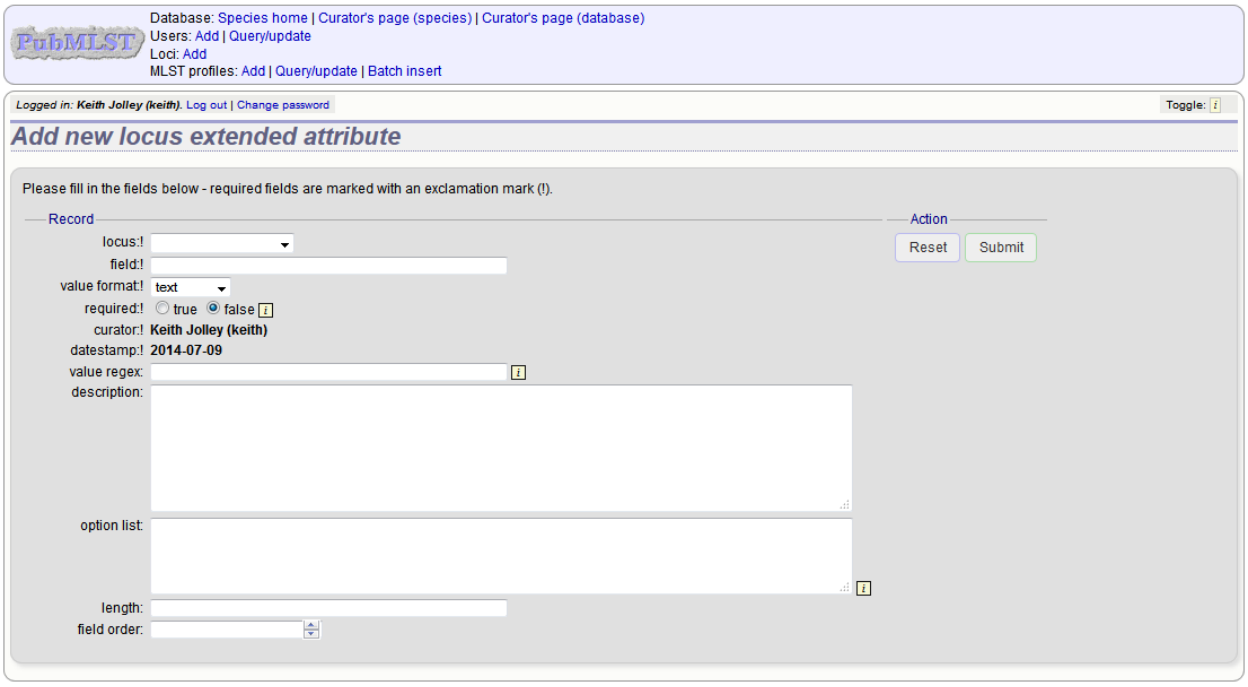
user groups	+	++	?	Users can be members of these groups - use for setting access permissions.
user group members	+	++	?	Add users to groups for setting access permissions.
user permissions	+	++	?	Set curator permissions for individual users - these are only active for users with a status of 'curator' in the users table.
locus descriptions	+	++	?	
scheme curator control list	+	++	query | batch	Define which curators can add or update profiles for particular schemes.
locus curator control list	+	++	query | batch	Define which curators can add or update sequences for particular loci.
sequences (all loci)	+	++ | FASTA	?	
accession number links	+	++	?	Associate sequences with Genbank/EMBL accession number.
PubMed links (to sequences)	+	++	?	
MLST profiles	+	++	query | browse | list | batch update	
test profiles	+	++	query | browse | list | batch update	
test2 profiles	+	++	query | browse | list | batch update	
test2 profiles	+	++	query | browse | list | batch update	
test3 profiles	+	++	query | browse | list | batch update	
PubMed links (to profiles)	+	++	?	

Database configuration

Table	Add	Batch Add	Update or delete	Comments
loci	+	++	?	
locus aliases	+	++	?	Add alternative names for loci. These can also be set when you batch add loci.
locus extended attributes	+	++	?	Define additional fields to associate with sequences of a particular locus.
client databases	+	++	?	Add isolate databases that use locus allele or scheme profile definitions defined in this database - this enables backlinks and searches of these databases when you query sequences or profiles in this database.
client database loci	+	++	?	Define loci that are used in client databases.
client database schemes	+	++	?	Define schemes that are used in client databases. You will need to add the appropriate loci to the client database loci table.
client database fields linked to loci	+	++	?	Define fields in client database whose value can be displayed when isolate has matching allele.
sets	+	++	?	Sets describe a collection of loci and schemes that can be treated like a stand-alone database.
set loci	+	++	?	Add loci to sets.
set schemes	+	++	?	Add schemes to sets.
schemes	+	++	?	Describes schemes consisting of collections of loci, e.g. MLST.
scheme members	+	++	?	Defines which loci belong to a scheme.
scheme fields	+	++	?	Defines which fields belong to a scheme.
scheme groups	+	++	?	Describes groups in to which schemes can belong - groups can also belong to other groups.
scheme group scheme members	+	++	?	Defines which schemes belong to a group.
scheme group group members	+	++	?	Defines which scheme groups belong to a parent group.

- Set user passwords - Set a user password to enable them to log on or change an existing password.
- Configuration check - Checks database connectivity for loci and schemes and that required helper applications are properly installed.
- Configuration repair - Rebuild scheme tables

Fill in the web form with appropriate values. Required fields have an exclamation mark (!) next to them:



- locus - Select locus from dropdown box.
  - Allowed: existing locus name.
- field - Name of extended attributes.
  - Allowed: any value.
- value_format - Data type of attribute.
  - Allowed: integer/text/boolean.
- required - Specifies whether the attribute value but be defined when adding a new sequence.
  - Allowed: true/false.
- value_regex - Regular expression to enforce allele id naming (optional).
  - ^: the beginning of the string
  - $:the end of the string
  - d: digit
  - D: non-digit
  - s: white space character
  - S: non white space character
  - w: alpha-numeric plus '_'
  - .: any character
  - *: 0 or more of previous character
  - +: 1 or more of previous character
- description - Description that will appear within the web form when adding new sequences (optional).
  - Allowed: any value.

- option_list - Pipe (|) separated list of allowed values (optional).
- length - Maximum length of value (optional).
  - Allowed: any integer.
- field_order - Integer that sets the position of the field within scheme values in any results (optional).
  - Allowed: any integer.

Once extended attributes have been defined, they will appear in the web form when adding new sequences for that locus. The values are searchable when using a *locus-specific sequence query*, and they will appear within query results and allele information pages.

5.14 Defining schemes

Schemes are collections of loci that may be associated with particular fields - one of these fields can be a primary key, i.e. a field that uniquely defines a particular combination of alleles at the associated loci.

A specific example of a scheme is MLST - *see workflow for setting up a MLST scheme*.

To set up a new scheme, you need to:

1. Add a new scheme description.
2. Define loci as 'scheme members'.
3. Add 'scheme fields' associated with the scheme.

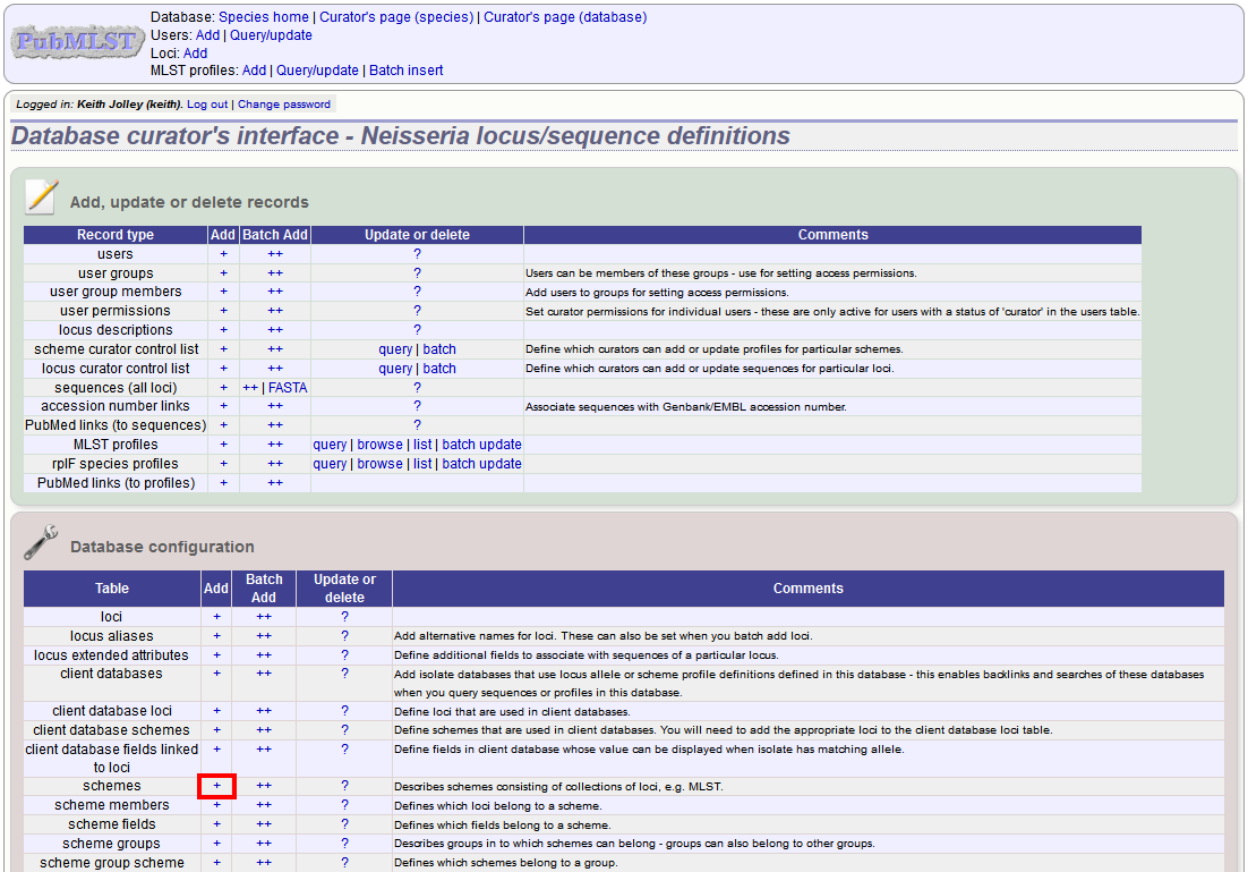
See also:

Schemes (concept)

5.14.1 Sequence definition databases

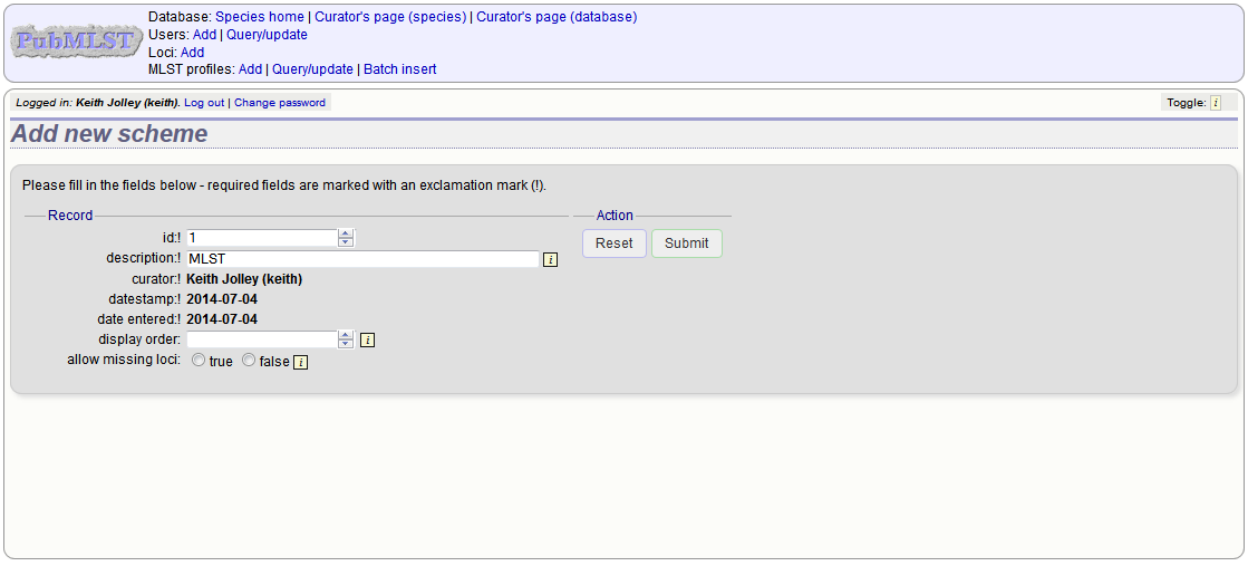
As with all configuration, tables can be populated using the batch interface (++) or one at a time (+). Details for the latter are described below:

Click the add (+) scheme link on the curator's interface contents page.

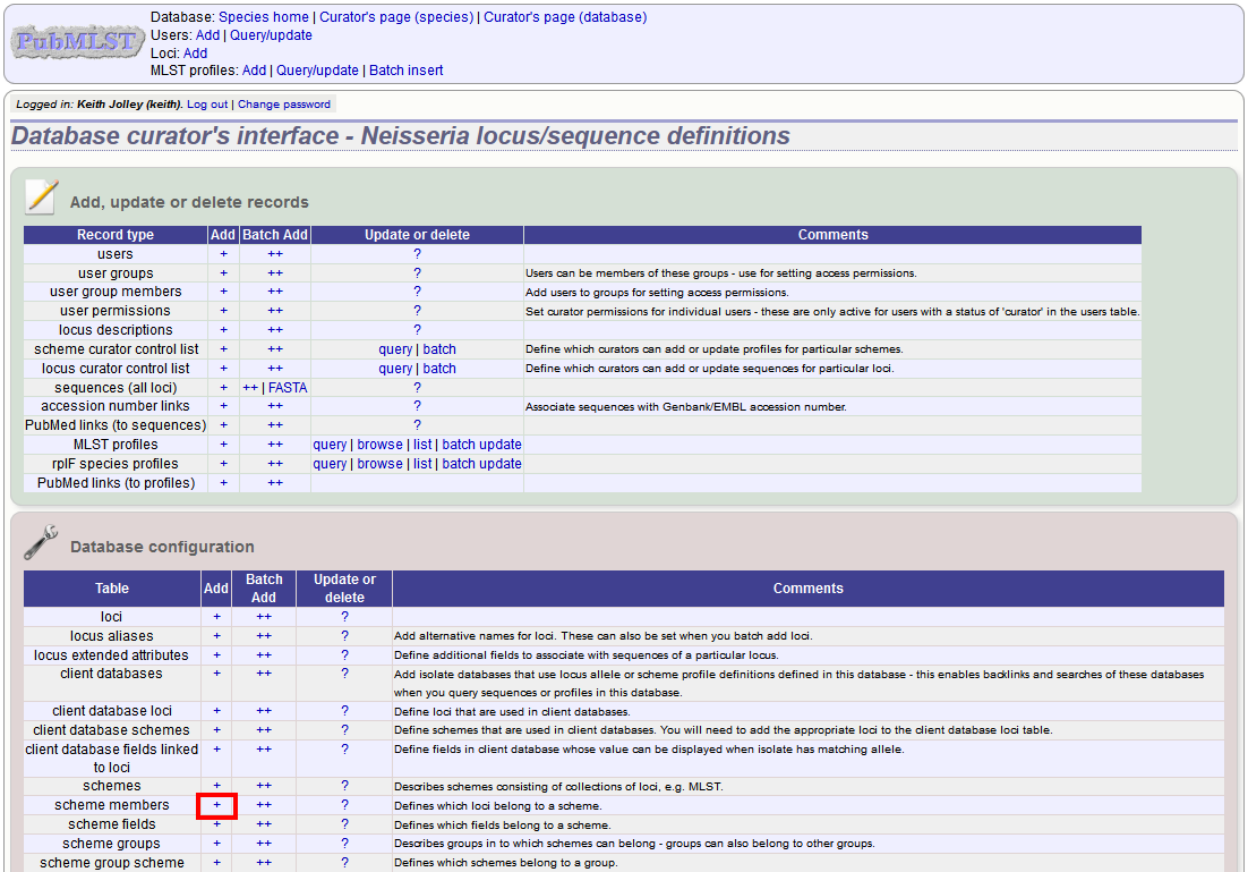


Fill in the scheme description in the web form. The next available scheme id number will be filled in already.

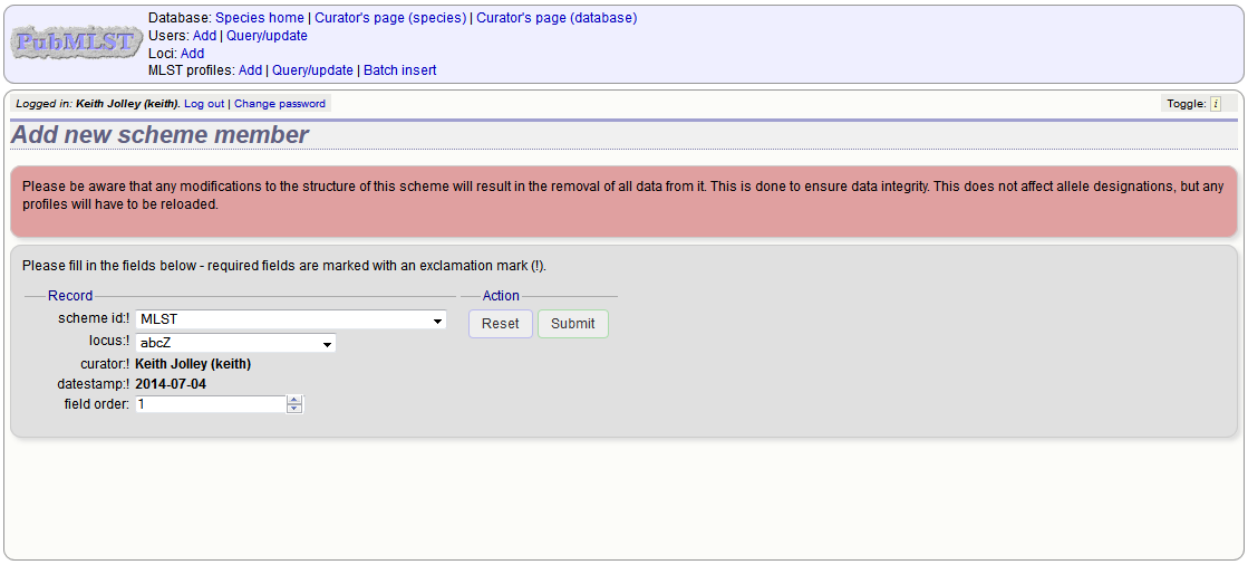
The display_order field accepts an integer that can be used to order the display of schemes in the interface - this can be left blank if you wish.



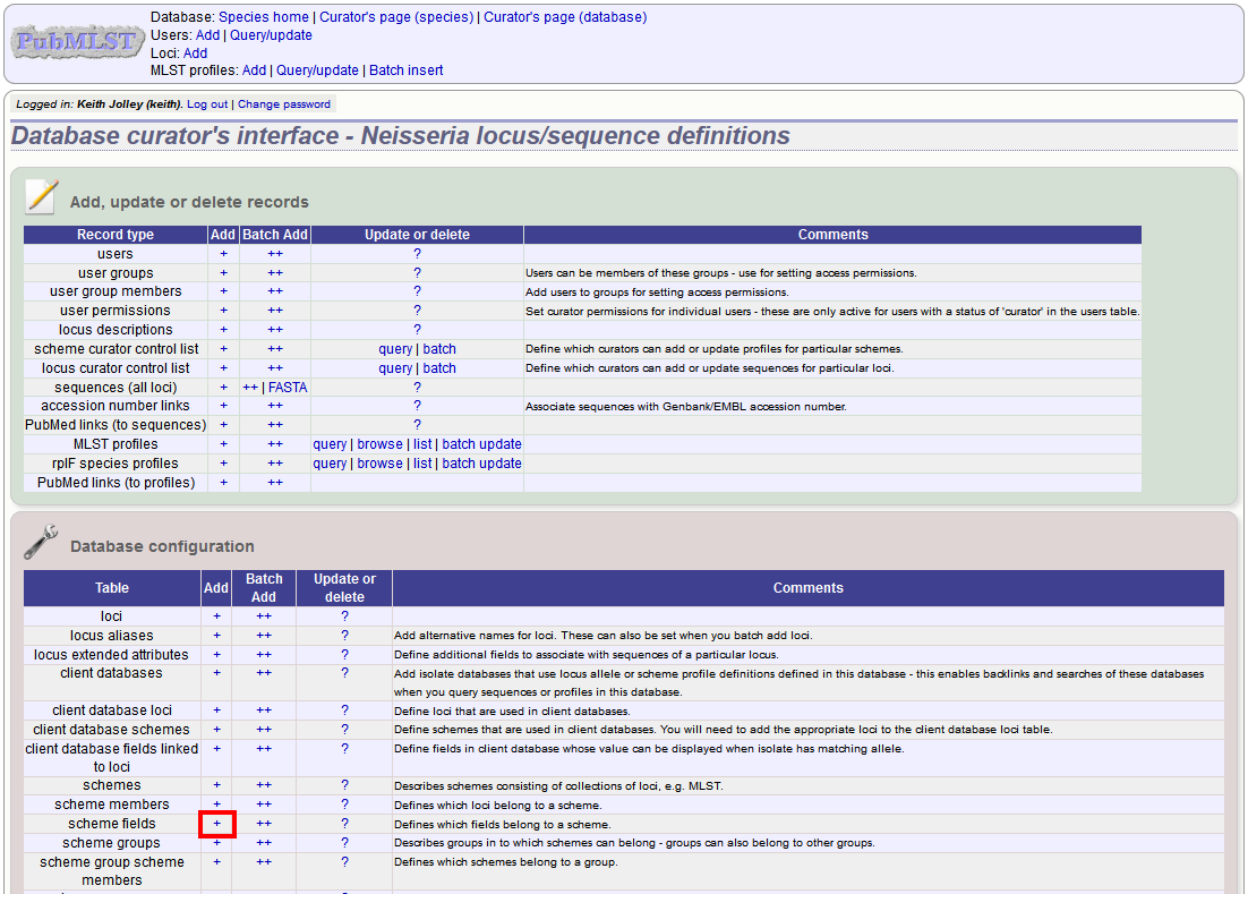
To add loci to the scheme, click the add (+) scheme members link on the curator's interface contents page.



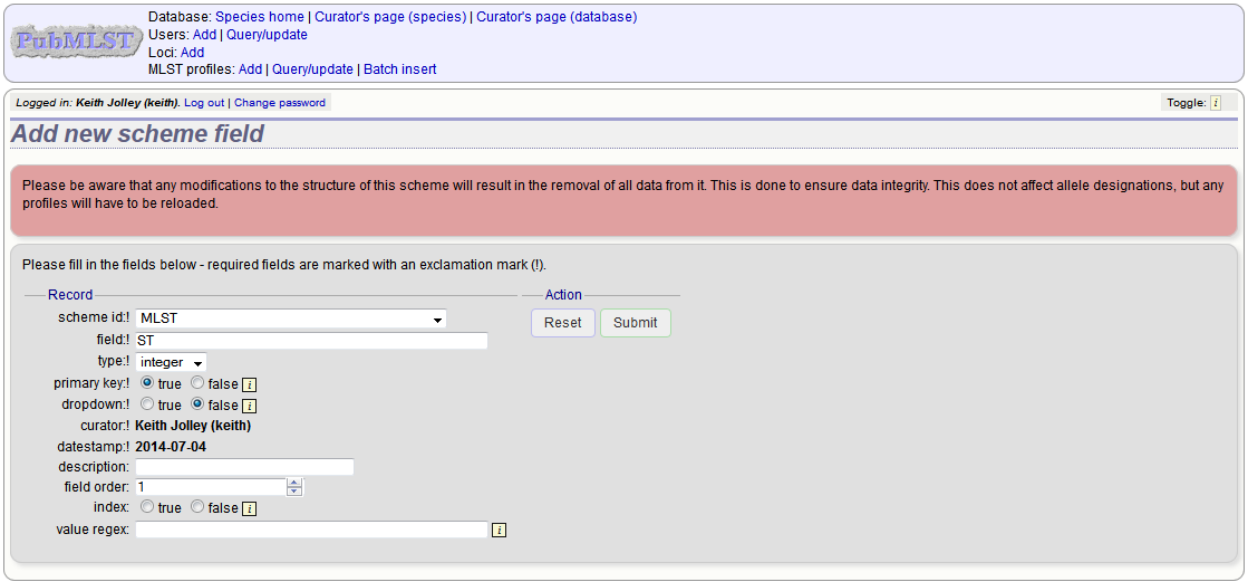
Select the scheme name and a locus that you wish to add to the scheme from the appropriate drop-down boxes. *Loci need to have already been defined*. The field_order field allows you to set the display order of the locus within a profile - if these are left blank that alphabetical ordering is used.



To add scheme fields, click the add (+) scheme fields link on the curator's interface contents page.



Fill in the web form with appropriate values. Required fields have an exclamation mark (!) next to them:



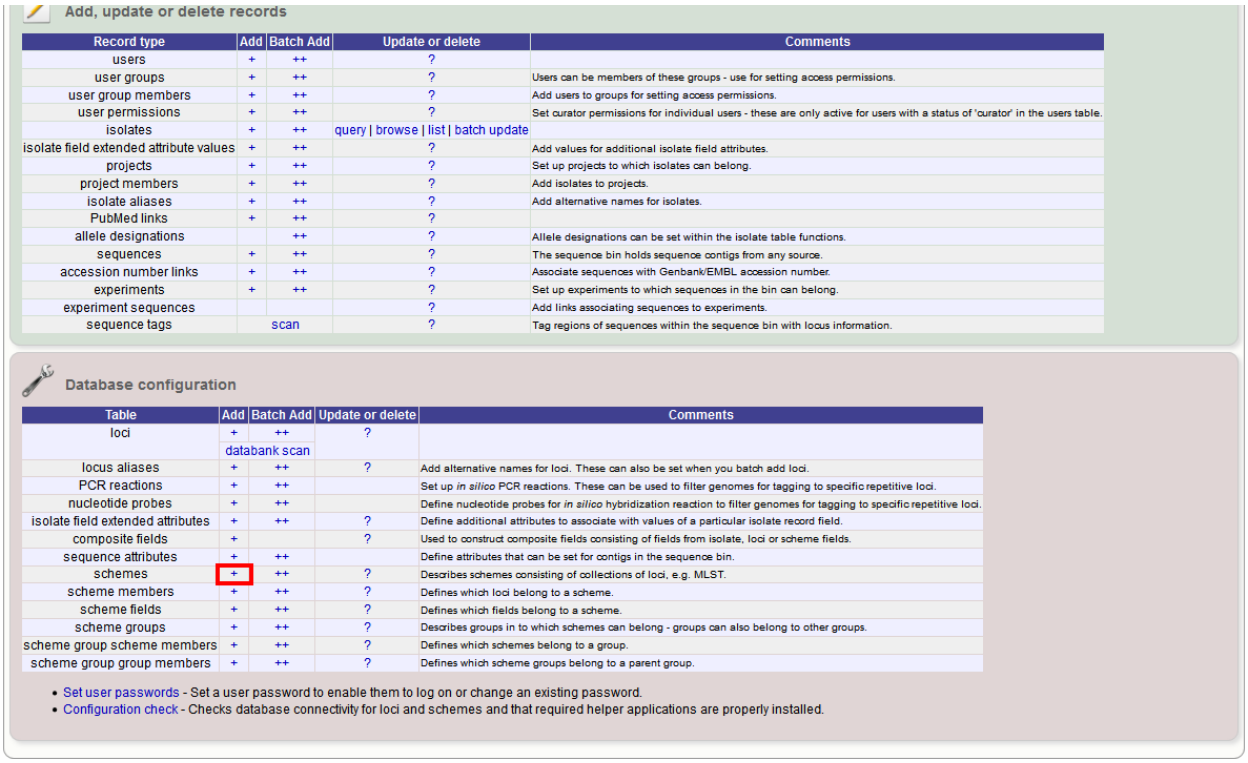
- scheme_id - Dropdown box of scheme names.
  - Allowed: selection from list.
- field - Field name.

  - Allowed: any value.
- type - Format for values.
  - Allowed: text/integer/date.
- primary_key - Set to true if field is the primary key. There can only be one primary key for a scheme.
  - Allowed: true/false.
- dropdown - Set to true if a dropdown box is displayed in the query interface, by default, for values of this field to be quickly selected. This option can be overridden by user preferences.
  - Allowed: true/false.
- description - This field isn't currently used.
- field_order - Integer that sets the position of the field within scheme values in any results.
  - Allowed: any integer.
- value_regex - Regular expression to enforce field values.
  - ^: the beginning of the string
  - $:the end of the string
  - d: digit
  - D: non-digit
  - s: white space character
  - S: non white space character
  - w: alpha-numeric plus '_'
  - .: any character
  - *: 0 or more of previous character
  - +: 1 or more of previous character

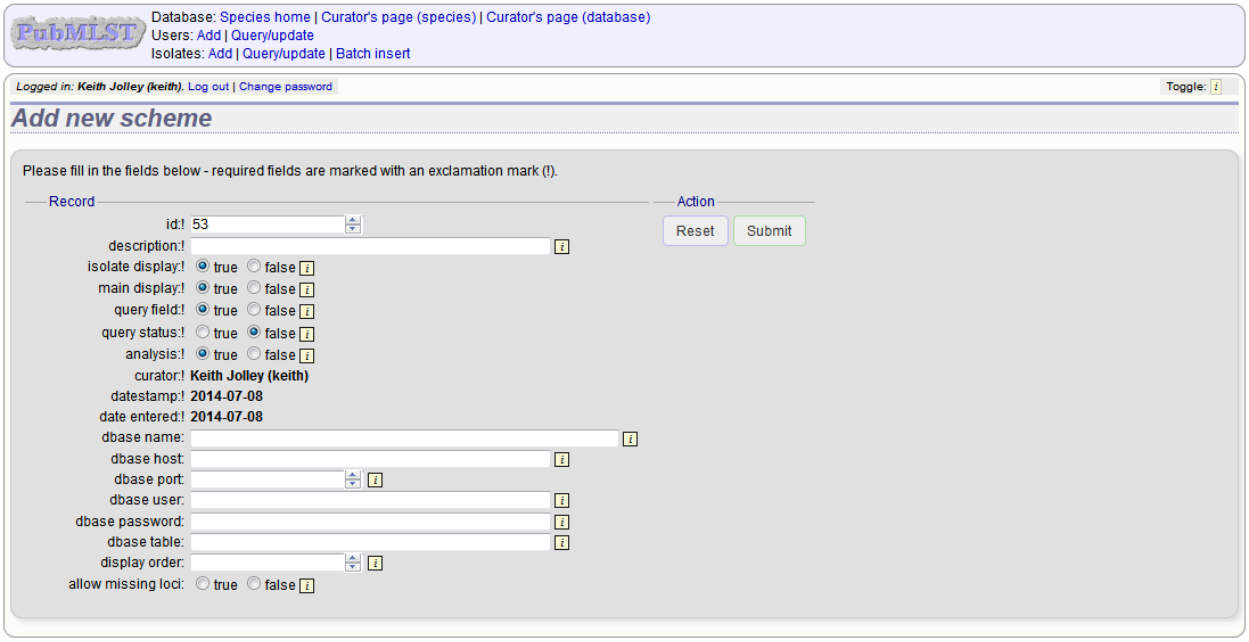
5.14.2 Isolate databases

As with all configuration, tables can be populated using the batch interface (++) or one at a time (+). Details for the latter are described below:

Click the add (+) scheme link on the curator's interface contents page.



Fill in the scheme description in the web form. Required fields have an exclamation mark (!) next to them:



- id - Index number of scheme - the next available number will be entered automatically.
  - Allowed: any positive integer.
- description - Short description - this is used in tables so make sure it's not too long.
  - Allowed: any text.
- isolate_display - Sets whether or not fields for this scheme are displayed in a detailed isolate record - this can be

overridden by user preference.

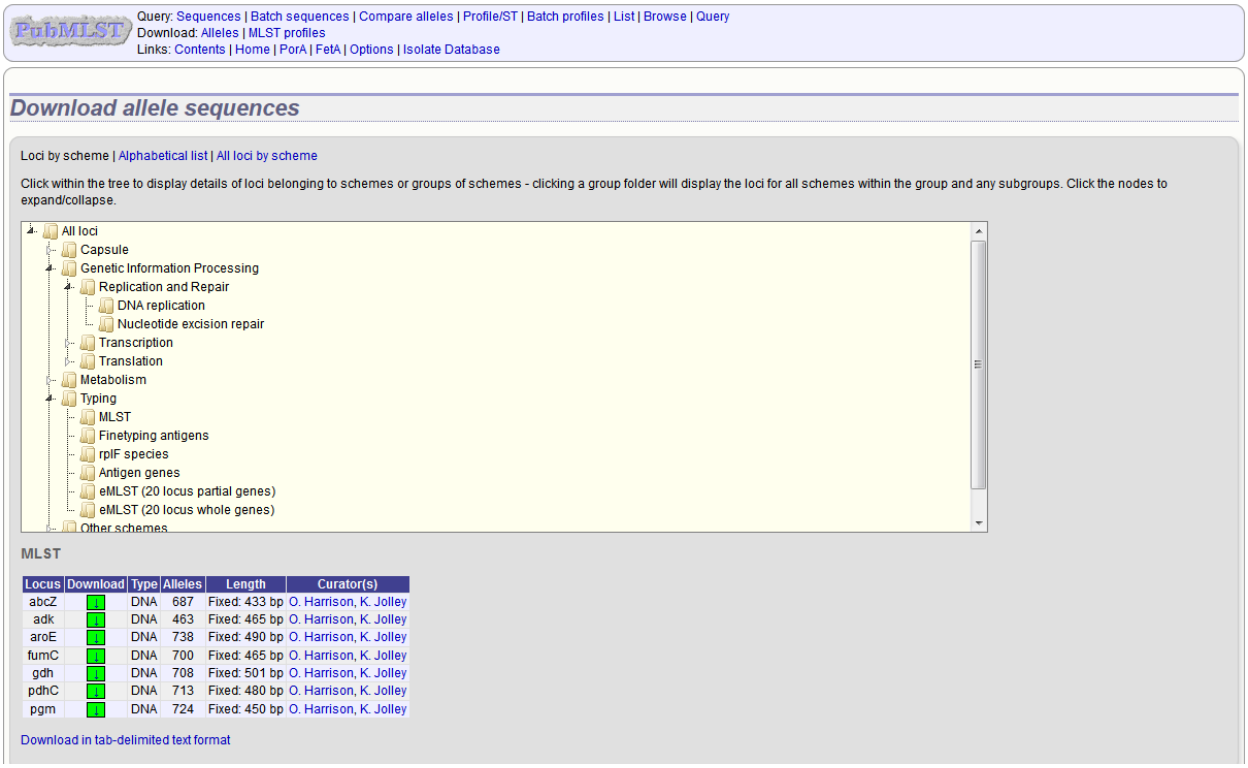
  - Allowed: allele only/sequence/hide.

- main_display - Sets whether or not fields for this scheme are displayed in a main results table by default - this can be overridden by user preference.
  - Allowed: true/false.
- query_field - Sets whether or not fields for this scheme can be used in queries by default - this can be overridden by user preference.
  - Allowed: true/false.
- query_status - Sets whether a dropdown list box should be displayed in the query interface to filter results based on profile completion for this scheme - this can be overridden by user preference.
  - Allowed: true/false.
- analysis - Sets whether or not alleles for this locus can be used in analysis functions by default - this can be overridden by user preference.
  - Allowed: true/false.
- dbase_name - Name of seqdef database (system name) containing scheme profiles (optional).
  - Allowed: any text.
- dbase_host - Resolved name of IP address of database host - leave blank if running on the same machine as the isolate database (optional).
  - Allowed: network address, e.g. 129.67.26.52 or zoo-oban.zoo.ox.ac.uk
- dbase_port - Network port on which the sequence definition database server is listening - leave blank unless using a non-standard port, 5432 (optional).
  - Allowed: integer.
- dbase_user - Name of user with permission to access the sequence definition database - depending on the database configuration you may be able to leave this blank (optional).
  - Allowed: any text (no spaces).
- dbase_password - Password of database user - again depending on the database configuration you may be able to leave this blank (optional).
  - Allowed: any text (no spaces).
- dbase_table - Table in the sequence definition database that contains profiles for this scheme. If the definition database uses BIGSdb this will be 'scheme_X' where X is the scheme id number in the seqdef database.
  - Allowed: any text (no spaces).
- display_order - Integer reflecting the display position for this scheme within the interface (optional).
  - Allowed: any integer.
- allow_missing_loci - Allow profile definitions to contain '0' (locus missing) or 'N' (any allele).

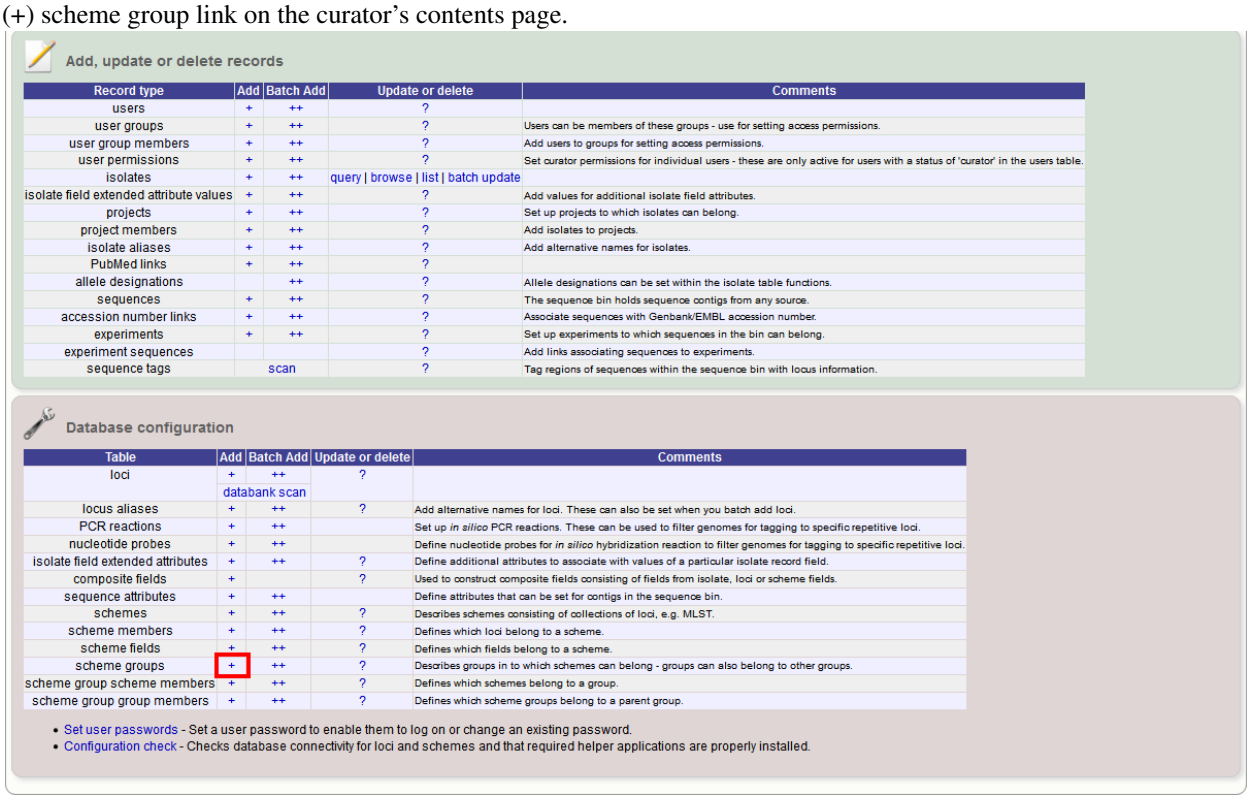
5.15 Organizing schemes into hierarchical groups

Schemes can be organized in to groups, and these groups can in turn be members of other groups. This faciliates hierarchical ordering of loci, but with the flexibility to allow loci and schemes to belong to multiple groups.

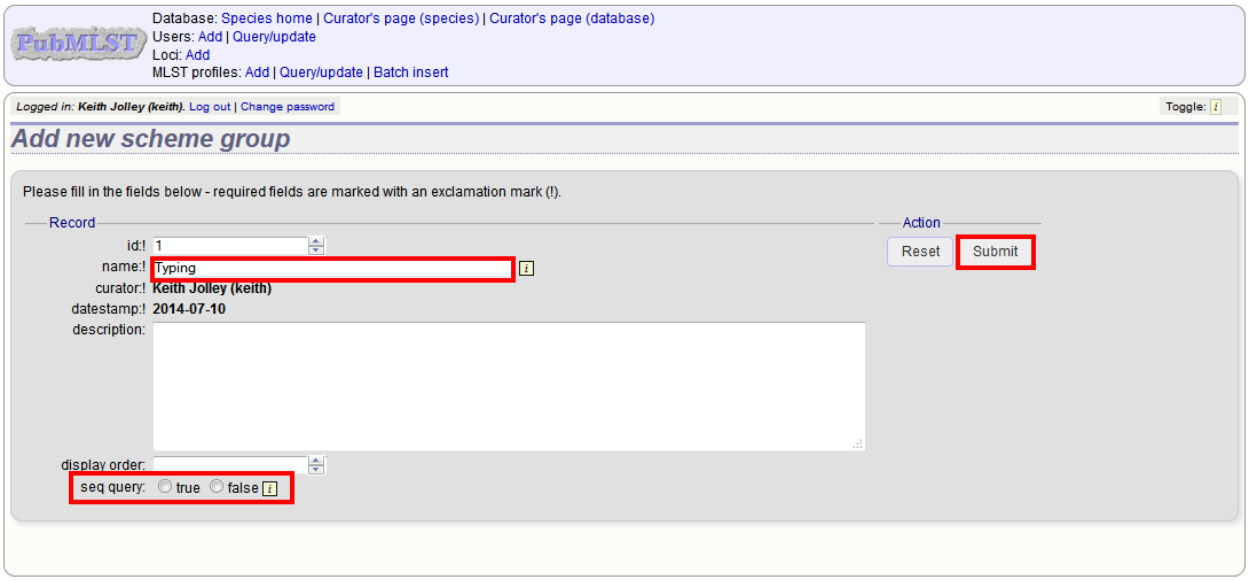
This hierarchical structuring can be seen in various places within BIGSdb, for example the *allele download* page.



Scheme groups can be added in both the sequence definition and isolate databases. To add a new group, click the add (+) scheme group link on the curator's contents page.



Enter a short name for the group - this will appear within drop-down list boxes and the hierarchical tree, so it needs to be fairly short.



If you are creating a scheme group in the sequence definition database, there is an additional field called 'seq_query'. Set this to true to add the scheme group to the dropdown lists in the *sequence query* page. This enables all loci belonging to schemes within the group to be queried together.

Schemes can be added to groups by clicking the add (+) scheme group scheme members link.

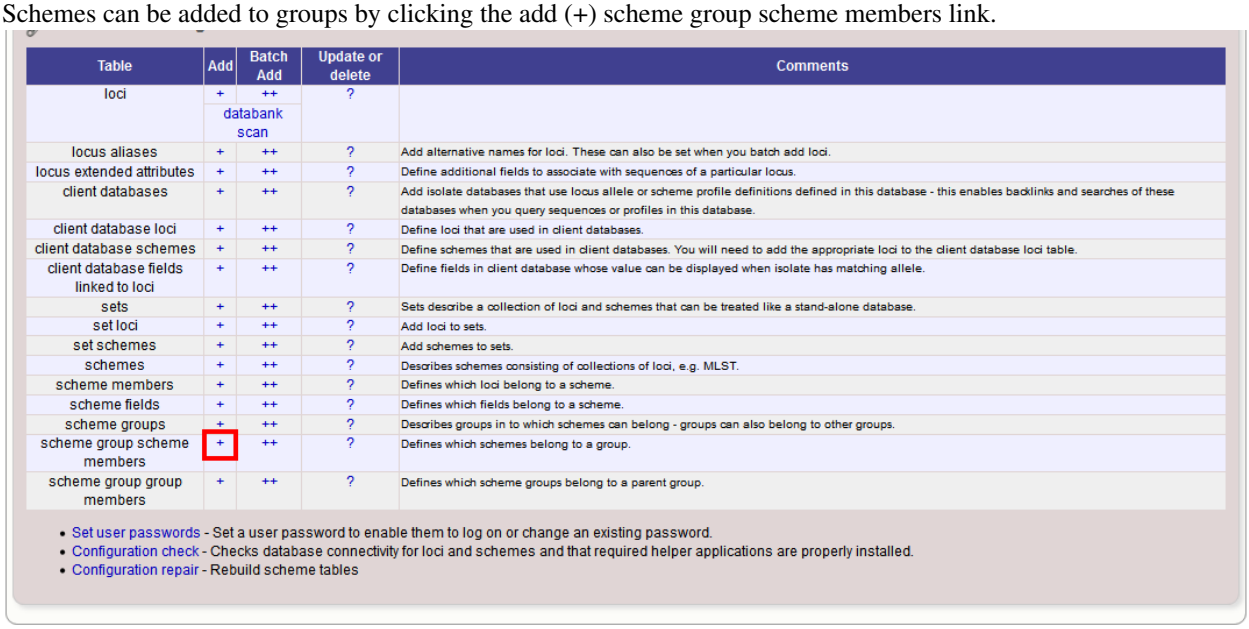
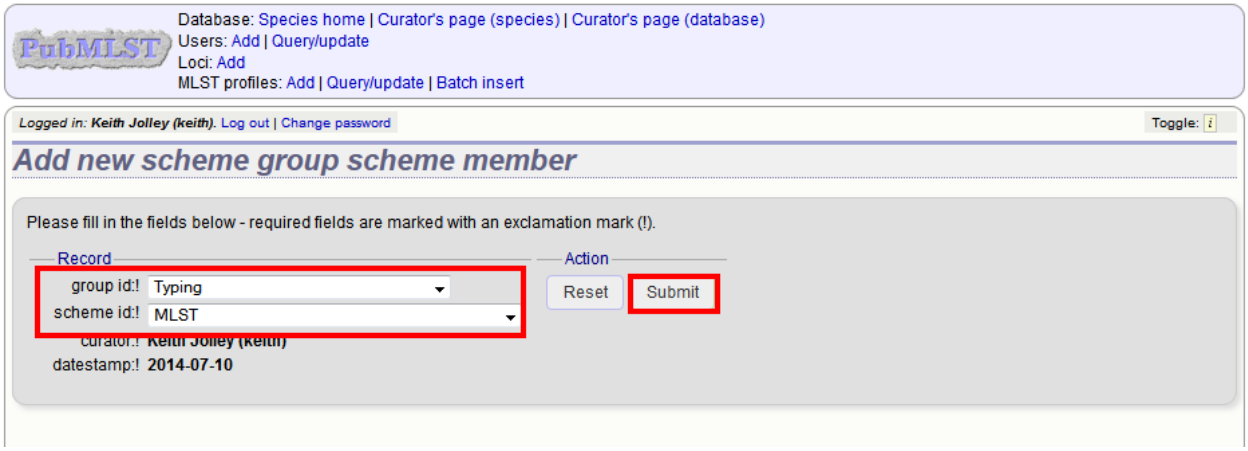


Table	Add	Batch Add	Update or delete	Comments
loci	+	++	?	
	databank scan			
locus aliases	+	++	?	Add alternative names for loci. These can also be set when you batch add loci.
locus extended attributes	+	++	?	Define additional fields to associate with sequences of a particular locus.
client databases	+	++	?	Add isolate databases that use locus allele or scheme profile definitions defined in this database - this enables backlinks and searches of these databases when you query sequences or profiles in this database.
client database loci	+	++	?	Define loci that are used in client databases.
client database schemes	+	++	?	Define schemes that are used in client databases. You will need to add the appropriate loci to the client database loci table.
client database fields linked to loci	+	++	?	Define fields in client database whose value can be displayed when isolate has matching allele.
sets	+	++	?	Sets describe a collection of loci and schemes that can be treated like a stand-alone database.
set loci	+	++	?	Add loci to sets.
set schemes	+	++	?	Add schemes to sets.
schemes	+	++	?	Describes schemes consisting of collections of loci, e.g. MLST.
scheme members	+	++	?	Defines which loci belong to a scheme.
scheme fields	+	++	?	Defines which fields belong to a scheme.
scheme groups	+	++	?	Describes groups in to which schemes can belong - groups can also belong to other groups.
scheme group scheme members	+	++	?	Defines which schemes belong to a group.
scheme group group members	+	++	?	Defines which scheme groups belong to a parent group.

- Set user passwords - Set a user password to enable them to log on or change an existing password.
- Configuration check - Checks database connectivity for loci and schemes and that required helper applications are properly installed.
- Configuration repair - Rebuild scheme tables

Select the scheme and the group to add it to, then click 'Submit'.



Scheme groups can be added to other scheme groups in the same way by clicking the add (+) scheme group group members link.

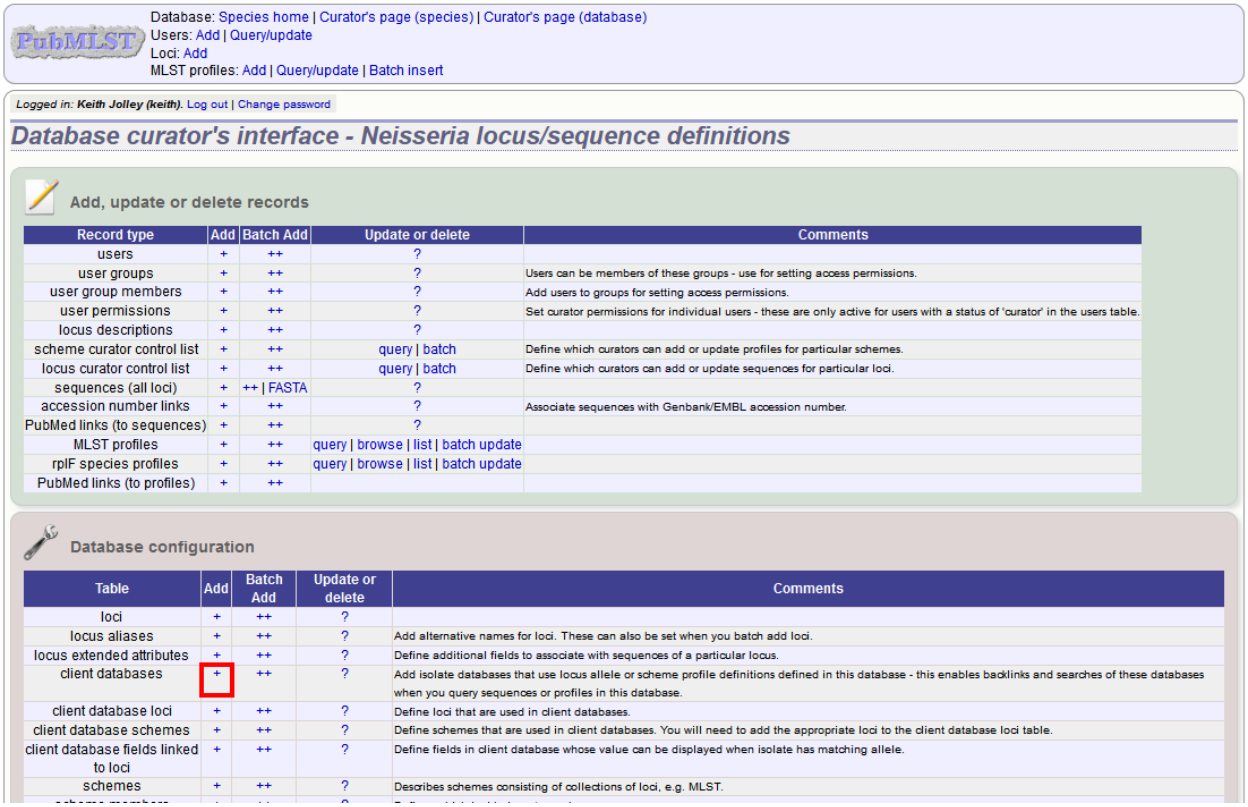
5.16 Setting up client databases

Sequence definition databases can have any number of isolate databases that connect as clients. Registering these databases allows the software to perform isolate data searches relevant to results returned by the sequence definition database, for example:

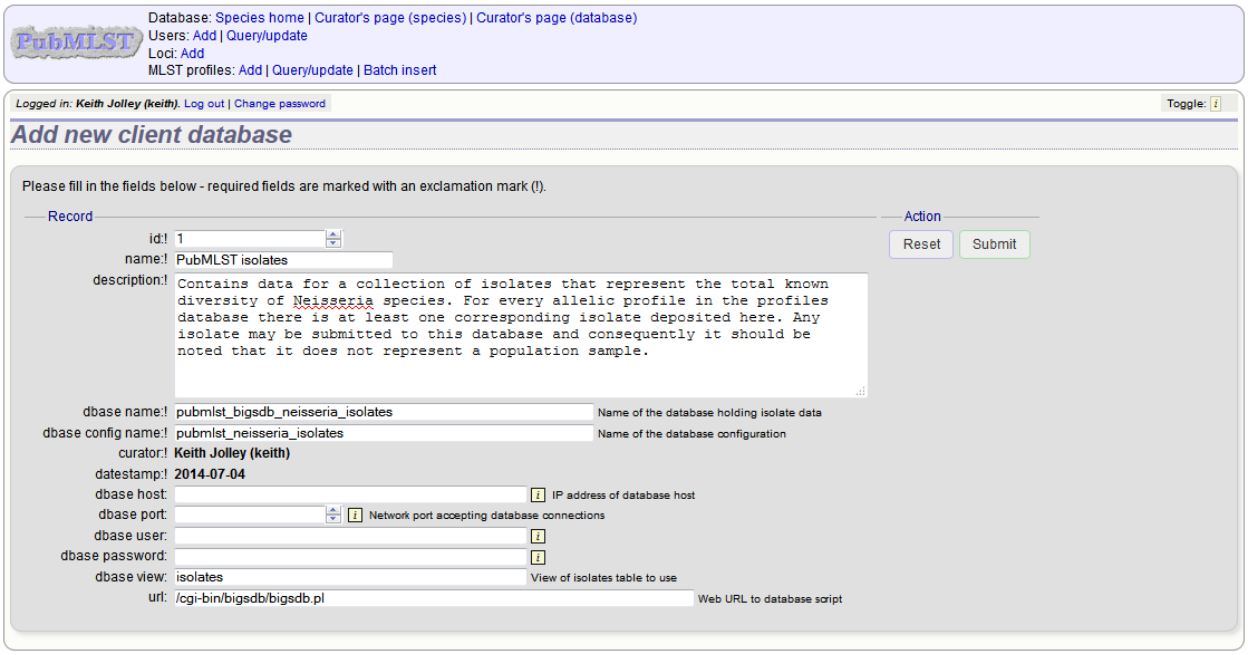
- Determine the number of isolates that a given allele is found in and link to these.
- Determine the number of isolates that a given scheme field, e.g. a sequence type, is found in and link to these.
- Retrieve specific attributes of isolates that have a given allele, e.g. species that have a particular 16S allele, or penicillin resistance given a particular penA allele.

Multiple client databases can be queried simultaneously.

To register a client isolate database for a sequence definition database, click the add (+) client database link on the curator's interface contents page.



Fill in the web form with appropriate values. Required fields have an exclamation mark (!) next to them:

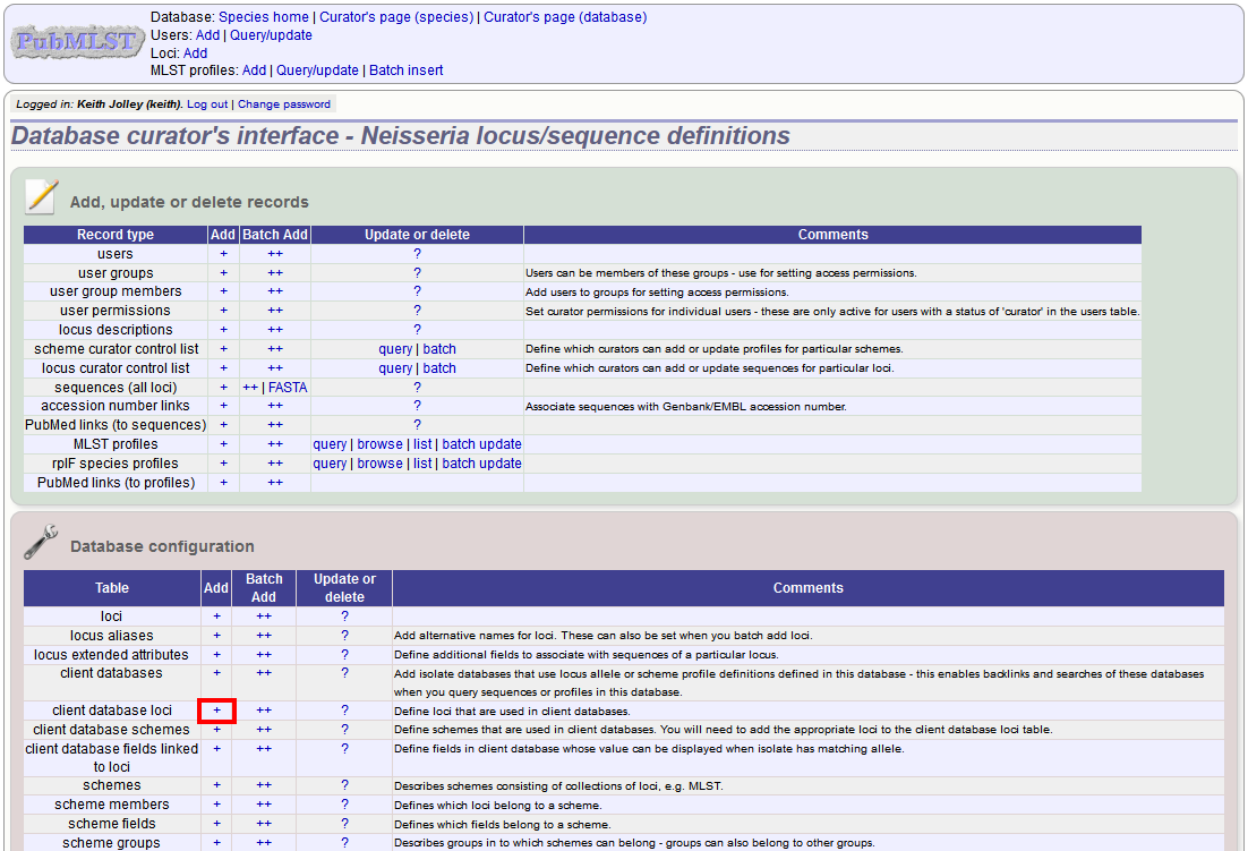


- id - Index number of client database. The next available number is entered automatically but can be overridden.
  - Allowed: any positive integer.
- name - Short description of database. This is used within the interface result tables so it is better to make it as short as possible.

  - Allowed: any text.
- description - Longer description of database.
  - Allowed: any text.
- dbase_name - Name of database (system name).
  - Allowed: any text.
- dbase_config_name - Name of database configuration - this is the text string that appears after the db= part of script URLs.
  - Allowed: any text (no spaces)
- dbase_host - Resolved name of IP address of database host (optional).
  - Allowed: Network address, e.g. 129.67.26.52 or zoo-oban.zoo.ox.ac.uk
  - Leave blank if running on the same machine as the seqdef database.
- dbase_port - Network port on which the client database server is listening (optional)
  - Allowed: integer.
  - Leave blank unless using a non-standard port (5432).
- dbase_user - Name of user with permission to access the client database
  - Allowed: any text (no spaces).
  - Depending on the database configuration you may be able to leave this blank.
- dbase_password - Password of database user
  - Allowed: any text (no spaces).
  - Depending on the database configuration you may be able to leave this blank.
- url - URL of client database bigsdb.pl script
  - Allowed: valid script path.
  - This can be relative (e.g. /cgi-bin/bigsdb/bigsdb.pl) if running on the same machine as the seqdef database or absolute (including http://) if on a different machine.

5.16.1 Look up isolates with given allele

To link a locus, click the add (+) client database loci link on the curator's interface contents page.



Link the locus to the appropriate client database using the dropdown list boxes. If the locus is named differently in the client database, fill this name in the locus_alias.

Now when information on a given allele is shown following a query, the software will list the number of isolates with that allele and link to a search on the database to retrieve these.

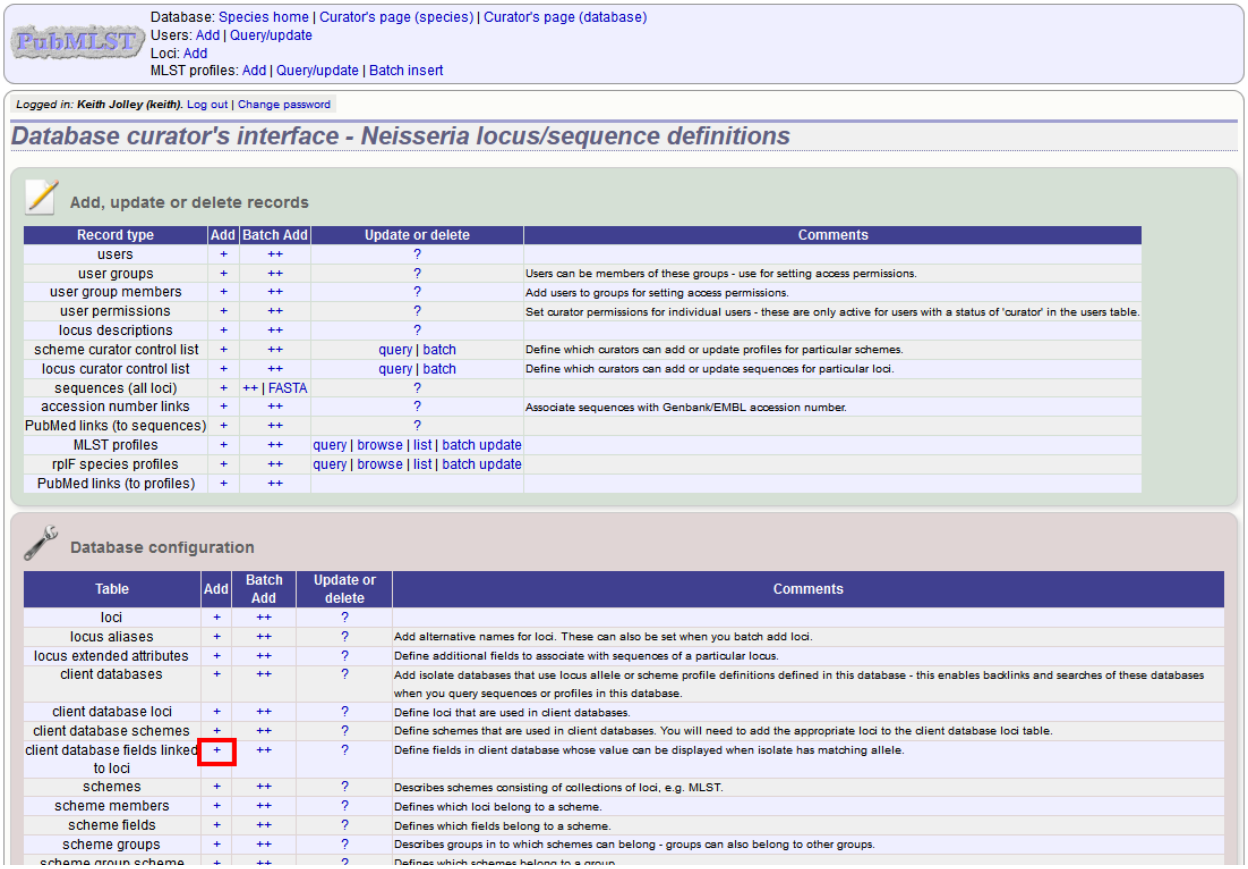
5.16.2 Look up isolates with a given scheme primary key

Setting this up is identical to setting up for alleles (see above) except you click on the add (+) client database schemes link and choose the scheme and client databases in the dropdown list boxes.

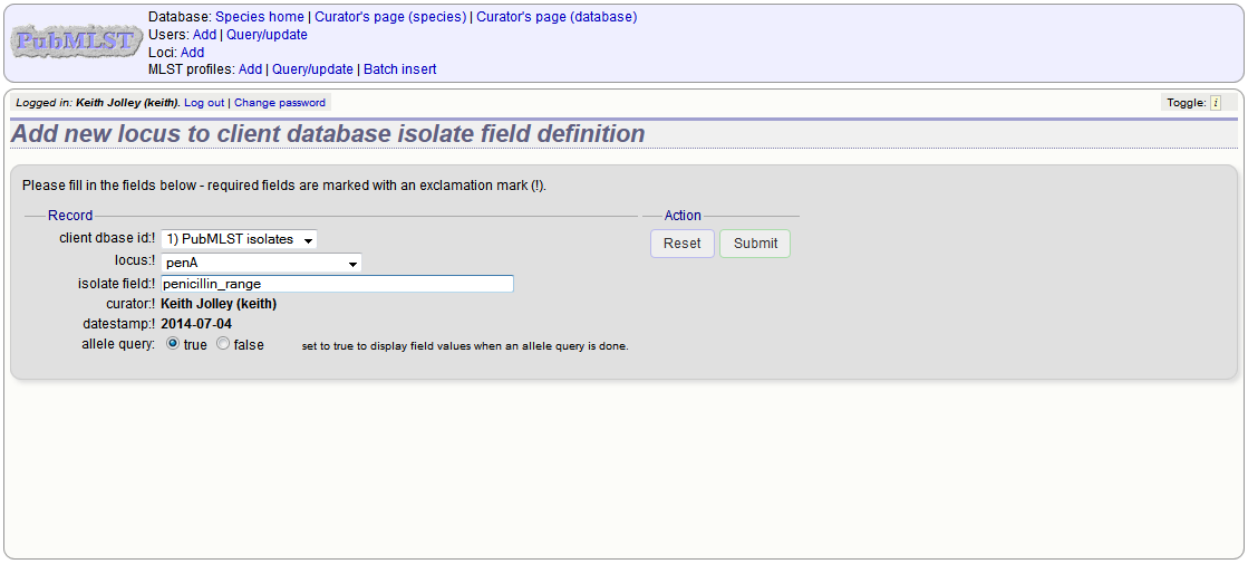
Now when information on a given scheme profile (e.g. MLST sequence type) is shown following a query, the software will list the number of isolates with that profile and link to a search on the database to retrieve these.

5.16.3 Look up specific isolate database fields linked to a given allele

To link an allele to an isolate field, click the add (+) 'client database fields linked to loci' link on the curator's interface contents page.

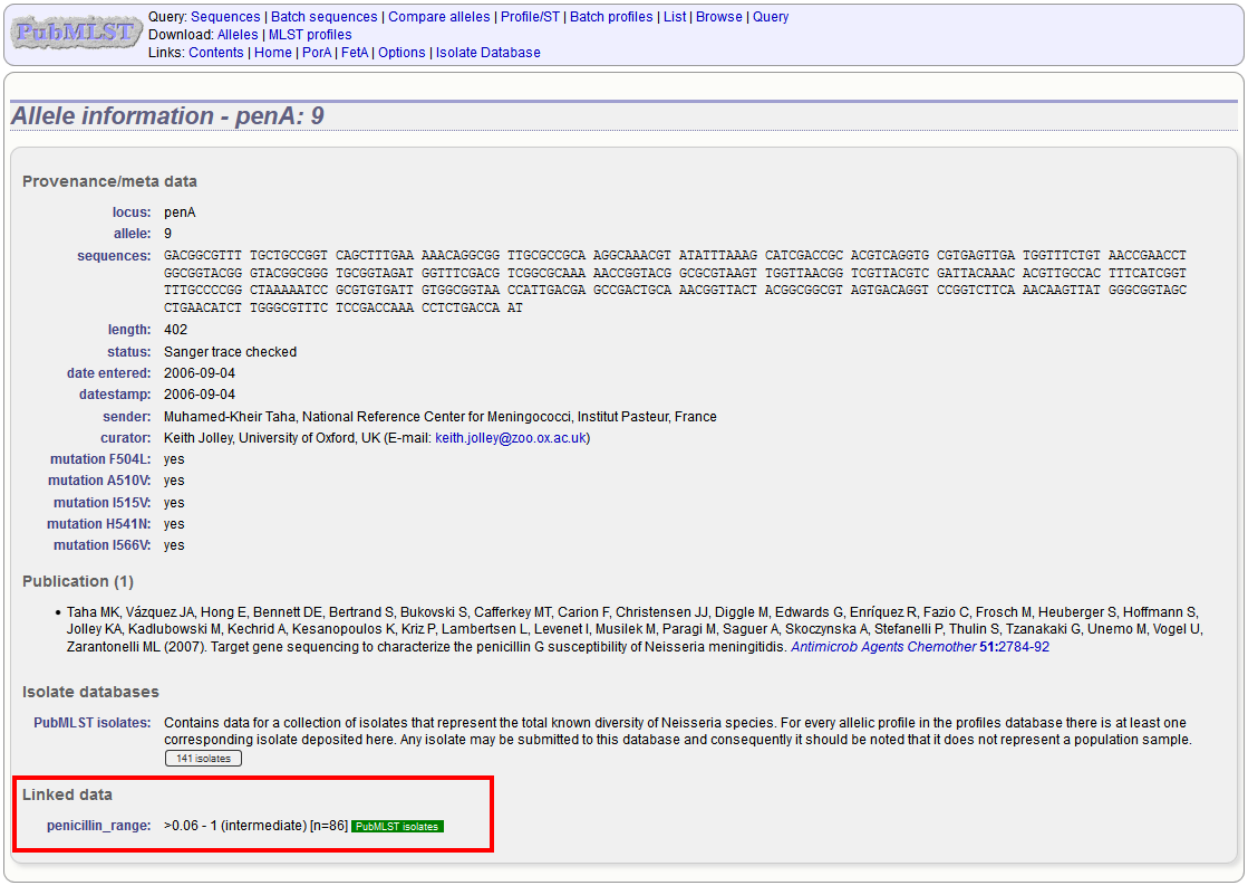


Select the client database and locus from the dropdown lists and enter the isolate database field that you'd like to link. The 'allele_query' field should be set to true.



Now, in the allele record or following a sequence query that identifies an allele, all values for the chosen field from

isolates with the corresponding allele are shown.



5.17 Rule-based sequence queries

The RuleQuery plugin has been designed to extract information from a pasted-in genome sequence, look up scheme fields and client database fields, and then format the output in a specified manner.

Rules are written in Perl, allowing the full power of this scripting language to be utilised. Helper functions that perform specific actions are available to the script (see example).

Please note that direct access to the database is prevented as are system calls.

5.17.1 Example rule code

An example can be found on the Neisseria sequence database that takes a genome sequence and determines a fine type and antibiotic resistance.

The code for this rule is as follows:

```
#Clinical identification rule

#Update job viewer status
update_status({stage=>'Scanning MLST loci'});

#Scan genome against all scheme 1 (MLST) loci
```

```
scan_scheme(1);

#Update job viewer status
update_status({percent_complete=>30, stage=>'Scanning PorA and FetA VRs'});

#Scan genome against the PorA VR and FetA VR loci
scan_locus($_) foreach qw(PorA_VR1 PorA_VR2 FetA_VR);

Add text to main output
append_html("<h1>Strain type</h1>");

#Set variables for the scanned results.  These can be found in the
#$results->{'locus'} hashref
my %alleles;
$alleles{$_} = $results->{'locus'}->{$_} // 'ND' foreach qw(PorA_VR1 PorA_VR2);
$alleles{'FetA_VR'} = $results->{'locus'}->{'FetA_VR'} // 'F-ND';

#Scheme field values are automatically determined if a complete
#profile is available.  These are stored in the $results->{'scheme'} hashref
my $st = $results->{'scheme'}->{1}->{'ST'} // 'ND';
append_html("<ul><li>P1.$alleles{'PorA_VR1'}, $alleles{'PorA_VR2'}; $alleles{'FetA_VR'}; ST-$st ");

#Reformat clonal complex using a regular expression, e.g.
#'ST-11 clonal complex/ET-37 complex' gets rewritten to 'cc11'
my $cc =  $results->{'scheme'}->{1}->{'clonal_complex'} // '-';
$cc =~ s/ST-(\S+) complex.*/cc$1/;

append_html("($cc)</li></ul>");
if ($st eq 'ND'){
  append_html("<p>ST not defined.  If individual MLST loci have been found "
  . "they will be displayed below:</p>");

  #The get_scheme_html function automatically formats output for a scheme.
  #Select whether to display in a table rather than a list, list all loci, and/or list fields.
  append_html(get_scheme_html(1, {table=>1, loci=>1, fields=>0}));
}

#Antibiotic resistance
update_status({percent_complete=>80, stage=>'Scanning penA and rpoB'});
scan_locus($_) foreach qw(penA rpoB);
if (defined $results->{'locus'}->{'penA'} || defined $results->{'locus'}->{'rpoB'} ){
  append_html("<h1>Antibiotic resistance</h1><ul>");
  if (defined $results->{'locus'}->{'penA'}){
    append_html("<li><i>penA</i> allele: $results->{'locus'}->{'penA'}");

    #If a client isolate database has been defined and values have been defined in
    #the client_dbase_loci_fields table, the values for a field in the isolate database can be
    #retrieved based on isolates that have a particular allele designated.
    #The min_percentage attribute states that only values that are represented by at least that
    #proportion of all isolates that had a value set are returned (null values are ignored).
    my $range = get_client_field(1,'penA','penicillin_range',{min_percentage => 75});
    append_html(" (penicillin MIC: $range->[0]->{'penicillin_range'})") if @$range;
    append_html("</li>");
  }
  if (defined $results->{'locus'}->{'rpoB'}){
    append_html("<li><i>rpoB</i> allele: $results->{'locus'}->{'rpoB'}");
    my $range = get_client_field(1,'rpoB','rifampicin_range',{min_percentage => 75});
    append_html(" (rifampicin MIC: $range->[0]->{'rifampicin_range'})") if @$range;
```

```
    append_html("</li>");
  }
  append_html("</ul>");
}
```

Rule files

The rule file is placed in a rules directory within the database configuration directory, e.g. /etc/bigsdb/dbase/pubmlst_neisseri_seqdef/rules. Rule files are suffixed with '.rule' and their name should be descriptive since it is used within the interface, i.e. the above rule file is named Clinical_identification.rule (underscores are converted to spaces in the web interface).

Linking to the rule query

Links to the rule query are not automatically placed within the web interface. The above rule query can be called using the following URL:

http://pubmlst.org/perl/bigsdb/bigsdb.pl?db=pubmlst_neisseria_seqdef&page=plugin&name=RuleQuery&ruleset=Clinical_identificatio

To place a link to this within the database contents page an HTML file called job_query.html can be placed in a contents directory within the database configuration directory, e.g. in /etc/bigsdb/dbases/pubmlst_neisseria_seqdef/contents/job_query.html. This file should contain a list entry (i.e. surrounded with <li> and tags) that will appear in the 'Query database' section of the contents page.

Adding descriptive text

Descriptive text for the rule, which will appear on the rule query page, can be placed in a file called description.html in a directory with the same name as the rule within the rule directory, e.g. in /etc/bigsdb/dbases/pubmlst_neisseria_seqdef/rules/Clinical_identification/description.html.

5.18 Workflow for setting up a MLST scheme

The workflow for setting up a MLST scheme is as follows (the example seqdef database is called seqdef_db):

Seqdef database

1. Create appropriate loci
2. Create new scheme 'MLST'
3. Add scheme_field 'ST' with primary_key=TRUE (add clonal_complex if you want; set this with primary_key=FALSE)
4. Add each locus as a scheme_member
5. You'll then be able to add profiles

Isolate database

1. Create the same loci with the following additional parameters (example locus 'atpD')

- dbase_name: seqdef_db
- dbase_table: sequences
- dbase_id_field: allele_id

- dbase_id2_field: locus
- dbase_id_value: atpD
- dbase_seq_field: sequence
- url: something like /cgi-bin/bigsdb/bigsdb.pl?db=seqdef_db&page=alleleInfo&locus=atpD&allele_id=[?]

2. Create scheme 'MLST' with:

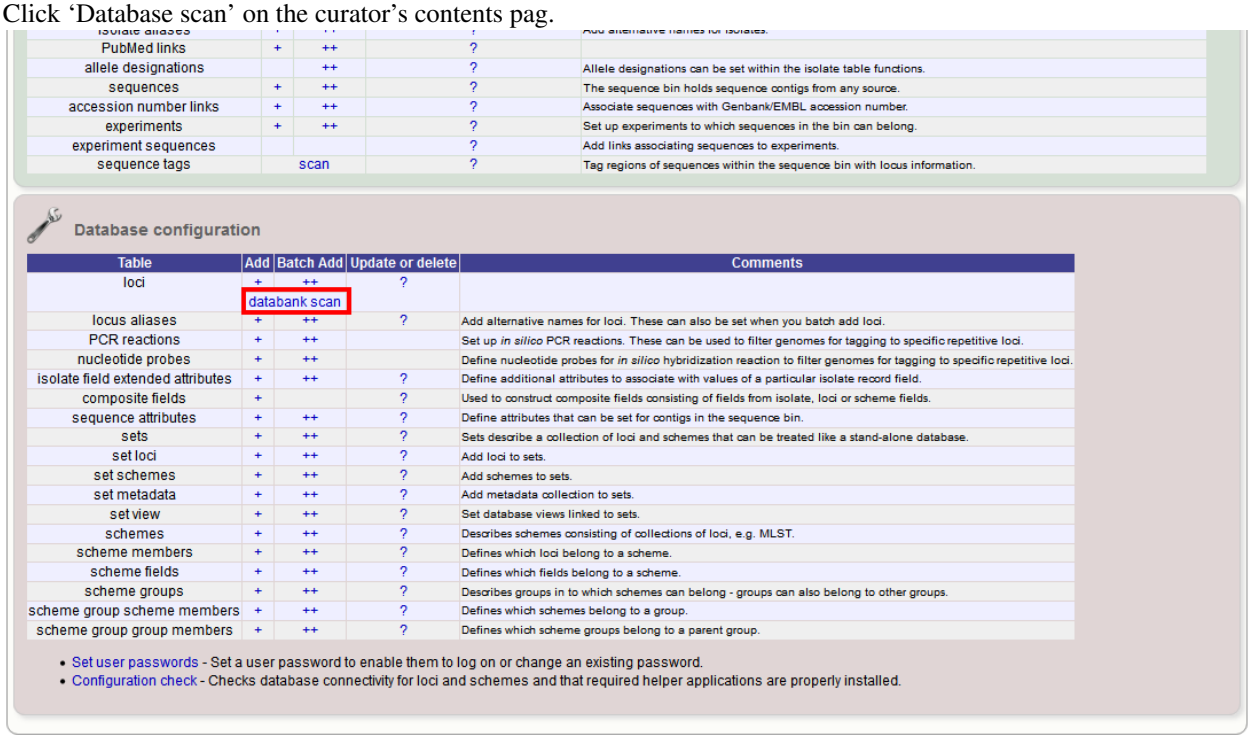
- dbase_name: seqdef_db
- dbase_table: scheme_1 (or whatever the id of your seqdef scheme is)

3. Add scheme_field ST as before
4. Add loci as scheme_members

5.19 Defining new loci based on annotated reference genome

An annotated reference genome can be used as the basis of defining loci. The 'Databank scan' function will create an upload table suitable for pasting directly in to the batch locus add form of the *sequence definition* or *isolate* databases.

Click 'Database scan' on the curator's contents pag.



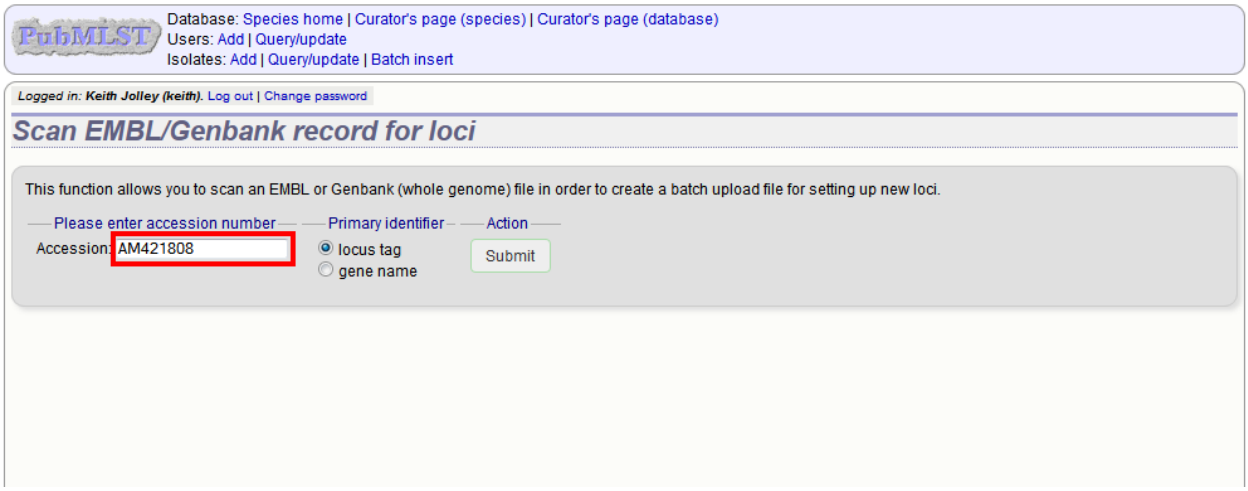
PubMed links	+	++	?	
allele designations		++	?	Allele designations can be set within the isolate table functions.
sequences	+	++	?	The sequence bin holds sequence contigs from any source.
accession number links	+	++	?	Associate sequences with Genbank/EMBL accession number.
experiments	+	++	?	Set up experiments to which sequences in the bin can belong.
experiment sequences			?	Add links associating sequences to experiments.
sequence tags		scan	?	Tag regions of sequences within the sequence bin with locus information.

Database configuration

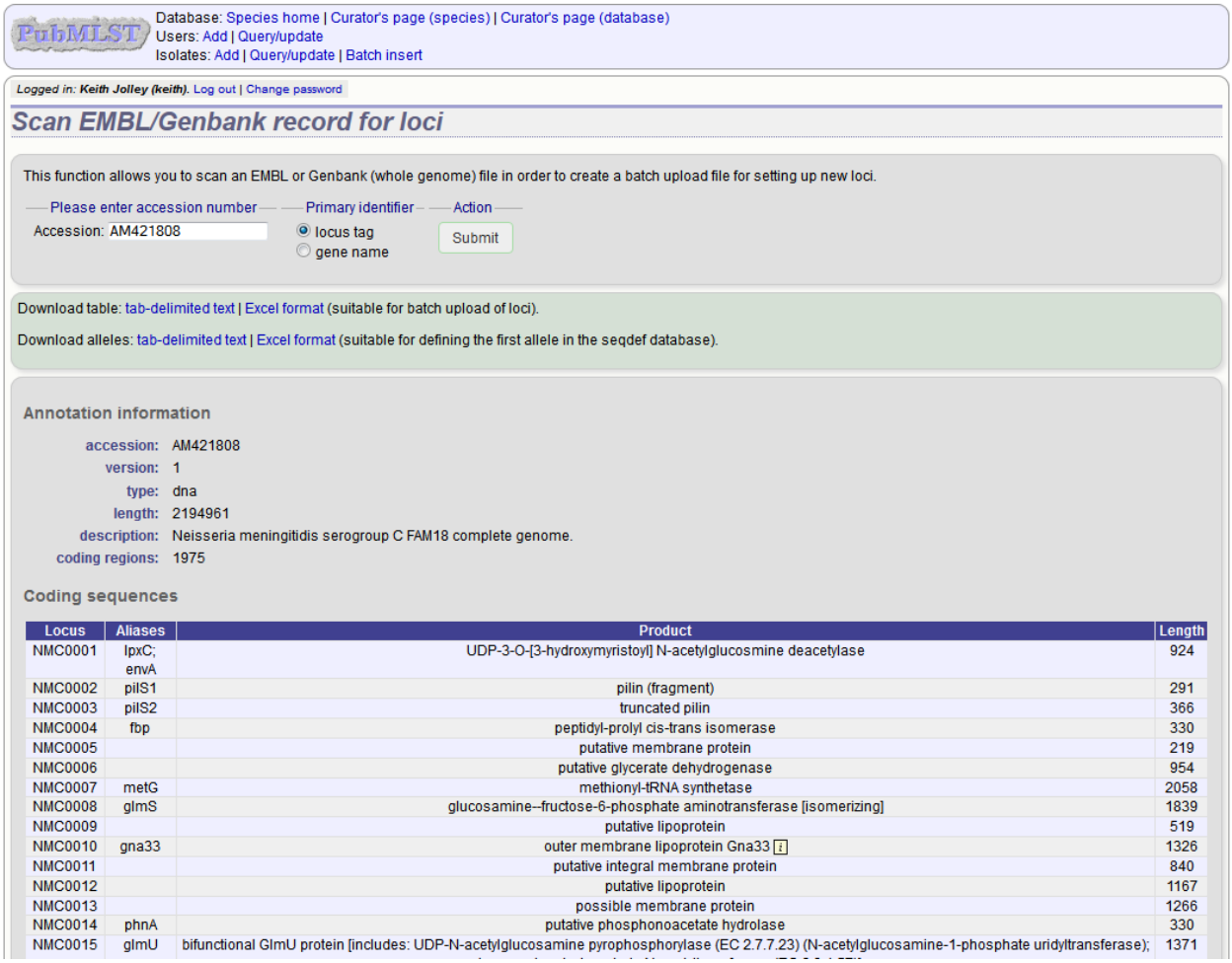
Table	Add	Batch Add	Update or delete	Comments
loci	+	++	?	
	databank scan			
locus aliases	+	++	?	Add alternative names for loci. These can also be set when you batch add loci.
PCR reactions	+	++		Set up *in silico* PCR reactions. These can be used to filter genomes for tagging to specific repetitive loci.
nucleotide probes	+	++		Define nucleotide probes for *in silico* hybridization reaction to filter genomes for tagging to specific repetitive loci.
isolate field extended attributes	+	++	?	Define additional attributes to associate with values of a particular isolate record field.
composite fields	+		?	Used to construct composite fields consisting of fields from isolate, loci or scheme fields.
sequence attributes	+	++	?	Define attributes that can be set for contigs in the sequence bin.
sets	+	++	?	Sets describe a collection of loci and schemes that can be treated like a stand-alone database.
set loci	+	++	?	Add loci to sets.
set schemes	+	++	?	Add schemes to sets.
set metadata	+	++	?	Add metadata collection to sets.
set view	+	++	?	Set database views linked to sets.
schemes	+	++	?	Describes schemes consisting of collections of loci, e.g. MLST.
scheme members	+	++	?	Defines which loci belong to a scheme.
scheme fields	+	++	?	Defines which fields belong to a scheme.
scheme groups	+	++	?	Describes groups in to which schemes can belong - groups can also belong to other groups.
scheme group scheme members	+	++	?	Defines which schemes belong to a group.
scheme group group members	+	++	?	Defines which scheme groups belong to a parent group.

- Set user passwords - Set a user password to enable them to log on or change an existing password.
- Configuration check - Checks database connectivity for loci and schemes and that required helper applications are properly installed.

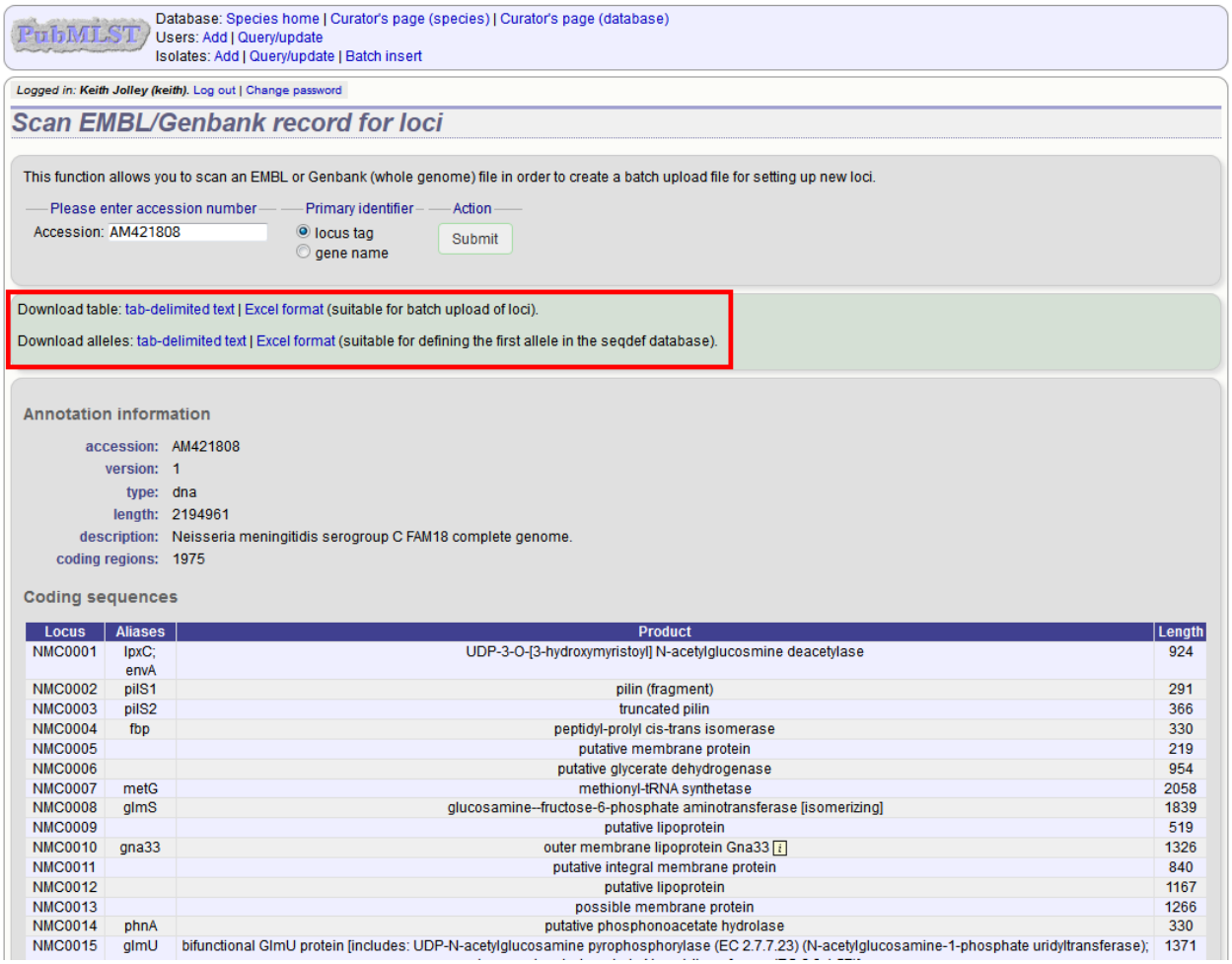
Enter an EMBL or Genbank accession number for a complete annotated genome and press 'Submit'.



A table of loci will be generated provided a valid accession number is provided.



Tab-delimited text and Excel format files will be created to be used as the basis for upload files for the sequence definition and isolate databases. Batch sequence files, in text and Excel formats, are also created for defining the first allele once the locus has been set up in the sequence definition database.



5.20 Genome filtering

Within a genome there may be multiple loci that share allele pools. If an allele sequence is tagged from a genome using only BLAST then there is no way to determine which locus has been identified. It is, however, possible to further define loci by their context, i.e. surrounding sequence.

5.20.1 Filtering by in silico PCR

Provided a locus can be predicted to be specifically amplifed by a PCR reaction, the genome can be filtered to only look at regions prediced to fall within amplification products of one or more PCR reactions. Since this is in silico we don't need to worry about problems such as sequence secondary structure and primers can be any length.

To define a PCR reaction that can be linked to a locus definition, click the add (+) PCR reaction link on the curator's main page.

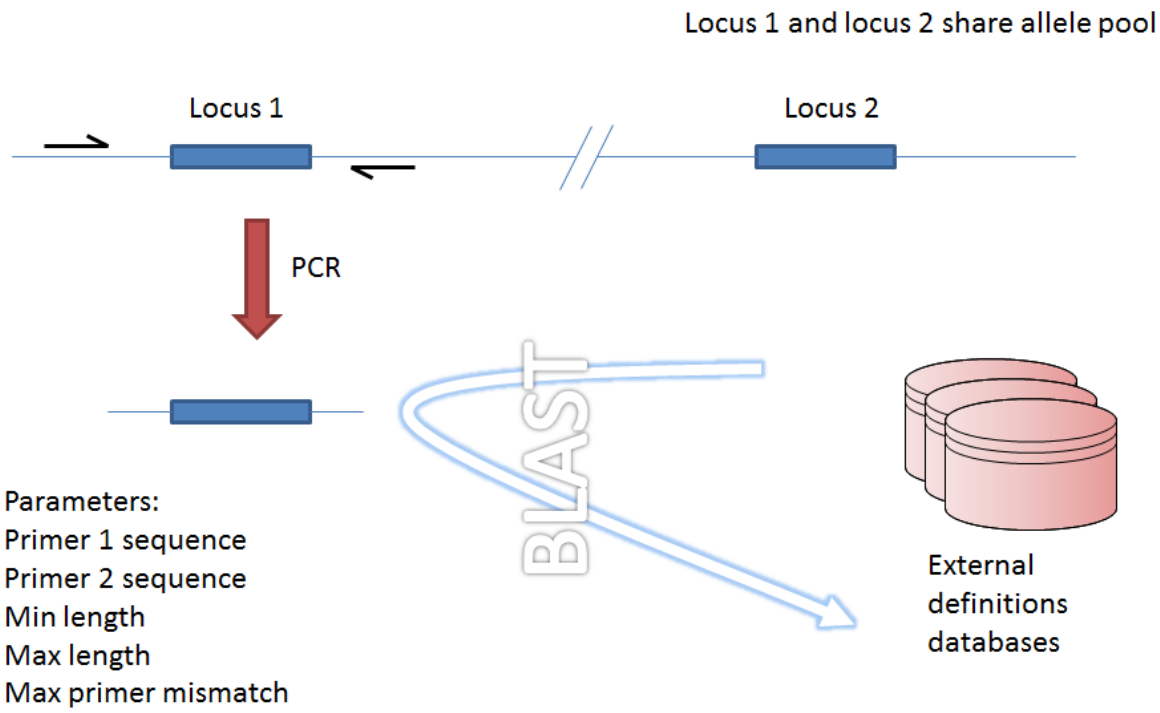
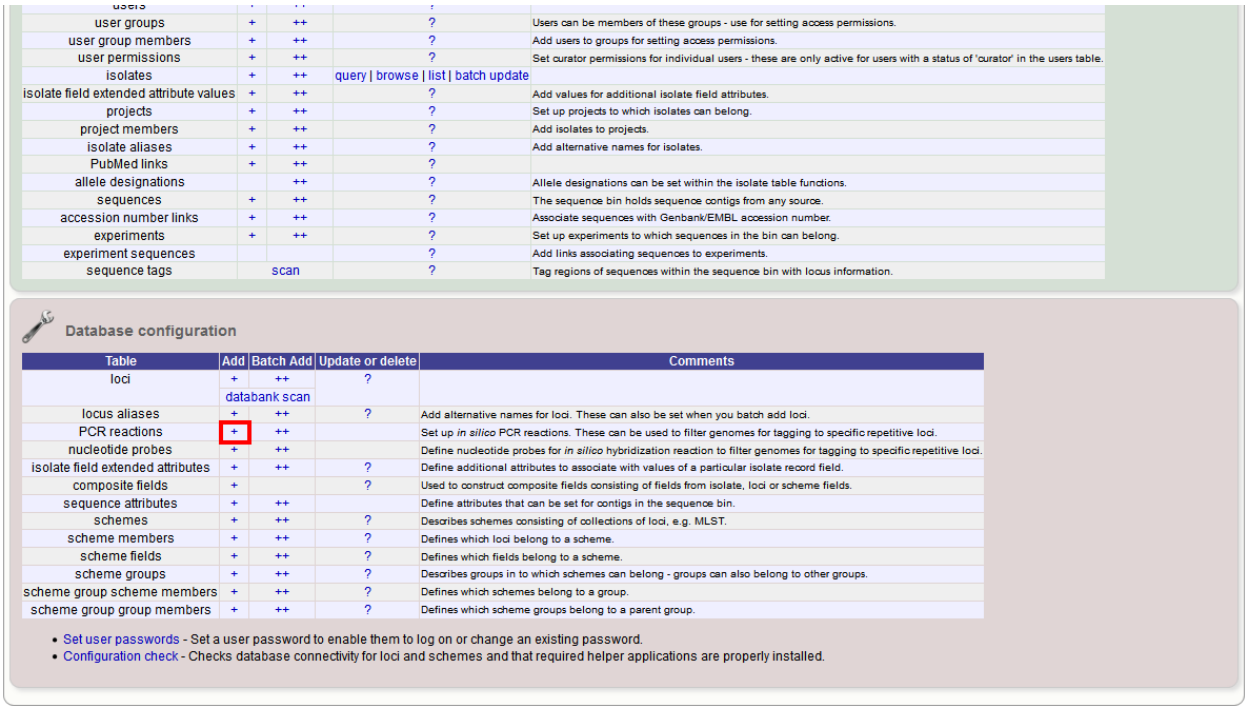


Figure 5.1: Genome filtering by in silico PCR.



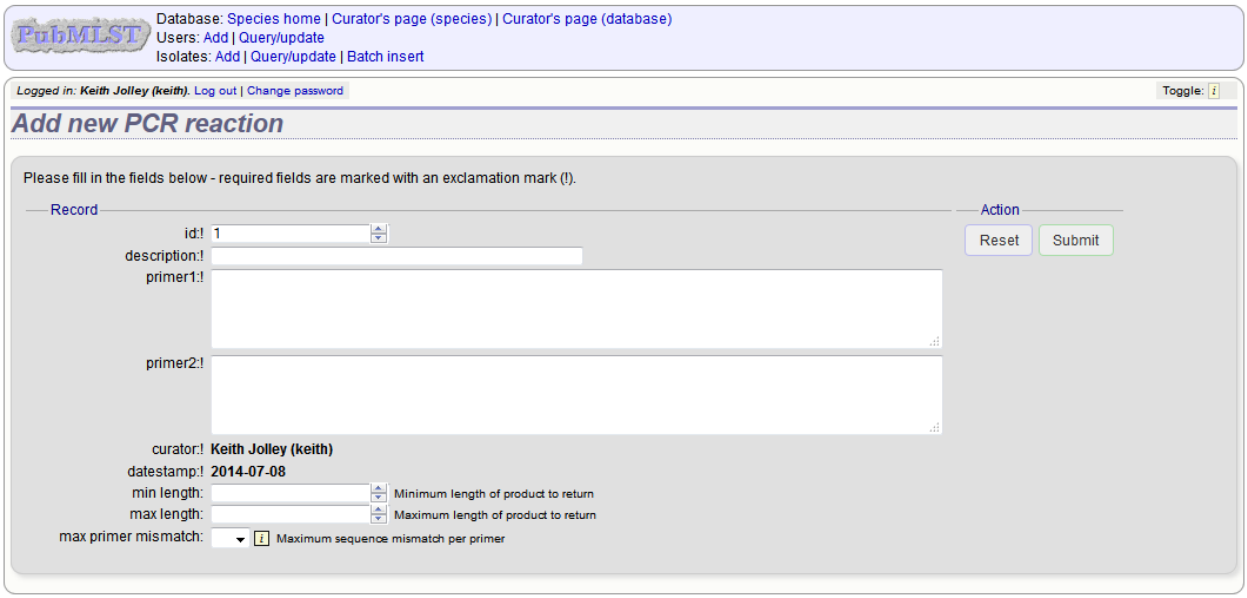
user groups	+	++	?	Users can be members of these groups - use for setting access permissions.
user group members	+	++	?	Add users to groups for setting access permissions.
user permissions	+	++	?	Set curator permissions for individual users - these are only active for users with a status of 'curator' in the users table.
isolates	+	++	query | browse | list | batch update	
isolate field extended attribute values	+	++	?	Add values for additional isolate field attributes.
projects	+	++	?	Set up projects to which isolates can belong.
project members	+	++	?	Add isolates to projects.
isolate aliases	+	++	?	Add alternative names for isolates.
PubMed links	+	++	?	
allele designations		++	?	Allele designations can be set within the isolate table functions.
sequences	+	++	?	The sequence bin holds sequence contigs from any source.
accession number links	+	++	?	Associate sequences with Genbank/EMBL accession number.
experiments	+	++	?	Set up experiments to which sequences in the bin can belong.
experiment sequences			?	Add links associating sequences to experiments.
sequence tags		scan	?	Tag regions of sequences within the sequence bin with locus information.

Database configuration

Table	Add	Batch Add	Update or delete	Comments
loci	+	++	?	
		databank scan		
locus aliases	+	++	?	Add alternative names for loci. These can also be set when you batch add loci.
PCR reactions	+	++		Set up *in silico* PCR reactions. These can be used to filter genomes for tagging to specific repetitive loci.
nucleotide probes	+	++		Define nucleotide probes for *in silico* hybridization reaction to filter genomes for tagging to specific repetitive loci.
isolate field extended attributes	+	++	?	Define additional attributes to associate with values of a particular isolate record field.
composite fields	+		?	Used to construct composite fields consisting of fields from isolate, loci or scheme fields.
sequence attributes	+	++		Define attributes that can be set for contigs in the sequence bin.
schemes	+	++	?	Describes schemes consisting of collections of loci, e.g. MLST.
scheme members	+	++	?	Defines which loci belong to a scheme.
scheme fields	+	++	?	Defines which fields belong to a scheme.
scheme groups	+	++	?	Describes groups in to which schemes can belong - groups can also belong to other groups.
scheme group scheme members	+	++	?	Defines which schemes belong to a group.
scheme group group members	+	++	?	Defines which scheme groups belong to a parent group.

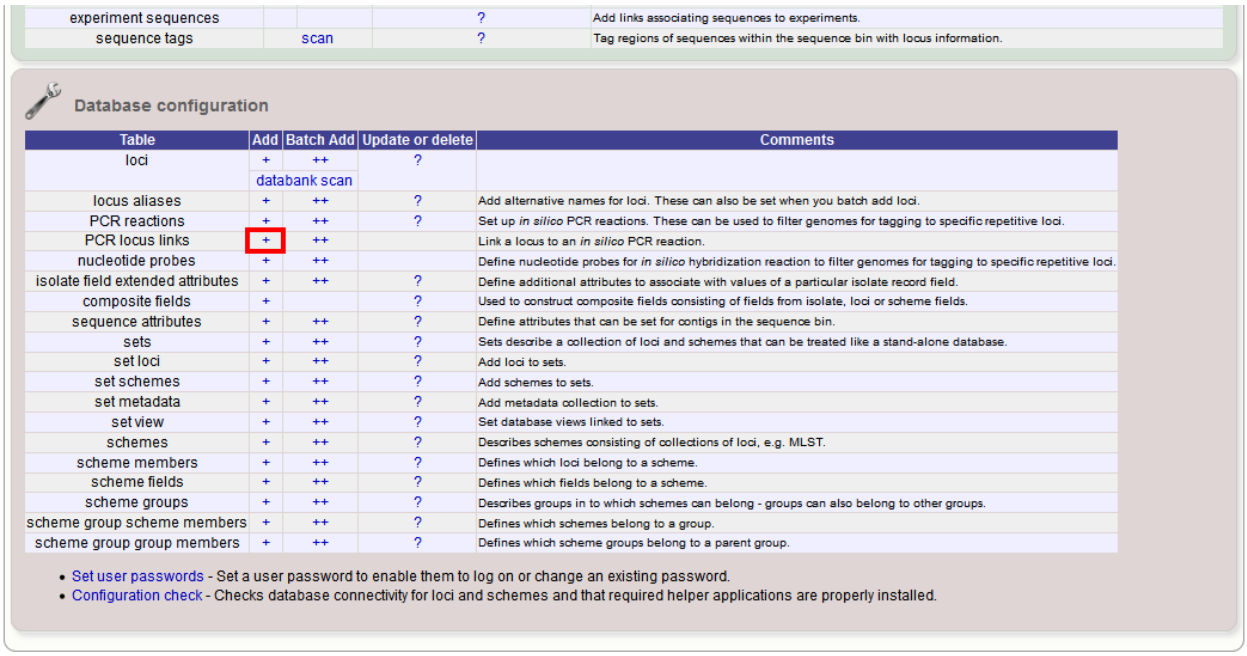
- Set user passwords - Set a user password to enable them to log on or change an existing password.
- Configuration check - Checks database connectivity for loci and schemes and that required helper applications are properly installed.

In the resulting web form you can enter values for your two primer sequences (which can be any length), the minimum and maximum lengths of reaction products you wish to consider and a value for the allowed number of mismatches per primer.



- id - PCR reaction identifier number.
  - Allowed: integer.
- description - Description of PCR reaction product.
  - Allowed: any text.
- primer1 - Primer 1 sequences
  - Allowed: nucleotide sequence (IUPAC ambiguous characters allowed).
- primer2 - Primer 2 sequence.
  - Allowed: nucleotide sequence (IUPAC ambiguous characters allowed).
- min_length - Minimum length of predicted PCR product.
  - Allowed: integer.
- max_length - Maximum length of predicted PCR product.
- max_primer_mismatch - Number of mismatches allowed in primer sequence.
  - Allowed: integer.
  - Do not set this too high or the simulation will run slowly.

Associating this with a particular locus is a two step process. First, create a locus link by clicking the add (+) PCR locus link on the curator's main page. This link will only appear once a PCR reaction has been defined.



experiment sequences			?	Add links associating sequences to experiments.
sequence tags		scan	?	Tag regions of sequences within the sequence bin with locus information.

Database configuration

Table	Add	Batch Add	Update or delete	Comments
loci	+	++	?	
		databank scan		
locus aliases	+	++	?	Add alternative names for loci. These can also be set when you batch add loci.
PCR reactions	+	++	?	Set up *in silico* PCR reactions. These can be used to filter genomes for tagging to specific repetitive loci.
PCR locus links	+	++		Link a locus to an *in silico* PCR reaction.
nucleotide probes	+	++		Define nucleotide probes for *in silico* hybridization reaction to filter genomes for tagging to specific repetitive loci.
isolate field extended attributes	+	++	?	Define additional attributes to associate with values of a particular isolate record field.
composite fields	+		?	Used to construct composite fields consisting of fields from isolate, loci or scheme fields.
sequence attributes	+	++	?	Define attributes that can be set for contigs in the sequence bin.
sets	+	++	?	Sets describe a collection of loci and schemes that can be treated like a stand-alone database.
set loci	+	++	?	Add loci to sets.
set schemes	+	++	?	Add schemes to sets.
set metadata	+	++	?	Add metadata collection to sets.
set view	+	++	?	Set database views linked to sets.
schemes	+	++	?	Describes schemes consisting of collections of loci, e.g. MLST.
scheme members	+	++	?	Defines which loci belong to a scheme.
scheme fields	+	++	?	Defines which fields belong to a scheme.
scheme groups	+	++	?	Describes groups in to which schemes can belong - groups can also belong to other groups.
scheme group scheme members	+	++	?	Defines which schemes belong to a group.
scheme group group members	+	++	?	Defines which scheme groups belong to a parent group.

- Set user passwords - Set a user password to enable them to log on or change an existing password.
- Configuration check - Checks database connectivity for loci and schemes and that required helper applications are properly installed.

Select the locus and PCR reaction name from the dropdown lists to create the link. You also need to edit the locus table and set the pcr_filter field to 'true'.

Now when you next perform *tag scanning* there will be an option to use PCR filtering.

5.20.2 Filtering by in silico hybridization

An alternative is to define a locus by proximity to a single probe sequence. This is especially useful if you have multiple contigs and the locus in question may be at the end of a contig so that it doesn't have upstream or downstream sequence available for PCR filtering.

The process is very similar to setting up PCR filtering, but this time click the nucleotide probe link on the curator's content page.

Enter the nucleotide sequence and a name for the probe. Next you need to link this to the locus in question. Click the add (+) probe locus links link on the curator's main page. This link will only appear once a probe has been defined.

Fill in the web form with appropriate values. Required fields have an exclamation mark (!) next to them:

- probe_id - Dropdown list of probe names.
  - Allowed: selection from list.
- locus - Dropdown list of loci.
  - Allowed: selection from list.
- max_distance - Minimum distance of probe from end of locus.
  - Allowed: any positive integer.
- min_alignment - Minimum length of alignment allowed.
  - Allowed: any positive integer.
- max_mismatch - Maximum number of mismatches allowed in alignment.
  - Allowed: any positive integer.
- max_gaps - Maximum number of gaps allowed in alignment.

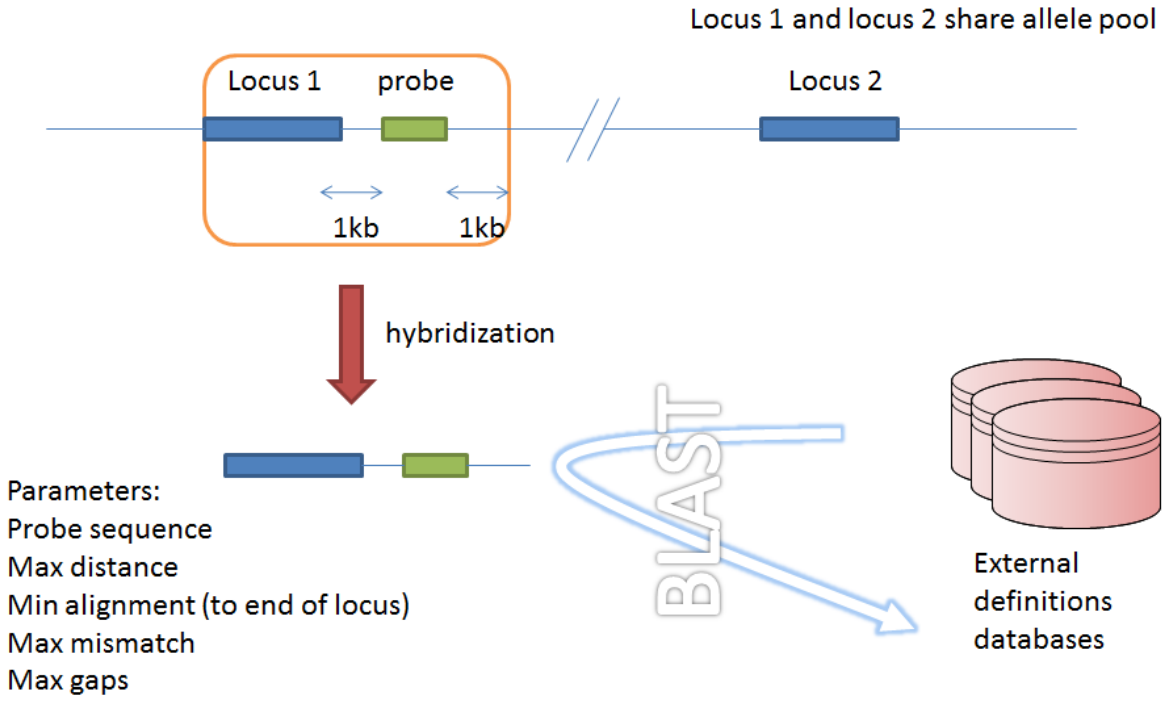
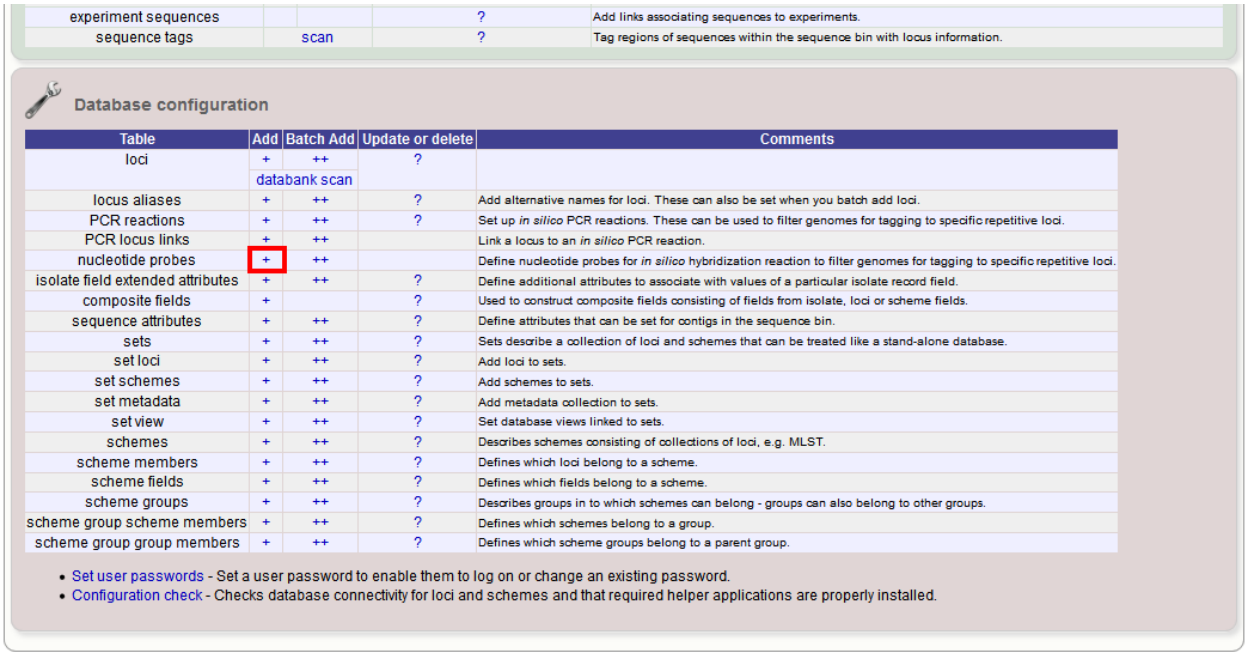


Figure 5.2: Filtering by in silico hybridization

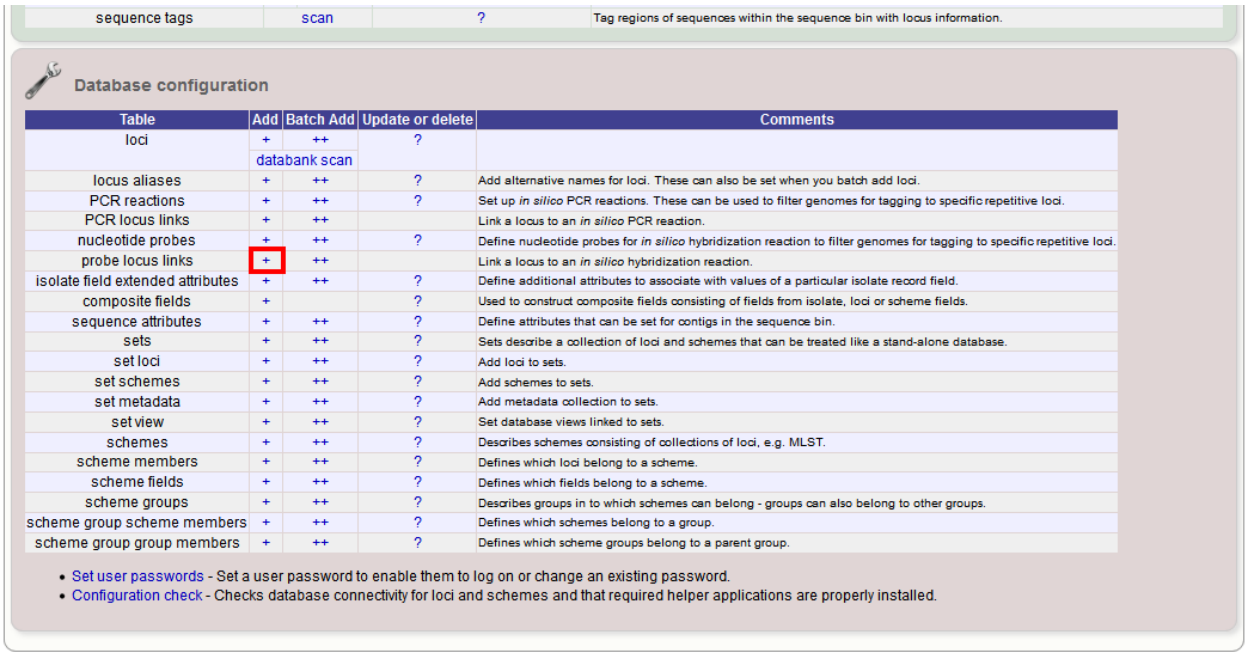


experiment sequences			?	Add links associating sequences to experiments.
sequence tags		scan	?	Tag regions of sequences within the sequence bin with locus information.

Database configuration

Table	Add	Batch Add	Update or delete	Comments
loci	+	++	?	
		databank scan		
locus aliases	+	++	?	Add alternative names for loci. These can also be set when you batch add loci.
PCR reactions	+	++	?	Set up *in silico* PCR reactions. These can be used to filter genomes for tagging to specific repetitive loci.
PCR locus links	+	++		Link a locus to an *in silico* PCR reaction.
nucleotide probes	+	++		Define nucleotide probes for *in silico* hybridization reaction to filter genomes for tagging to specific repetitive loci.
isolate field extended attributes	+	++	?	Define additional attributes to associate with values of a particular isolate record field.
composite fields	+		?	Used to construct composite fields consisting of fields from isolate, loci or scheme fields.
sequence attributes	+	++	?	Define attributes that can be set for contigs in the sequence bin.
sets	+	++	?	Sets describe a collection of loci and schemes that can be treated like a stand-alone database.
set loci	+	++	?	Add loci to sets.
set schemes	+	++	?	Add schemes to sets.
set metadata	+	++	?	Add metadata collection to sets.
set view	+	++	?	Set database views linked to sets.
schemes	+	++	?	Describes schemes consisting of collections of loci, e.g. MLST.
scheme members	+	++	?	Defines which loci belong to a scheme.
scheme fields	+	++	?	Defines which fields belong to a scheme.
scheme groups	+	++	?	Describes groups in to which schemes can belong - groups can also belong to other groups.
scheme group scheme members	+	++	?	Defines which schemes belong to a group.
scheme group group members	+	++	?	Defines which scheme groups belong to a parent group.

- Set user passwords - Set a user password to enable them to log on or change an existing password.
- Configuration check - Checks database connectivity for loci and schemes and that required helper applications are properly installed.



sequence tags	scan	?	Tag regions of sequences within the sequence bin with locus information.

Database configuration

Table	Add	Batch Add	Update or delete	Comments
loci	+	++	?	
	databank scan			
locus aliases	+	++	?	Add alternative names for loci. These can also be set when you batch add loci.
PCR reactions	+	++	?	Set up *in silico* PCR reactions. These can be used to filter genomes for tagging to specific repetitive loci.
PCR locus links	+	++		Link a locus to an *in silico* PCR reaction.
nucleotide probes	+	++	?	Define nucleotide probes for *in silico* hybridization reaction to filter genomes for tagging to specific repetitive loci.
probe locus links	+	++		Link a locus to an *in silico* hybridization reaction.
isolate field extended attributes	+	++	?	Define additional attributes to associate with values of a particular isolate record field.
composite fields	+		?	Used to construct composite fields consisting of fields from isolate, loci or scheme fields.
sequence attributes	+	++	?	Define attributes that can be set for contigs in the sequence bin.
sets	+	++	?	Sets describe a collection of loci and schemes that can be treated like a stand-alone database.
set loci	+	++	?	Add loci to sets.
set schemes	+	++	?	Add schemes to sets.
set metadata	+	++	?	Add metadata collection to sets.
set view	+	++	?	Set database views linked to sets.
schemes	+	++	?	Describes schemes consisting of collections of loci, e.g. MLST.
scheme members	+	++	?	Defines which loci belong to a scheme.
scheme fields	+	++	?	Defines which fields belong to a scheme.
scheme groups	+	++	?	Describes groups in to which schemes can belong - groups can also belong to other groups.
scheme group scheme members	+	++	?	Defines which schemes belong to a group.
scheme group group members	+	++	?	Defines which scheme groups belong to a parent group.

- Set user passwords - Set a user password to enable them to log on or change an existing password.
- Configuration check - Checks database connectivity for loci and schemes and that required helper applications are properly installed.

  - Allowed: any positive integer.

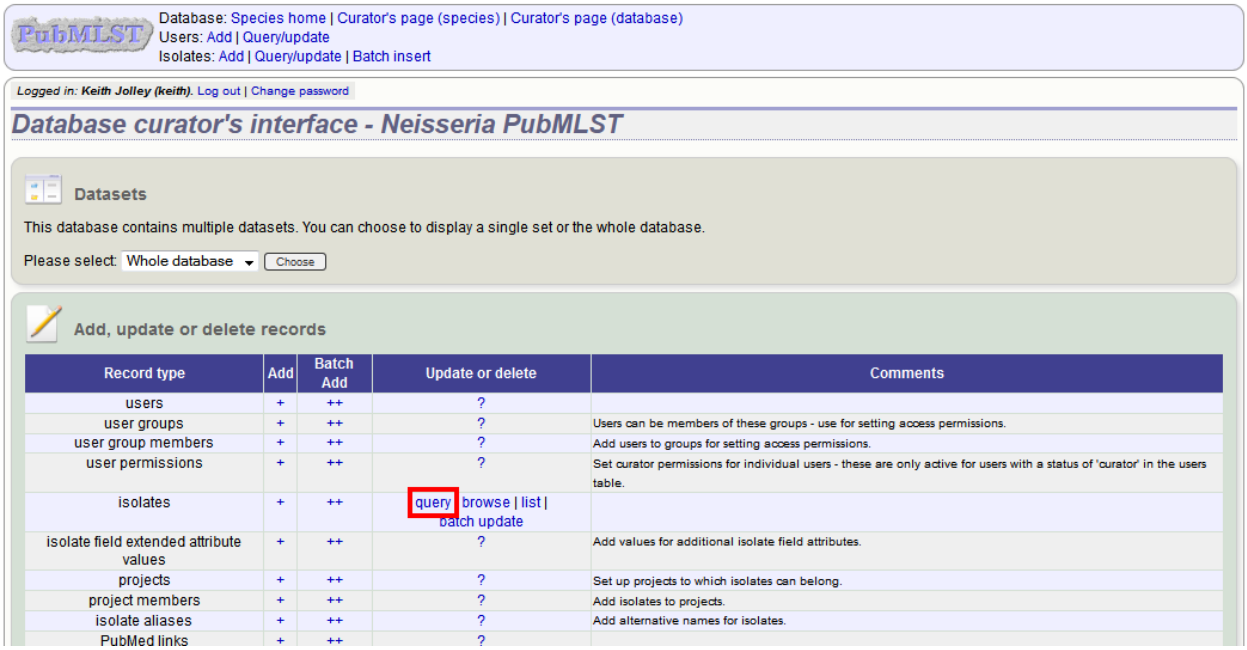
Finally edit the locus table and set the probe_filter field for the specified locus to 'true'.

Now when you next perform *tag scanning* there will be an option to use probe hybridization filtering.

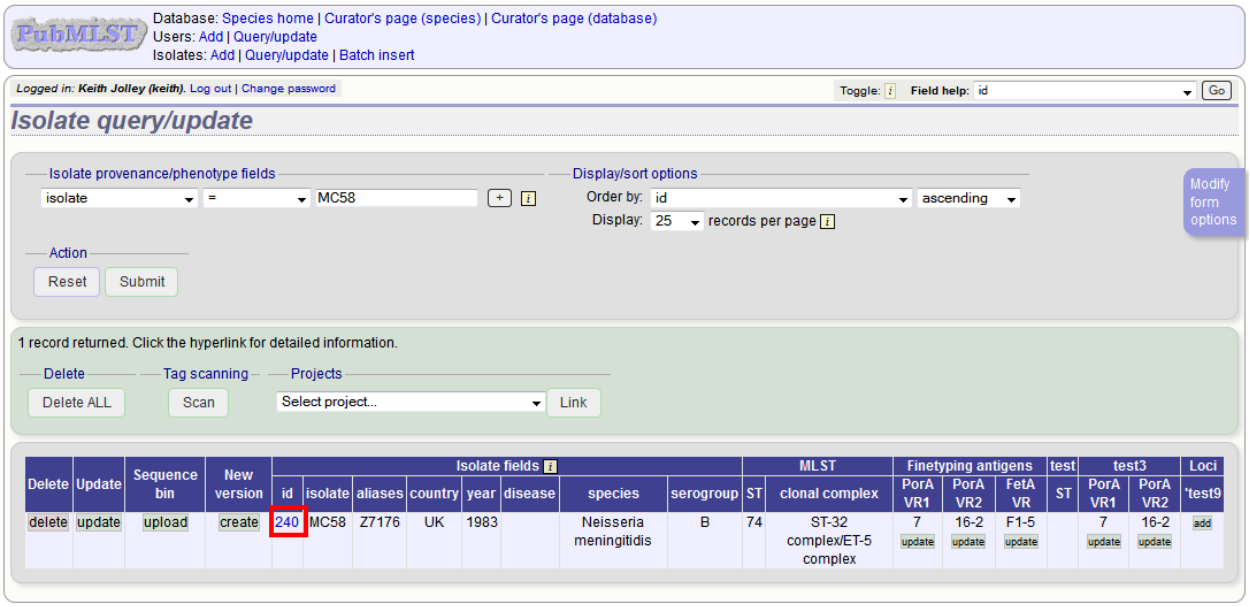
5.21 Setting locus genome positions

The genome position for a locus can be set directly by editing the locus record. To batch update multiple loci based on a tagged genome, however, a much easier way is possible. For this method to work, the reference genome must be represented by a single contig.

From the curator's main page, you need to do a query to find the isolate that you will base your numbering on. Click 'isolate query' to take you to a standard query form.



Perform your search and click the hyperlinked id number of the record.



In the isolate record, click the sequence bin 'Display' button to bring up details of the isolate contigs.

species: Neisseria meningitidis update history: 137 updates show details

Publications (4)

- Bennett JS, Bentley SD, Vernikos GS, Quail MA, Cherevach I, White B, Parkhill J, Maiden MC (2010). Independent evolution of the core and accessory gene sets in the genus Neisseria: insights gained from the genome of Neisseria lactamica isolate 020-06. *BMC Genomics* **11**:652 79 isolates
- Bennett JS, Jolley KA, Earle SG, Corton C, Bentley SD, Parkhill J, Maiden MC (2012). A genomic approach to bacterial taxonomy: an examination and proposed reclassification of species within the genus Neisseria. *Microbiology* **158**:1570-80 55 isolates
- Stabler RA, Marsden GL, Witney AA, Li Y, Bentley SD, Tang CM, Hinds J (2005). Identification of pathogen-specific genes through microarray analysis of pathogenic and commensal Neisseria species. *Microbiology* **151**:2907-22 3 isolates
- Tettelin H, Saunders NJ, Heidelberg J, Jeffries AC, Nelson KE, Eisen JA, Ketchum KA, Hood DW, Peden JF, Dodson RJ, Nelson WC, Gwinn ML, DeBoy R, Peterson JD, Hickey EK, Haft DH, Salzberg SL, White O, Fleischmann RD, Dougherty BA, Mason T, Ciecko A, Parksey DS, Blair E, Cittone H, Clark EB, Cotton MD, Utterback TR, Khouri H, Qin H, Vamathevan J, Gill J, Scarlato V, Masignani V, Pizza M, Grandi G, Sun L, Smith HO, Fraser CM, Moxon ER, Rappuoli R, Venter JC (2000). Complete genome sequence of Neisseria meningitidis serogroup B strain MC58. *Science* **287**:1809-15 1 isolate

Sequence bin

contigs: 1 detailed breakdown: Display
length: 2272360 bp
loci tagged: 1283

Schemes and loci

- All loci
  - Capsule
  - Genetic Information Processing
  - Metabolism
  - Typing
  - Other schemes
  - Loci not in schemes

Navigate and select schemes within tree to display allele designations

Click the 'Renumber' button:

PubMLST
Database: Species home | Curator's page (species) | Curator's page (database)
Users: Add | Query/update
Isolates: Add | Query/update | Batch insert

Logged in: **Keith Jolley (keith)**. Log out | Change password Toggle:

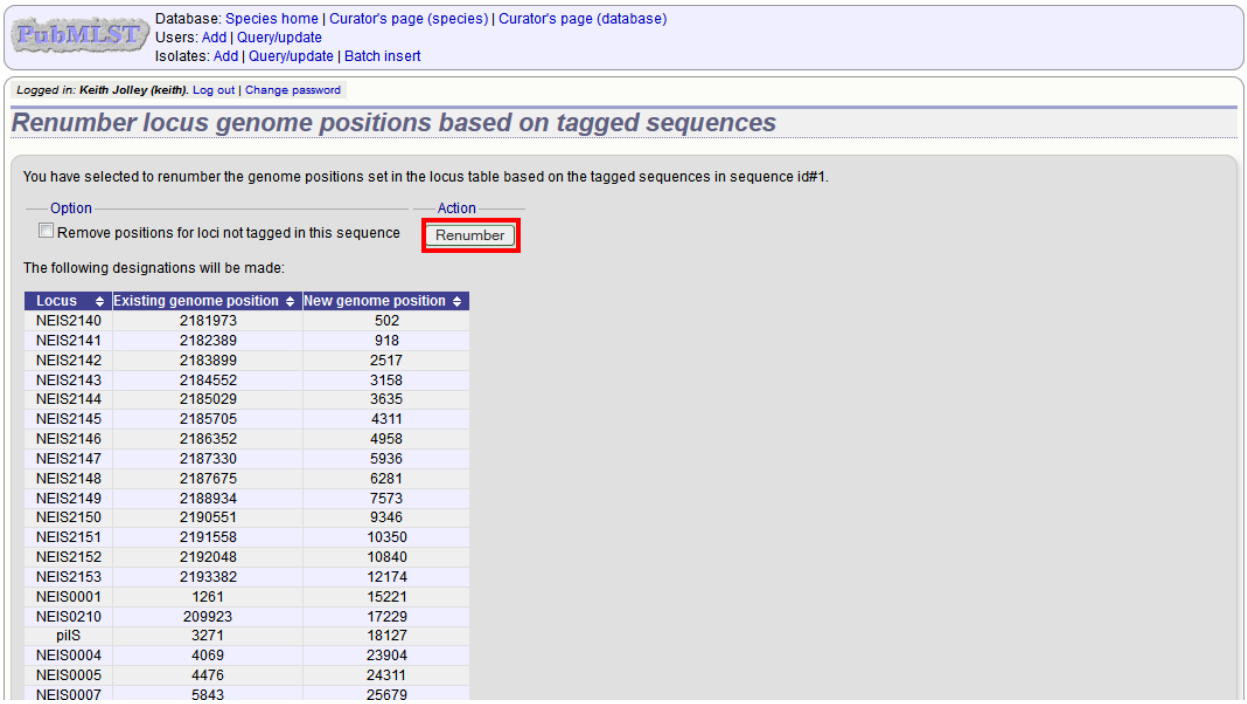
Sequence bin for MC58

Contig summary statistics

- Number of contigs: 1
- Length: 2272360
- Download sequences (FASTA format)
- Download sequences with annotations (EMBL format)

Sequence	Sequencing method	Original designation	Length	Comments	float test	SRA accession	test attribute	test date	test int	Locus	Start	End	Direction	EMBL format	Artemis	Renumber
1	Sanger		2272360	whole genome						NEIS2140	502	897	←	EMBL	Artemis	Renumber
										NEIS2141	918	2312	←			
										NEIS2142	2517	3161	←			
										NEIS2143	3158	3511	←			
										NEIS2144	3635	4117	→			
										NEIS2145	4311	4961	→			
										NEIS2146	4958	5875	→			
										NEIS2147	5936	6214	→			
										NEIS2148 (pgk)	6281	7492	←			
										NEIS2149	7573	8826	←			
										NEIS2150	9346	10317	←			
										NEIS2151	10350	10811	←			
										NEIS2152 (kdtA)	10840	12177	←			
										NEIS2153	12174	13622	←			
										NEIS0001	15221	16144				

A final confirmation screen is displayed with the option to remove existing numbering that doesn't appear within the reference genome. Click 'Renumber'.



Locus	Existing genome position	New genome position
NEIS2140	2181973	502
NEIS2141	2182389	918
NEIS2142	2183899	2517
NEIS2143	2184552	3158
NEIS2144	2185029	3635
NEIS2145	2185705	4311
NEIS2146	2186352	4958
NEIS2147	2187330	5936
NEIS2148	2187675	6281
NEIS2149	2188934	7573
NEIS2150	2190551	9346
NEIS2151	2191558	10350
NEIS2152	2192048	10840
NEIS2153	2193382	12174
NEIS0001	1261	15221
NEIS0210	209923	17229
pilS	3271	18127
NEIS0004	4069	23904
NEIS0005	4476	24311
NEIS0007	5843	25679

5.22 Defining composite fields

Composite fields are virtual fields that don't themselves exist within the database but are made up of values retrieved from other fields or schemes and formatted in a particular way. They are used for display and analysis purposes only and can not be searched against.

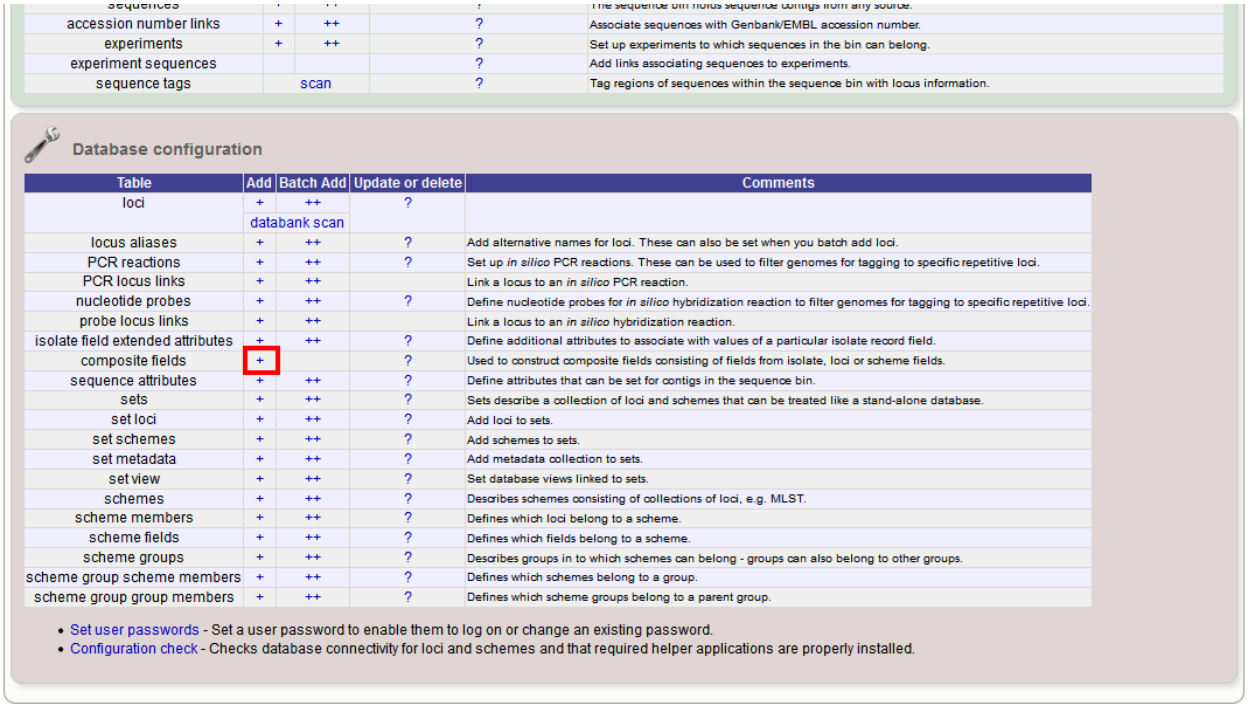
One example of a composite field is used in the Neisseria PubMLST database which has a strain designation composite field made up of serogroup, PorA VR1 and VR2, FetA VR, ST and clonal complex designations in the format:

[serogroup]: P1.[PorA_VR1],[PorA_VR2]: [FetA_VR]: ST-[ST] ([clonal_complex])

e.g. A: P1.5-2,10: F1-5: ST-4 (cc4)

Additionally, the clonal complex field in the above example is converted using a regular expression from 'ST-4 complex/subgroup IV' to 'cc4'.

Composite fields can be added to the database by clicking the add (+) composite fields link on the curator's main page.



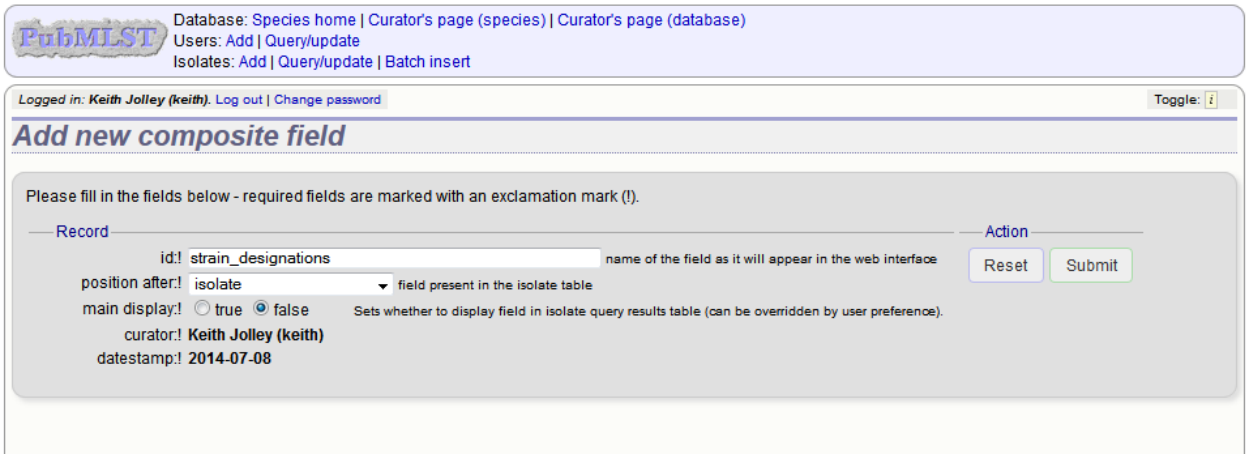
accession number links	+	++	?	Associate sequences with Genbank/EMBL accession number.
experiments	+	++	?	Set up experiments to which sequences in the bin can belong.
experiment sequences			?	Add links associating sequences to experiments.
sequence tags		scan	?	Tag regions of sequences within the sequence bin with locus information.

Database configuration

Table	Add	Batch Add	Update or delete	Comments
loci	+	++	?	
	databank scan			
locus aliases	+	++	?	Add alternative names for loci. These can also be set when you batch add loci.
PCR reactions	+	++	?	Set up *in silico* PCR reactions. These can be used to filter genomes for tagging to specific repetitive loci.
PCR locus links	+	++		Link a locus to an *in silico* PCR reaction.
nucleotide probes	+	++	?	Define nucleotide probes for *in silico* hybridization reaction to filter genomes for tagging to specific repetitive loci.
probe locus links	+	++		Link a locus to an *in silico* hybridization reaction.
isolate field extended attributes	+	++	?	Define additional attributes to associate with values of a particular isolate record field.
composite fields	+		?	Used to construct composite fields consisting of fields from isolate, loci or scheme fields.
sequence attributes	+	++	?	Define attributes that can be set for contigs in the sequence bin.
sets	+	++	?	Sets describe a collection of loci and schemes that can be treated like a stand-alone database.
set loci	+	++	?	Add loci to sets.
set schemes	+	++	?	Add schemes to sets.
set metadata	+	++	?	Add metadata collection to sets.
set view	+	++	?	Set database views linked to sets.
schemes	+	++	?	Describes schemes consisting of collections of loci, e.g. MLST.
scheme members	+	++	?	Defines which loci belong to a scheme.
scheme fields	+	++	?	Defines which fields belong to a scheme.
scheme groups	+	++	?	Describes groups in to which schemes can belong - groups can also belong to other groups.
scheme group scheme members	+	++	?	Defines which schemes belong to a group.
scheme group group members	+	++	?	Defines which scheme groups belong to a parent group.

- Set user passwords - Set a user password to enable them to log on or change an existing password.
- Configuration check - Checks database connectivity for loci and schemes and that required helper applications are properly installed.

Initially you just enter a name for the composite field and after which field it should be positioned. You can also set whether or not it should be displayed by default in main results tables following a query - this is overrideable by user preferences.



Database: Species home | Curator's page (species) | Curator's page (database)
Users: Add | Query/update
Isolates: Add | Query/update | Batch insert

Logged in: Keith Jolley (keith). Log out | Change password Toggle:

Add new composite field

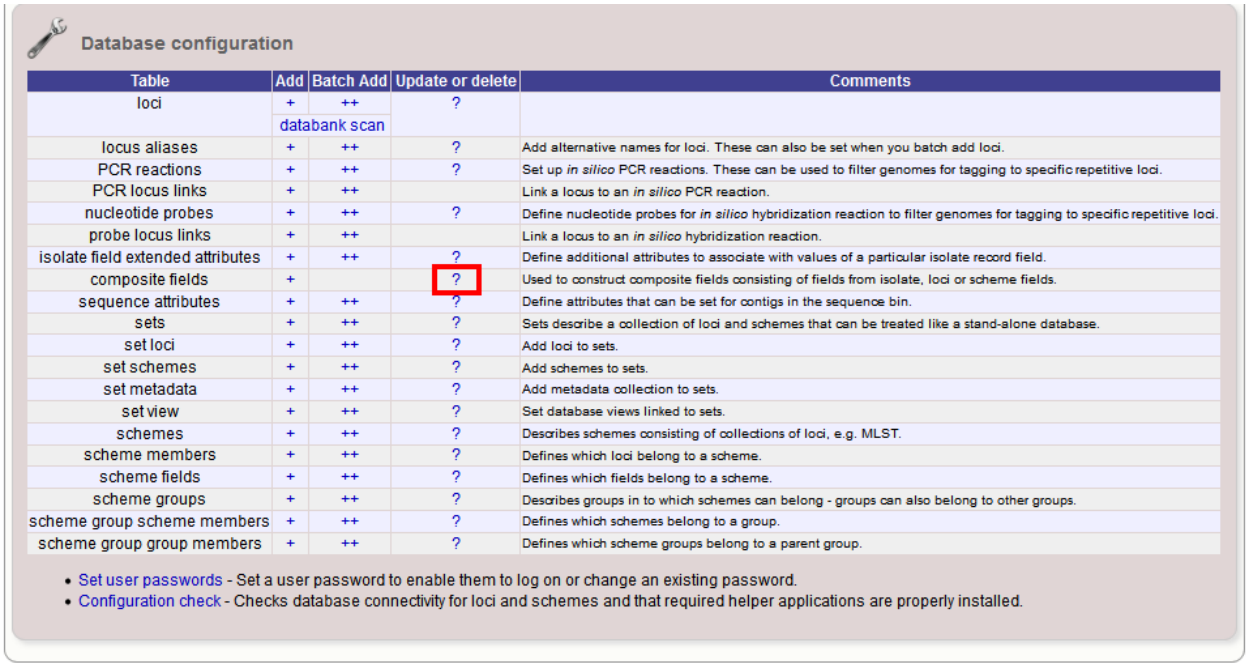
Please fill in the fields below - required fields are marked with an exclamation mark (!).

Record

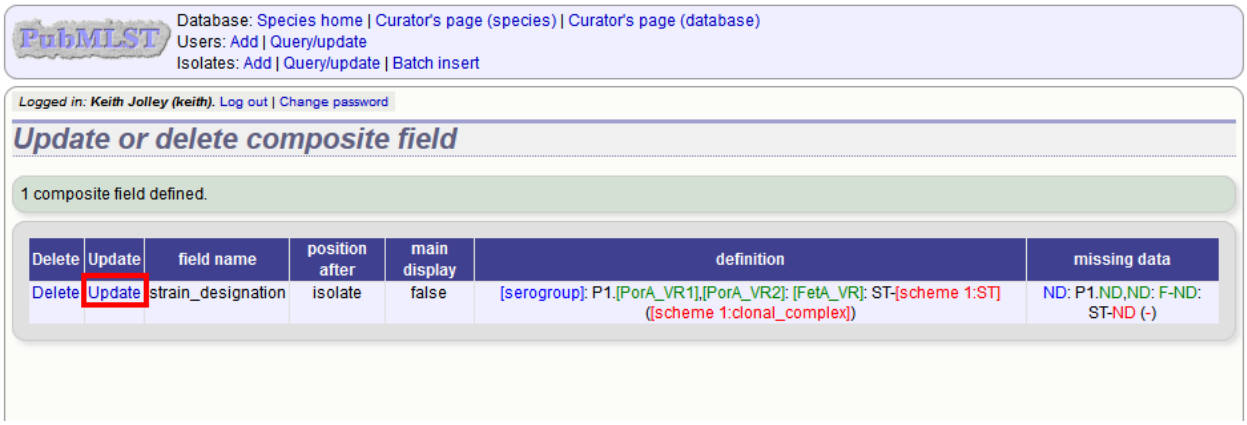
id:! strain_designations — name of the field as it will appear in the web interface
position after:! isolate — field present in the isolate table
main display:! true false — Sets whether to display field in isolate query results table (can be overridden by user preference).
curator:! **Keith Jolley (keith)**
datestamp:! **2014-07-08**

Action: Reset Submit

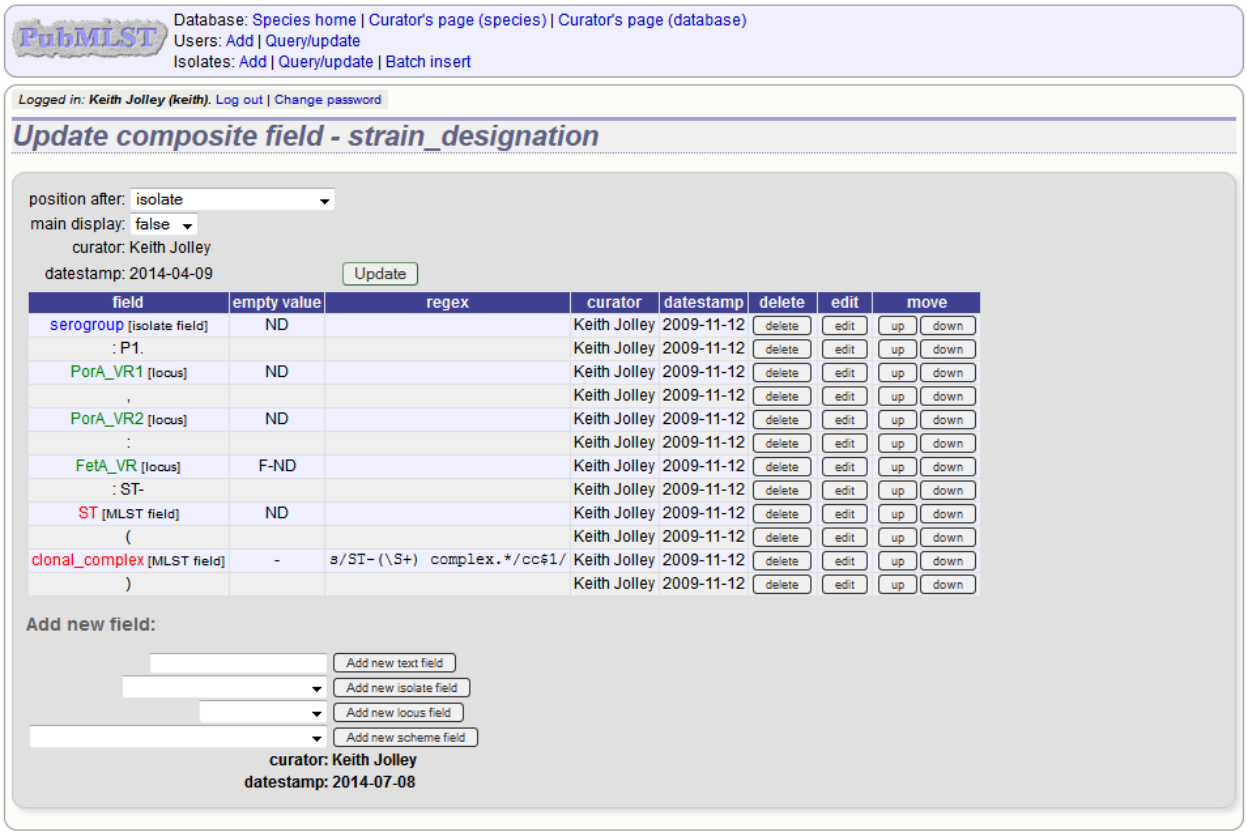
Once the field has been created it needs to be defined. This can be done from query composite field link on the main curator's page.



Select the composite field from the list and click 'Update'.



From this page you can build up your composite field from snippets of text, isolate field, locus and scheme field values. Enter new values in the boxes at the bottom of the page.



Once a field has been added to the composite field, it can be edited by clicking the 'edit' button next to it to add a regular expression to modify its value by specific rules, e.g. in the clonal complex field above, the regular expression is set as:

```
s/ST-(\S+) complex.*/cc$1/
```

which extracts one or more non-space characters following the 'ST-' in a string that then contains the work 'complex', and appends this to 'cc' to produce the final string.

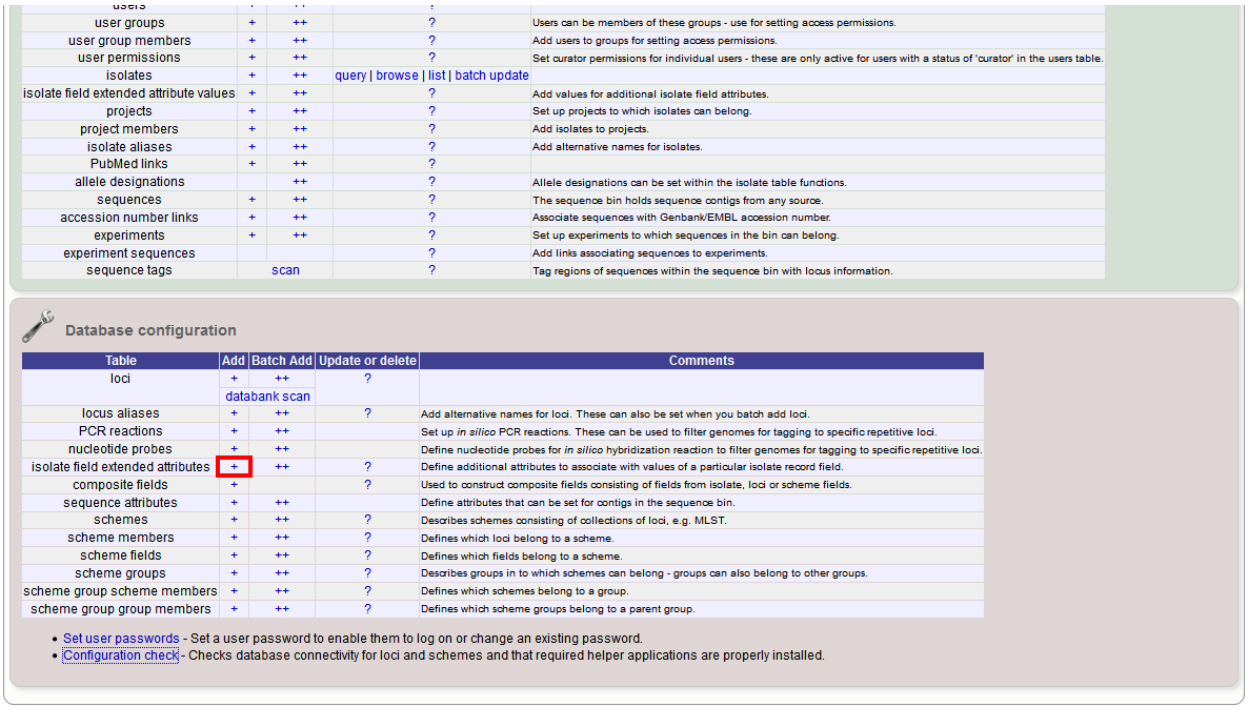
This will convert 'ST-4 complex/subgroup IV' to 'cc4'.

You can also define text to be used for when the field value is missing, e.g. 'ND'.

5.23 Extended provenance attributes (lookup tables)

Lookup tables can be associated with an isolate database field such that the database can be queried by extended attributes. An example of this is the relationship between continent and country - every country belongs to a continent but you wouldn't want to store the continent with each isolate record (not only could data be entered inconsistently but it's redundant). Instead, each record may have a country field and the continent is then determined from the lookup table, allowing, for example, a search of isolates limited to those from Europe.

To set up such an extended attribute, click the add (+) isolate field extended attributes link on the curator's main page.



user groups	+	++	?	Users can be members of these groups - use for setting access permissions.
user group members	+	++	?	Add users to groups for setting access permissions.
user permissions	+	++	?	Set curator permissions for individual users - these are only active for users with a status of 'curator' in the users table.
isolates	+	++	query | browse | list | batch update	
isolate field extended attribute values	+	++	?	Add values for additional isolate field attributes.
projects	+	++	?	Set up projects to which isolates can belong.
project members	+	++	?	Add isolates to projects.
isolate aliases	+	++	?	Add alternative names for isolates.
PubMed links	+	++	?	
allele designations		++	?	Allele designations can be set within the isolate table functions.
sequences	+	++	?	The sequence bin holds sequence contigs from any source.
accession number links	+	++	?	Associate sequences with Genbank/EMBL accession number.
experiments	+	++	?	Set up experiments to which sequences in the bin can belong.
experiment sequences			?	Add links associating sequences to experiments.
sequence tags	scan		?	Tag regions of sequences within the sequence bin with locus information.

Database configuration

Table	Add	Batch Add	Update or delete	Comments
loci	+	++	?	
	databank scan			
locus aliases	+	++	?	Add alternative names for loci. These can also be set when you batch add loci.
PCR reactions	+	++		Set up *in silico* PCR reactions. These can be used to filter genomes for tagging to specific repetitive loci.
nucleotide probes	+	++		Define nucleotide probes for *in silico* hybridization reaction to filter genomes for tagging to specific repetitive loci.
isolate field extended attributes	+	++	?	Define additional attributes to associate with values of a particular isolate record field.
composite fields	+		?	Used to construct composite fields consisting of fields from isolate, loci or scheme fields.
sequence attributes	+	++		Define attributes that can be set for contigs in the sequence bin.
schemes	+	++	?	Describes schemes consisting of collections of loci, e.g. MLST.
scheme members	+	++	?	Defines which loci belong to a scheme.
scheme fields	+	++	?	Defines which fields belong to a scheme.
scheme groups	+	++	?	Describes groups in to which schemes can belong - groups can also belong to other groups.
scheme group scheme members	+	++	?	Defines which schemes belong to a group.
scheme group group members	+	++	?	Defines which scheme groups belong to a parent group.

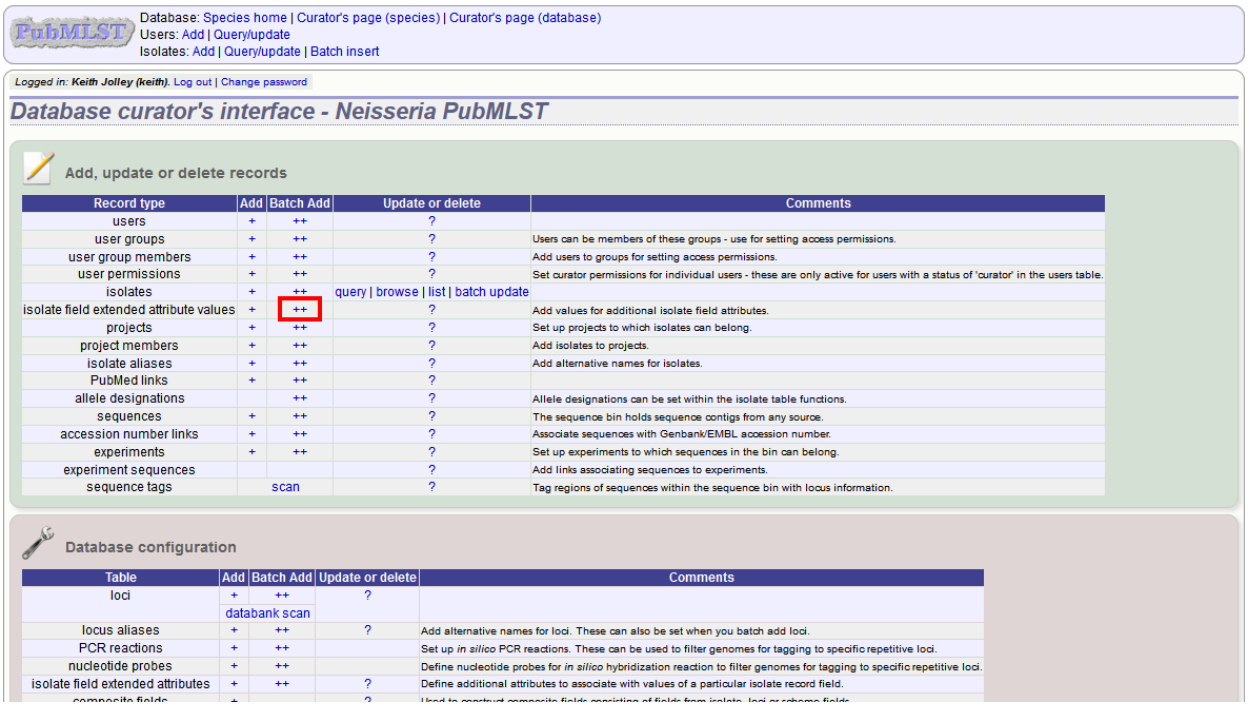
- Set user passwords - Set a user password to enable them to log on or change an existing password.
- Configuration check - Checks database connectivity for loci and schemes and that required helper applications are properly installed.

Fill in the web form with appropriate values. Required fields have an exclamation mark (!) next to them:

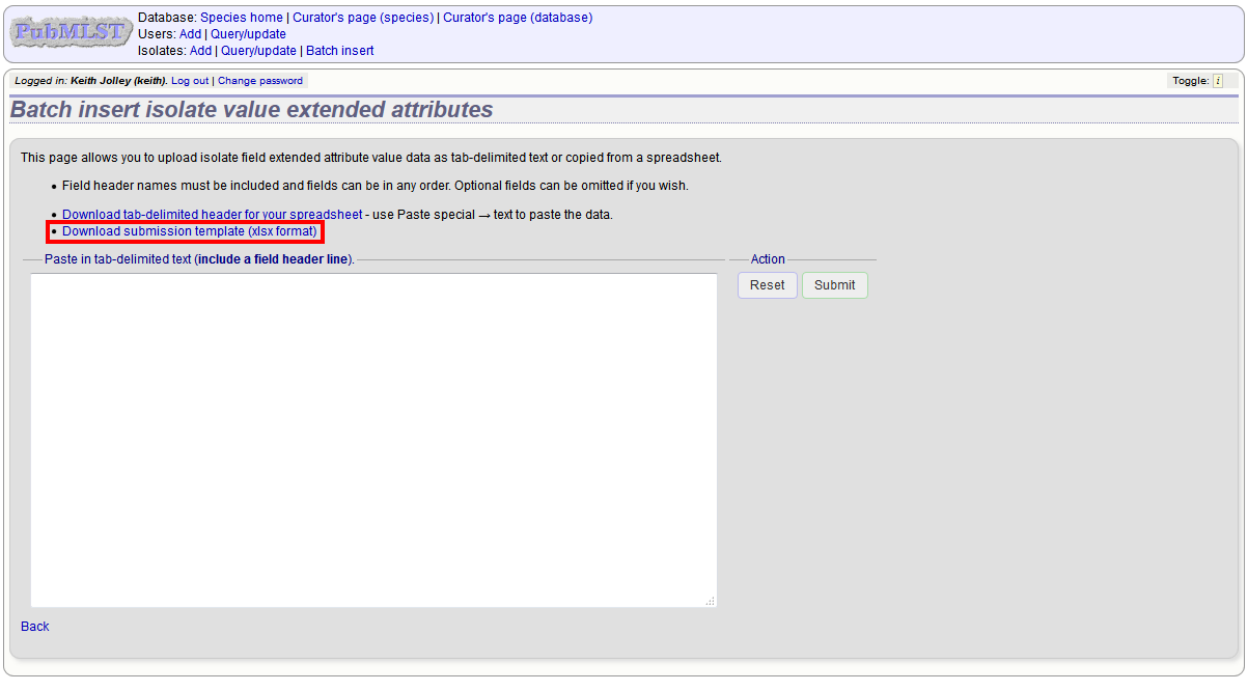
- isolate_field - Dropdown list of isolate fields.
  - Allowed: selection from list.
- attribute - Name of extended attribute, e.g. continent.
  - Allowed: any text (no spaces).
- value_format - Format for values.
  - Allowed: integer/float/text/date.
- value_regex - Regular expression to enforce allele id naming.
  - ^: the beginning of the string
  - $:the end of the string
  - d: digit
  - D: non-digit
  - s: white space character
  - S: non white space character
  - w: alpha-numeric plus '_'
  - .: any character
  - *: 0 or more of previous character
  - +: 1 or more of previous character
  - e.g. ^Fd-d+$ states that a value must begin with a F followed by a single digit, then a dash, then one or more digits, e.g. F1-12
- description - Long description - this isn't currently used but may be in the future.

  - Allowed: any text.
- url - URL used to hyperlink values in the isolate information page. Instances of [?] within the URL will be substituted with the value.
  - Allowed: any valid URL (either relative or absolute).
- length - Maximum length of extended attribute value.
  - Allowed: any positive integer.
- field_order - Integer that sets the order of the field following it's parent isolate field.
  - Allowed: any integer.

The easiest way to populate the lookup table is to do a batch update copied from a spreadsheet. Click the batch add (++) isolate field extended attribute values link on the curator's main page (this link will only appear once an extended attribute has been defined).



Download the Excel template:



Fill in the columns with your values, e.g.

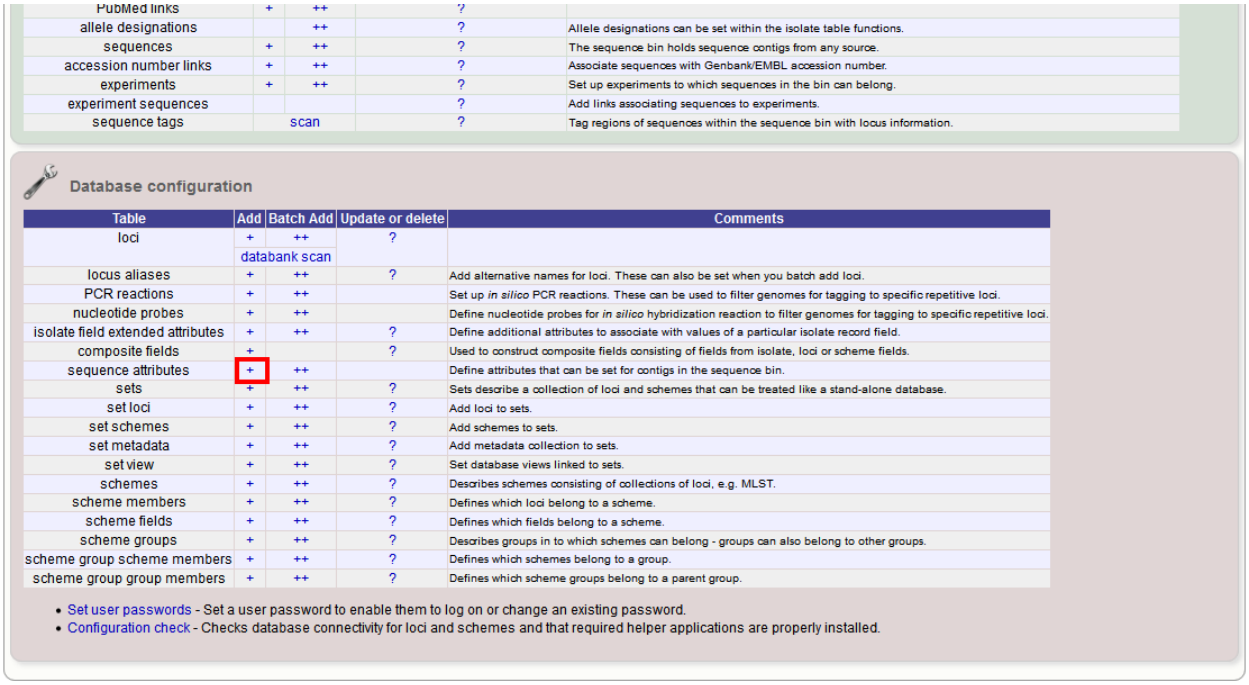
isolate_field	attribute	field_value	value
country	continent	Afghanistan	Asia
country	continent	Albania	Europe
country	continent	Algeria	Africa
country	continent	Andorra	Europe
country	continent	Angola	Africa

Paste from the spreadsheet in to the upload form and click 'Submit'.

5.24 Sequence bin attributes

It is possible that you will want to store extended attributes for sequence bin contigs when you upload them. Examples may be read length, assembler version, etc. Since there are almost infinite possibilities for these fields, and they are likely to change over time, they are not hard-coded within the database. An administrator can, however, create their own attributes for a specific database and these will then be available in the web form when uploading new contig data. The attributes are also searchable.

To set up new attributes, click the add (+) 'sequence attributes' link on the isolate database curator's index page.



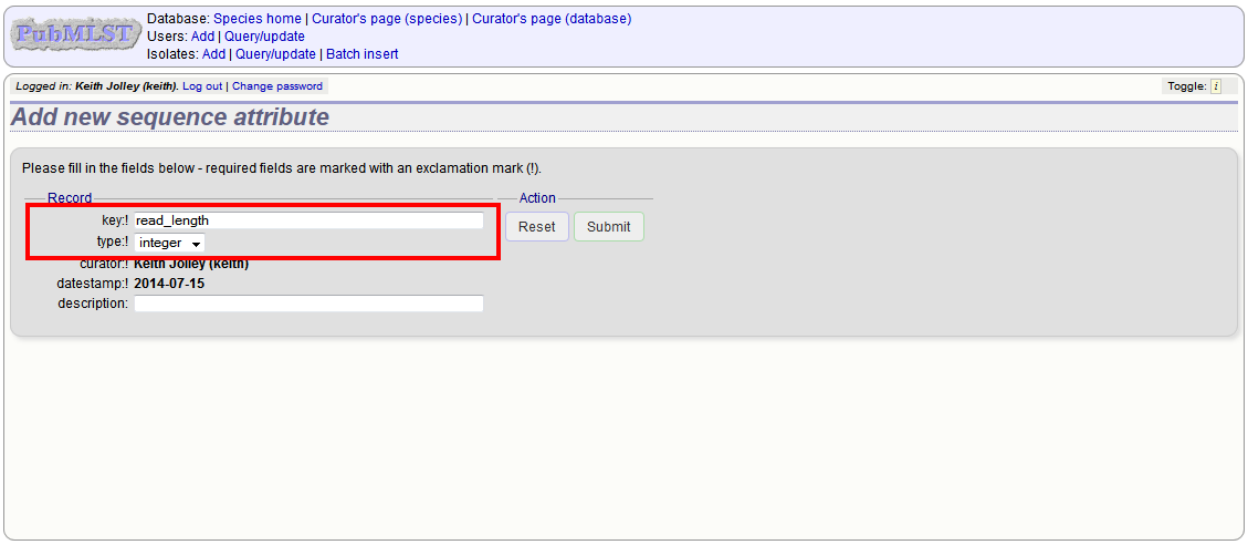
PubMed links	+	++	?	
allele designations		++	?	Allele designations can be set within the isolate table functions.
sequences	+	++	?	The sequence bin holds sequence contigs from any source.
accession number links	+	++	?	Associate sequences with Genbank/EMBL accession number.
experiments	+	++	?	Set up experiments to which sequences in the bin can belong.
experiment sequences			?	Add links associating sequences to experiments.
sequence tags		scan	?	Tag regions of sequences within the sequence bin with locus information.

Database configuration

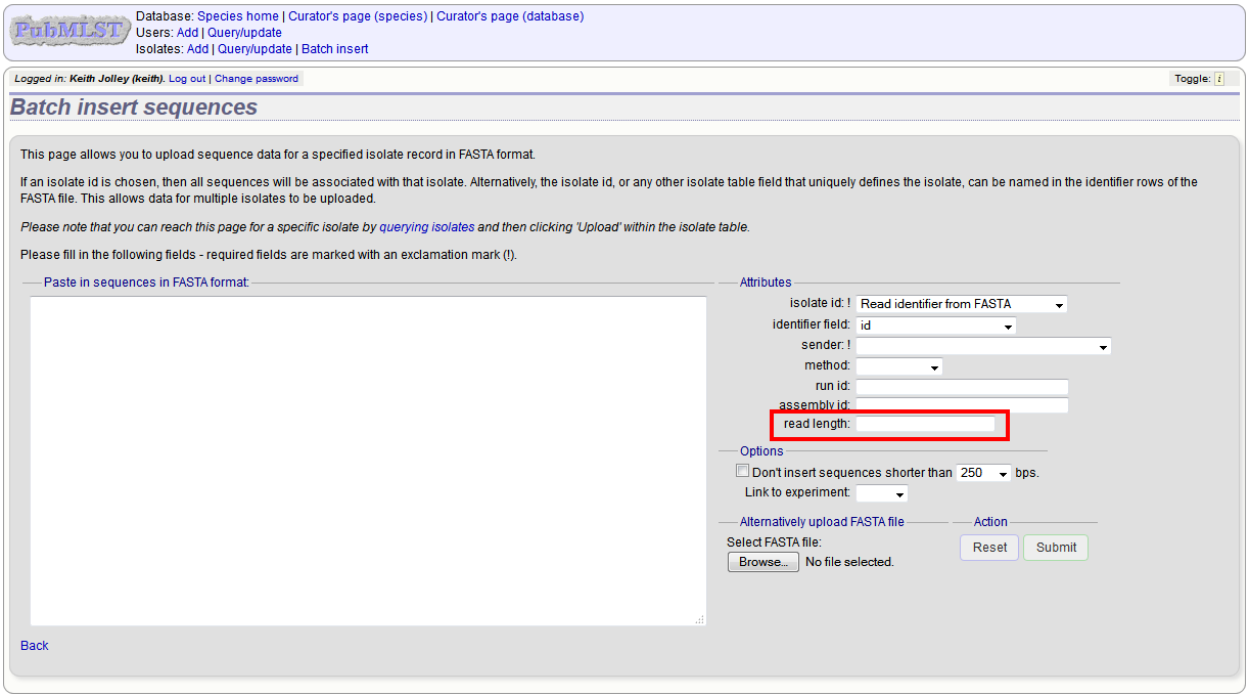
Table	Add	Batch Add	Update or delete	Comments
loci	+	++	?	
		databank scan		
locus aliases	+	++	?	Add alternative names for loci. These can also be set when you batch add loci.
PCR reactions	+	++		Set up *in silico* PCR reactions. These can be used to filter genomes for tagging to specific repetitive loci.
nucleotide probes	+	++		Define nucleotide probes for *in silico* hybridization reaction to filter genomes for tagging to specific repetitive loci.
isolate field extended attributes	+	++	?	Define additional attributes to associate with values of a particular isolate record field.
composite fields	+		?	Used to construct composite fields consisting of fields from isolate, loci or scheme fields.
sequence attributes	+	++		Define attributes that can be set for contigs in the sequence bin.
sets	+	++	?	Sets describe a collection of loci and schemes that can be treated like a stand-alone database.
set loci	+	++	?	Add loci to sets.
set schemes	+	++	?	Add schemes to sets.
set metadata	+	++	?	Add metadata collection to sets.
set view	+	++	?	Set database views linked to sets.
schemes	+	++	?	Describes schemes consisting of collections of loci, e.g. MLST.
scheme members	+	++	?	Defines which loci belong to a scheme.
scheme fields	+	++	?	Defines which fields belong to a scheme.
scheme groups	+	++	?	Describes groups in to which schemes can belong - groups can also belong to other groups.
scheme group scheme members	+	++	?	Defines which schemes belong to a group.
scheme group group members	+	++	?	Defines which scheme groups belong to a parent group.

- Set user passwords - Set a user password to enable them to log on or change an existing password.
- Configuration check - Checks database connectivity for loci and schemes and that required helper applications are properly installed.

Enter the name of the attribute as the 'key', select the type of data (text, integer, float, date) and an optional short description. Click 'Submit'.

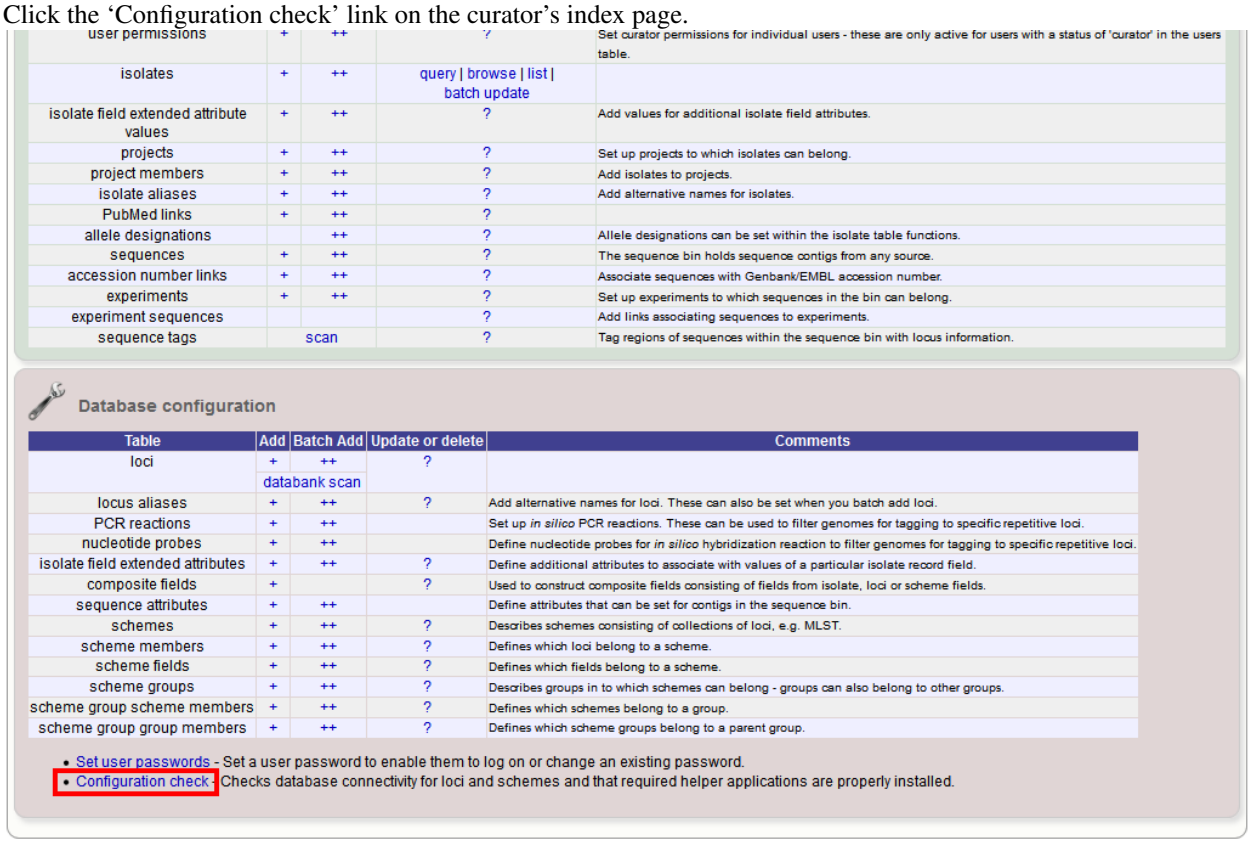


This new attribute will then be available when *uploading contig data*.



5.25 Checking external database configuration settings

Click the 'Configuration check' link on the curator's index page.



user permissions	+	++	?	Set curator permissions for individual users - these are only active for users with a status of 'curator' in the users table.
isolates	+	++	query | browse | list | batch update	
isolate field extended attribute values	+	++	?	Add values for additional isolate field attributes.
projects	+	++	?	Set up projects to which isolates can belong.
project members	+	++	?	Add isolates to projects.
isolate aliases	+	++	?	Add alternative names for isolates.
PubMed links	+	++	?	
allele designations		++	?	Allele designations can be set within the isolate table functions.
sequences	+	++	?	The sequence bin holds sequence contigs from any source.
accession number links	+	++	?	Associate sequences with Genbank/EMBL accession number.
experiments	+	++	?	Set up experiments to which sequences in the bin can belong.
experiment sequences			?	Add links associating sequences to experiments.
sequence tags	scan		?	Tag regions of sequences within the sequence bin with locus information.

Database configuration

Table	Add	Batch Add	Update or delete	Comments
loci	+	++	?	
	databank scan			
locus aliases	+	++	?	Add alternative names for loci. These can also be set when you batch add loci.
PCR reactions	+	++		Set up *in silico* PCR reactions. These can be used to filter genomes for tagging to specific repetitive loci.
nucleotide probes	+	++		Define nucleotide probes for *in silico* hybridization reaction to filter genomes for tagging to specific repetitive loci.
isolate field extended attributes	+	++	?	Define additional attributes to associate with values of a particular isolate record field.
composite fields	+		?	Used to construct composite fields consisting of fields from isolate, loci or scheme fields.
sequence attributes	+	++		Define attributes that can be set for contigs in the sequence bin.
schemes	+	++	?	Describes schemes consisting of collections of loci, e.g. MLST.
scheme members	+	++	?	Defines which loci belong to a scheme.
scheme fields	+	++	?	Defines which fields belong to a scheme.
scheme groups	+	++	?	Describes groups in to which schemes can belong - groups can also belong to other groups.
scheme group scheme members	+	++	?	Defines which schemes belong to a group.
scheme group group members	+	++	?	Defines which scheme groups belong to a parent group.

- Set user passwords - Set a user password to enable them to log on or change an existing password.
- Configuration check - Checks database connectivity for loci and schemes and that required helper applications are properly installed.

The software will check that required helper applications are installed and executable and, in isolate databases, test every locus and scheme external database to check for connectivity and that data can be retrieved.

PubMLST
Database: Species home | Curator's page (species) | Curator's page (database)
Users: Add | Query/update
Isolates: Add | Query/update | Batch insert

*Logged in: **Keith Jolley (keith)**.* Log out | Change password

Configuration check - Neisseria PubMLST

Helper applications

Program	Path	Installed	Executable
EMBOSS infoalign	/usr/bin/infoalign	ok	ok
EMBOSS sixpack	/usr/bin/sixpack	ok	ok
EMBOSS stretcher	/usr/bin/stretcher	ok	ok
blastn	/usr/local/ncbi-blast+/bin/blastn	ok	ok
blastp	/usr/local/ncbi-blast+/bin/blastp	ok	ok
blastx	/usr/local/ncbi-blast+/bin/blastx	ok	ok
ipcress	/usr/bin/ipcress	ok	ok
mafft	/usr/local/bin/mafft	ok	ok
makeblastdb	/usr/local/ncbi-blast+/bin/makeblastdb	ok	ok
mogrify	/usr/bin/mogrify	ok	ok
muscle	/usr/bin/muscle	ok	ok
tblastx	/usr/local/ncbi-blast+/bin/tblastx	ok	ok

Locus databases

Locus	Database	Host	Port	Table	Primary id field	Secondary id field	Secondary id field value	Sequence field	Database accessible	Sequence query	Sequences assigned
'16S rDNA	pubmlst_bigsdb_neisseria_seqdef	localhost	5432	sequences	allele_id	locus	'16S_rDNA	sequence	ok	ok	197
'porA	pubmlst_bigsdb_neisseria_seqdef	localhost	5432	sequences	allele_id	locus	'porA	sequence	ok	ok	164
'porB	pubmlst_bigsdb_neisseria_seqdef	localhost	5432	sequences	allele_id	locus	'porB	sequence	ok	ok	695
'rplF	pubmlst_bigsdb_neisseria_seqdef	localhost	5432	sequences	allele_id	locus	'rplF	sequence	ok	ok	109
BACT000001 (rpsA)	bigsdb_multispecies_seqdef	localhost	5432	sequences	allele_id	locus	BACT000001	sequence	ok	ok	8189
BACT000002 (rpsB)	bigsdb_multispecies_seqdef	localhost	5432	sequences	allele_id	locus	BACT000002	sequence	ok	ok	6567
BACT000003 (rpsC)	bigsdb_multispecies_seqdef	localhost	5432	sequences	allele_id	locus	BACT000003	sequence	ok	ok	5965
BACT000004 (rpsD)	bigsdb_multispecies_seqdef	localhost	5432	sequences	allele_id	locus	BACT000004	sequence	ok	ok	6195
BACT000005 (rpsE)	bigsdb_multispecies_seqdef	localhost	5432	sequences	allele_id	locus	BACT000005	sequence	ok	ok	5707
BACT000006 (rpsF)	bigsdb_multispecies_seqdef	localhost	5432	sequences	allele_id	locus	BACT000006	sequence	ok	ok	4918
BACT000007 (rpsG)	bigsdb_multispecies_seqdef	localhost	5432	sequences	allele_id	locus	BACT000007	sequence	ok	ok	5667
BACT000008 (rpsH)	bigsdb_multispecies_seqdef	localhost	5432	sequences	allele_id	locus	BACT000008	sequence	ok	ok	5260

Any problems will be highlighted with a red X.

CHAPTER 6

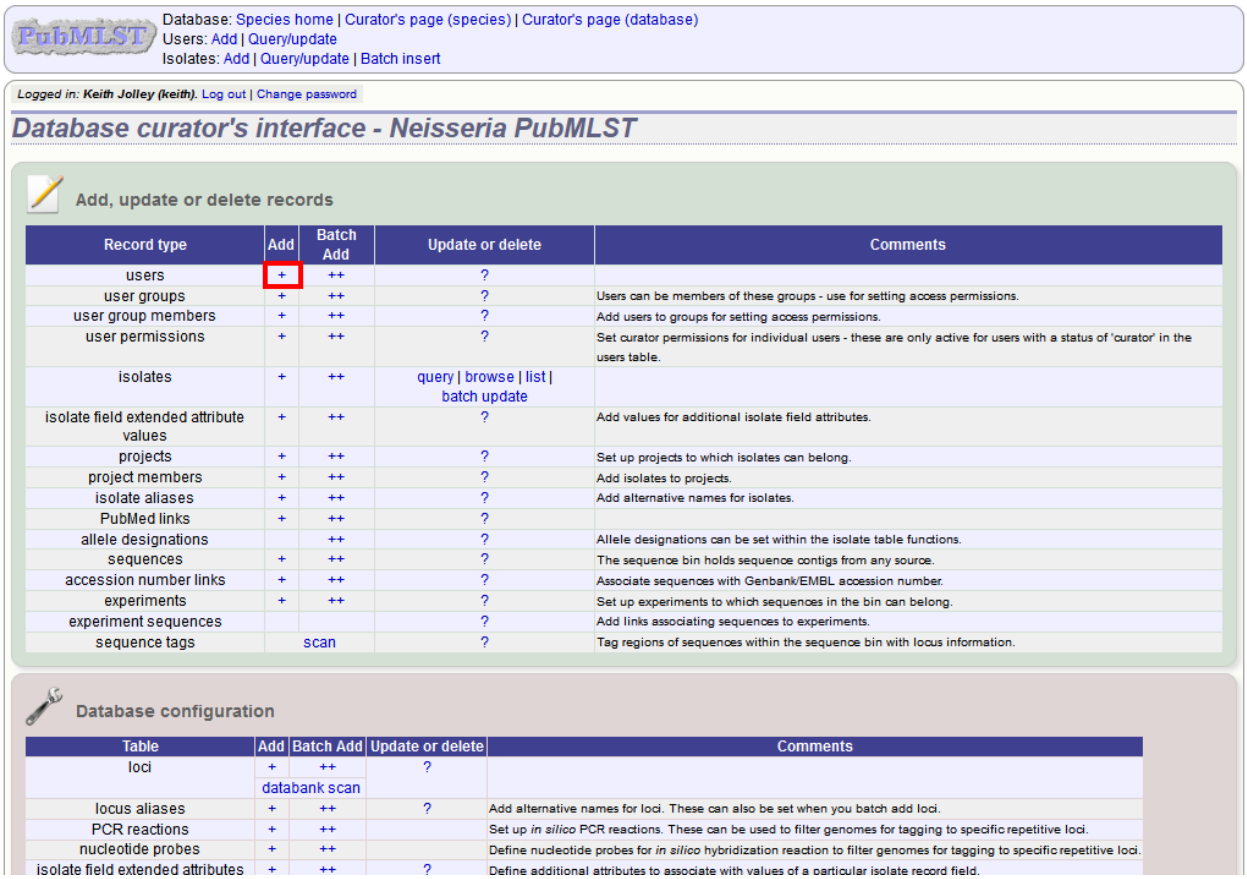
Curator's guide

Please note that links displayed within the curation interface will vary depending on database contents and the permissions of the curator.

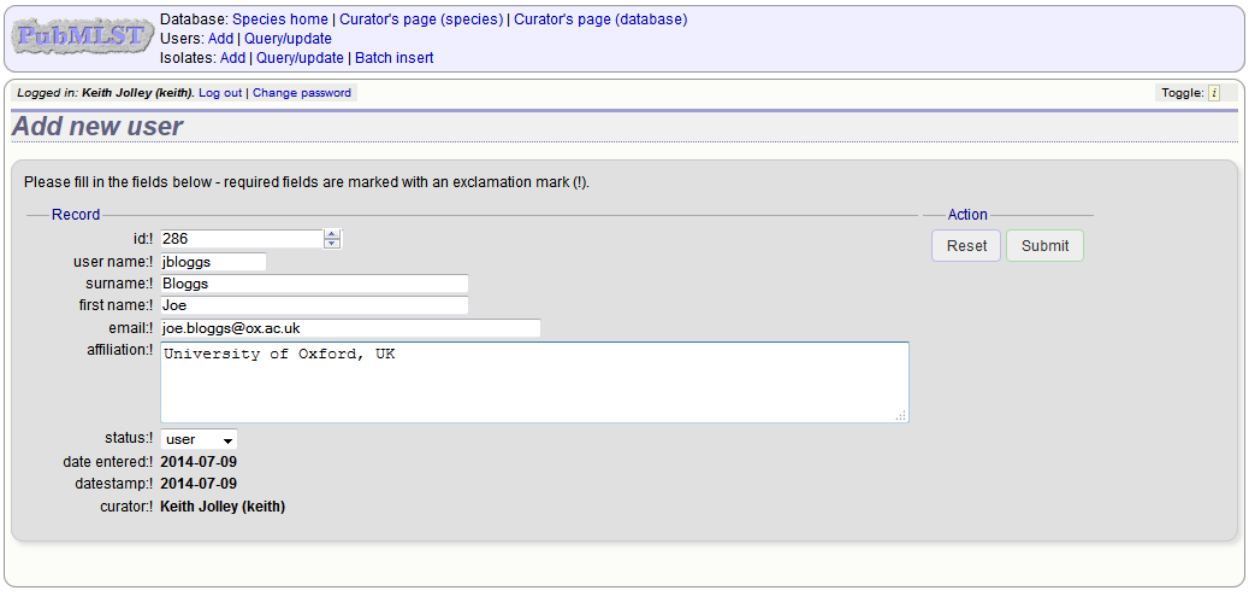
6.1 Adding new sender details

All records within the databases are associated with a sender. Whenever somebody new submits data, they should be added to the users table so that their name appears in the dropdown lists on the data upload forms.

To add a user, click the add users (+) link on the curator's contents page.



Enter the user's details in to the form.

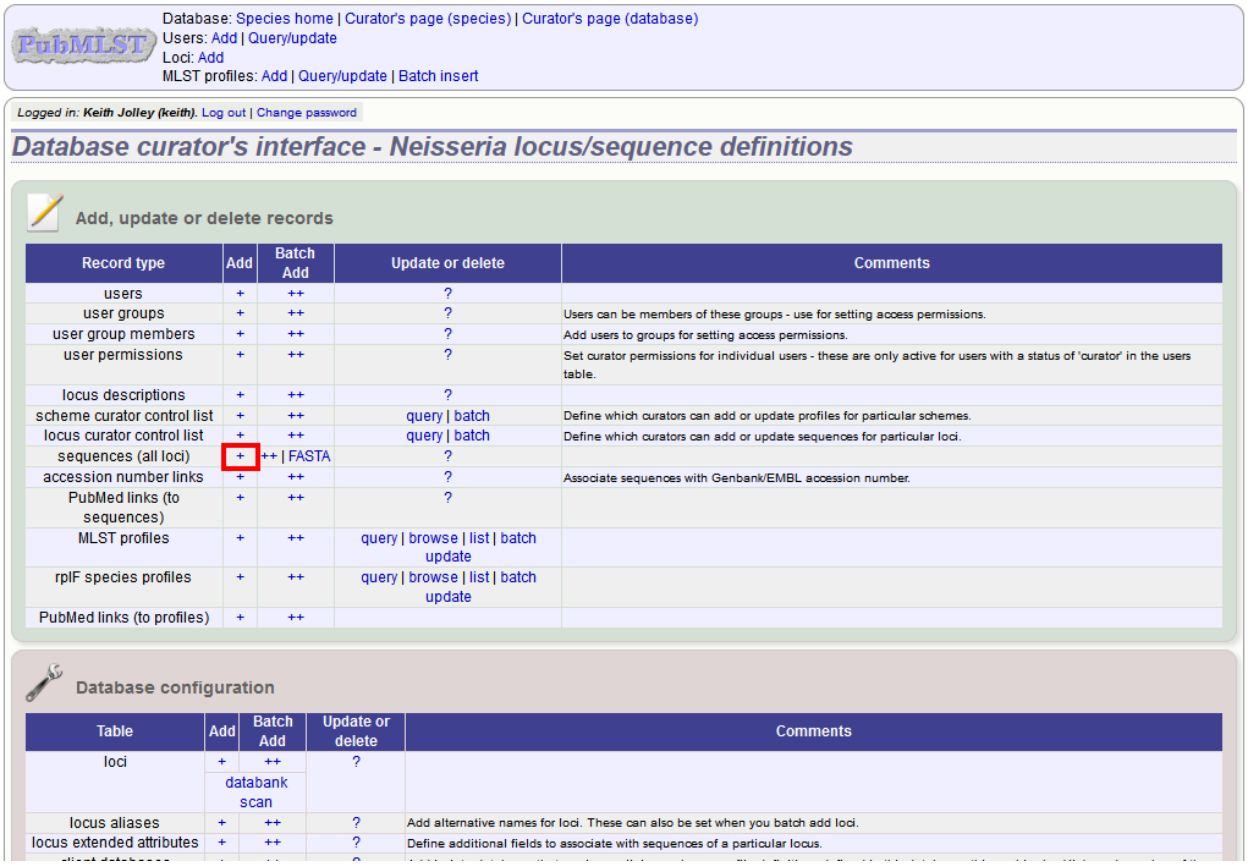


Normally the status should be set as 'user'. Only admins and curators with special permissions can create users with a status of curator or admin.

6.2 Adding new allele sequence definitions

6.2.1 Single allele

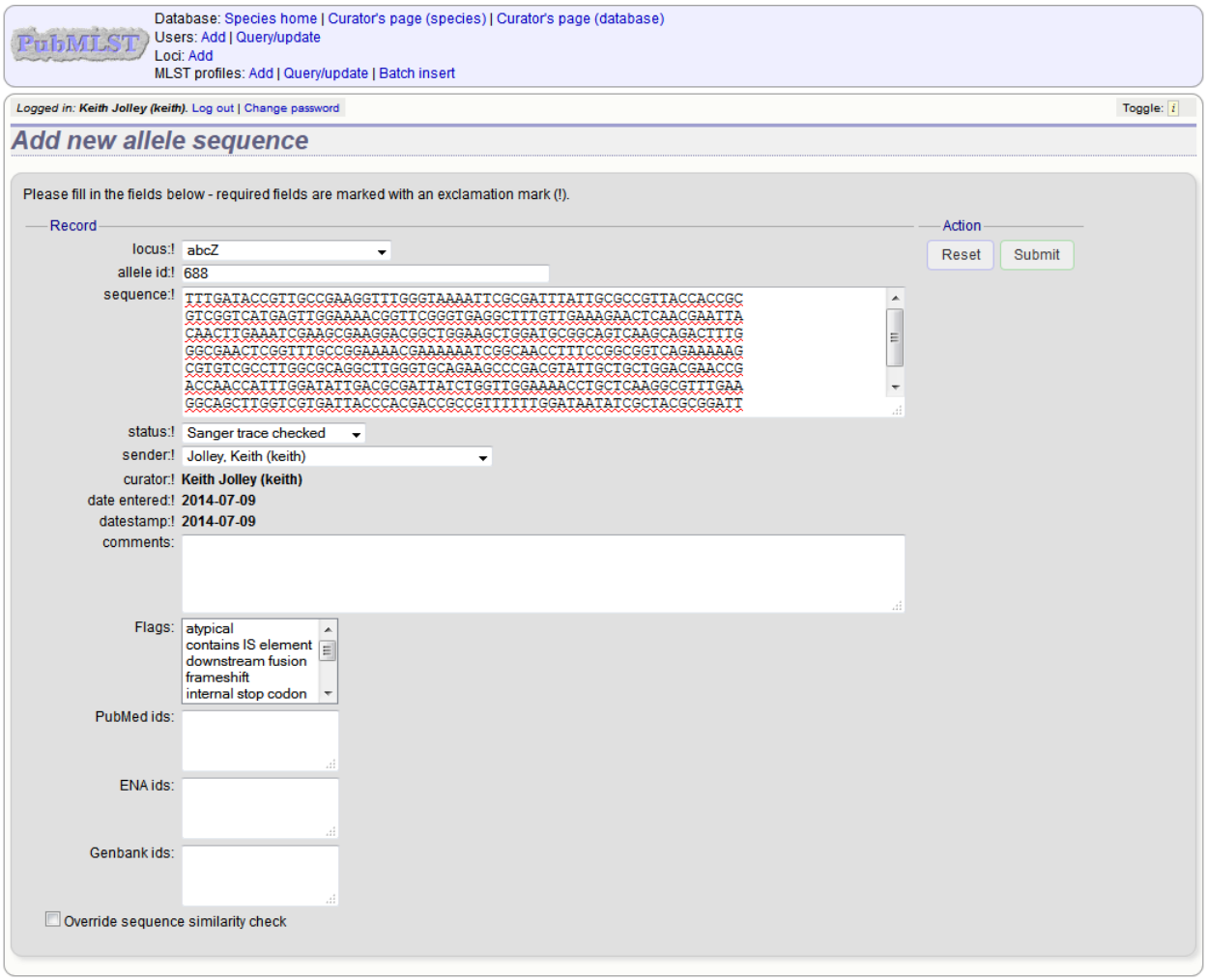
To add a single new allele, click the sequences (all loci) add (+) link on the curator's main page - if only a few loci are defined with permission for the current user to curate then they will be listed individually and the specific locus allele addition links can also be used.



Select the locus from the dropdown list box. The next available allele id will be entered automatically (if the allele id format is set to integer). Paste the sequence in to form, set the status and select the sender name from the dropdown box. If the sender does not appear in the box, you will need to add them to the registered users.

The status can either be:

- Sanger trace checked
- WGS: manual extract
- WGS: automated extract
- unchecked



Press submit. By default, the system will test whether your sequence is similar enough to existing alleles defined for that locus. The sequence will be rejected if it isn't considered similar enough. This test can be overridden by checking the 'Override sequence similarity check' checkbox at the bottom.

See also:

allele sequence flags

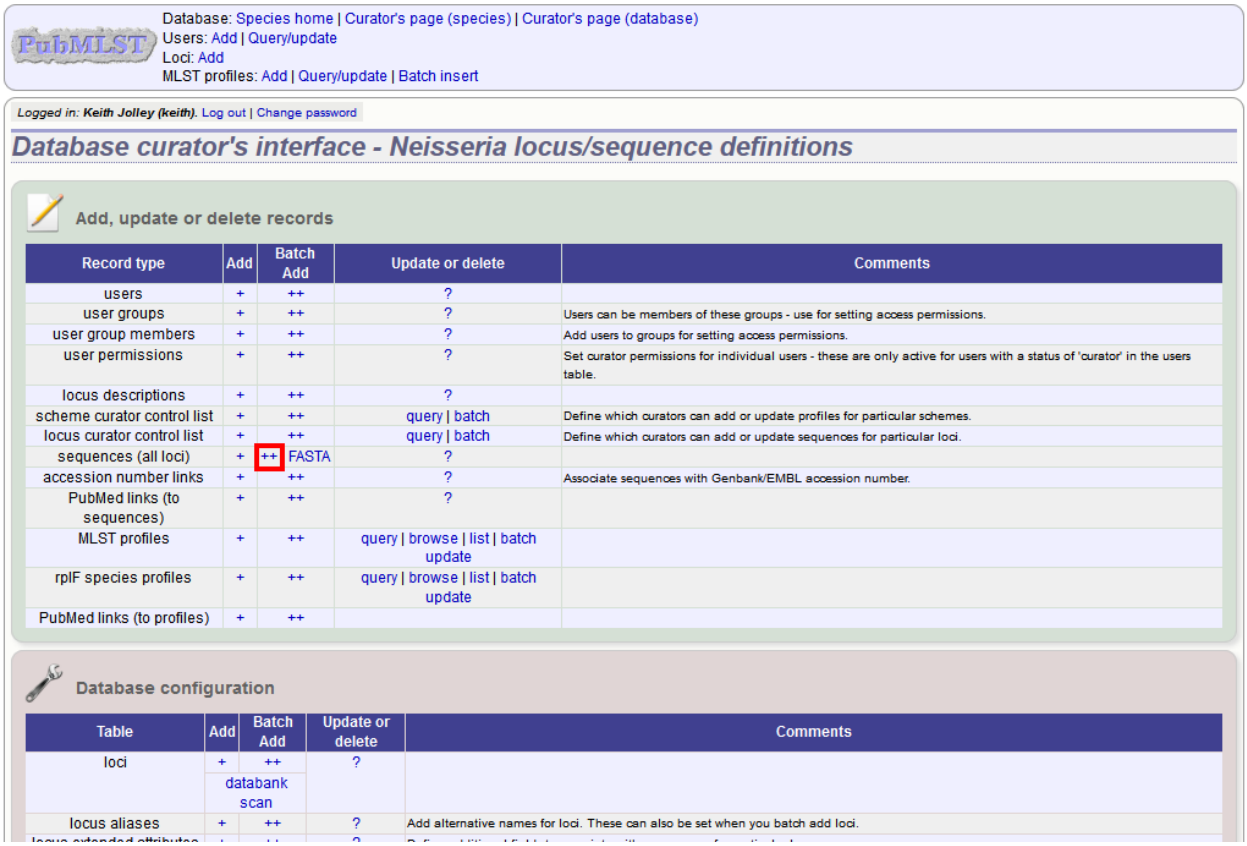
Sequences can also be associated with PubMed, ENA or Genbank id numbers by entering these as lists (one value per line) in the appropriate form box.

6.2.2 Batch adding multiple alleles

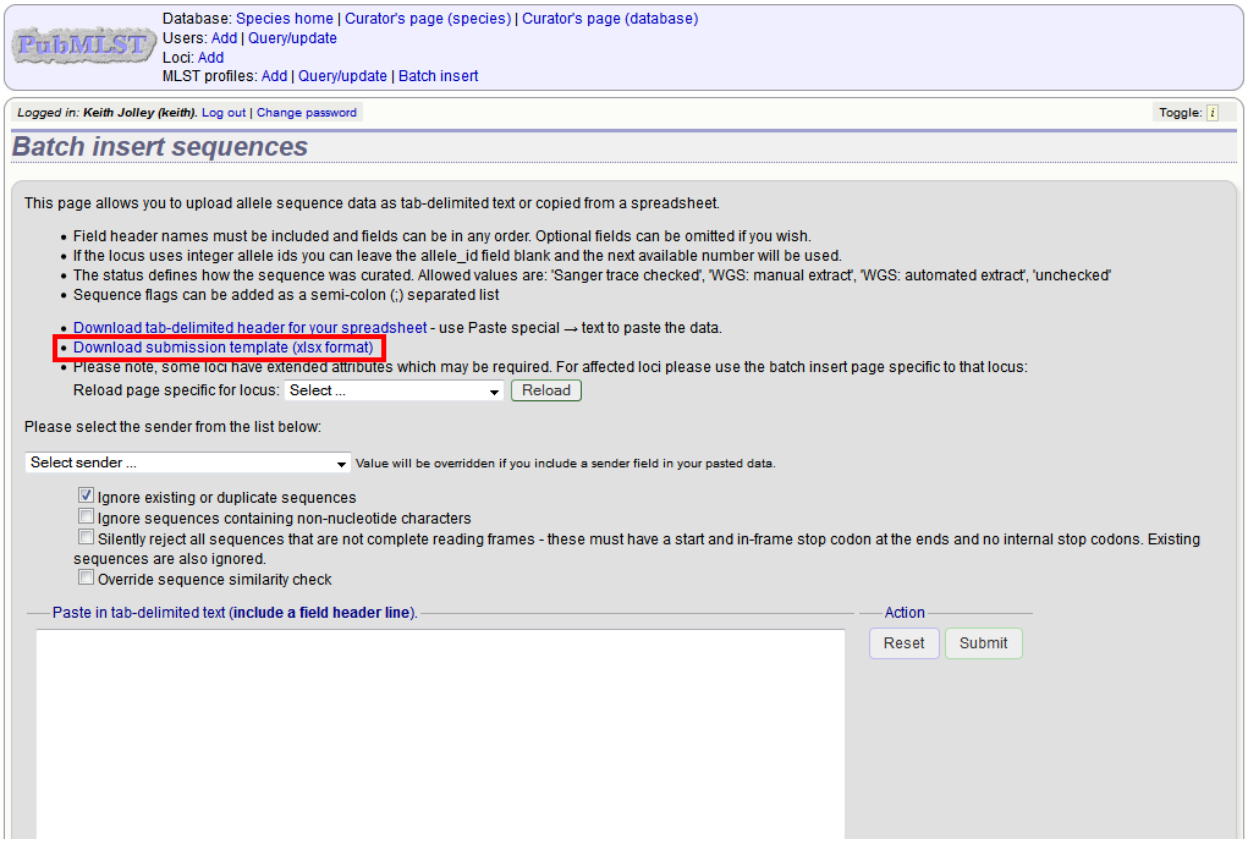
There are two methods of batch adding alleles. You can either upload a spreadsheet with all fields in tabular format, or you can upload a FASTA file provided all sequences are for the same locus and have the same status.

Upload using a spreadsheet

Click the batch add (++) sequences (all loci) link on the curator's main page.



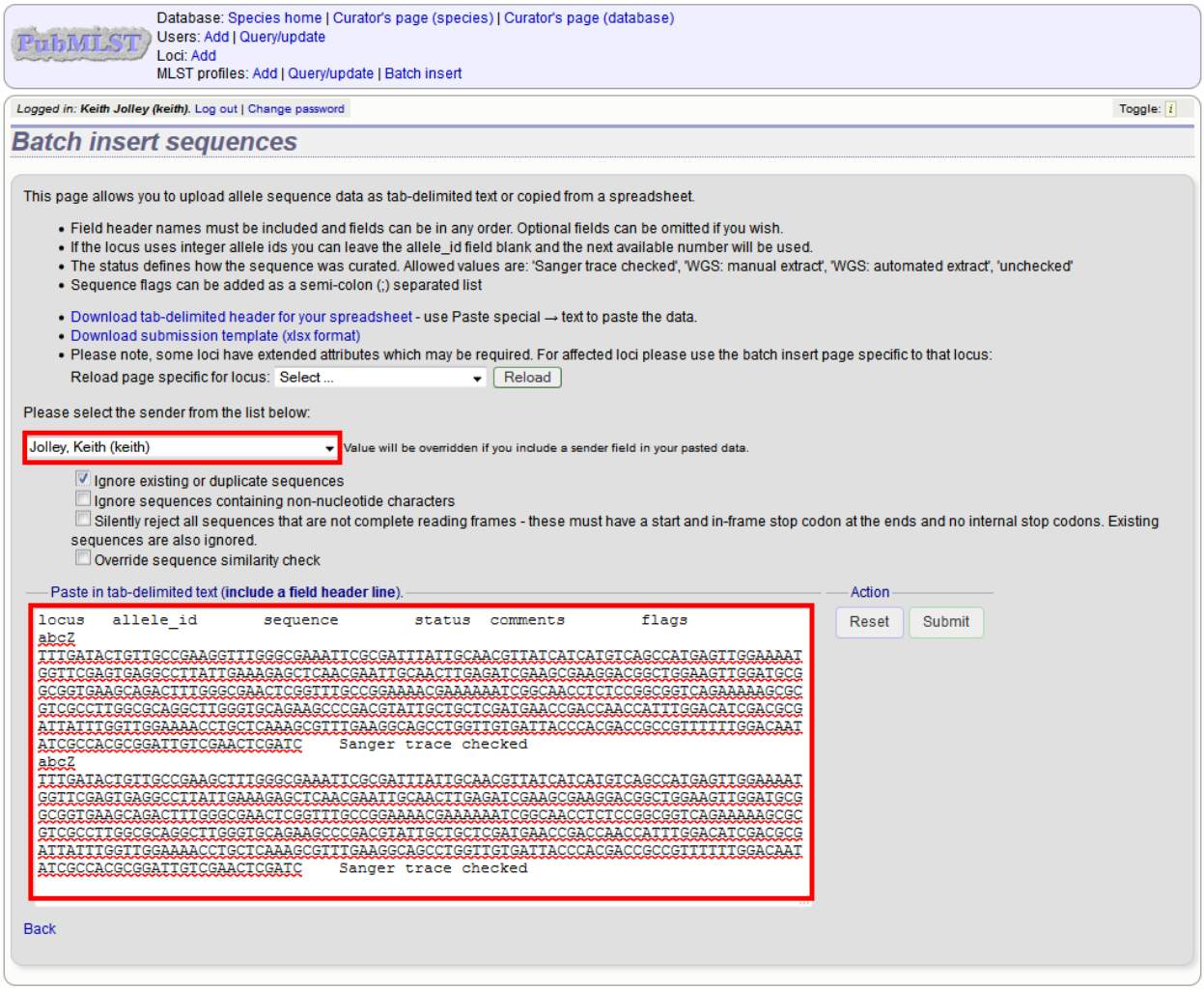
Download a template Excel file from the following page.



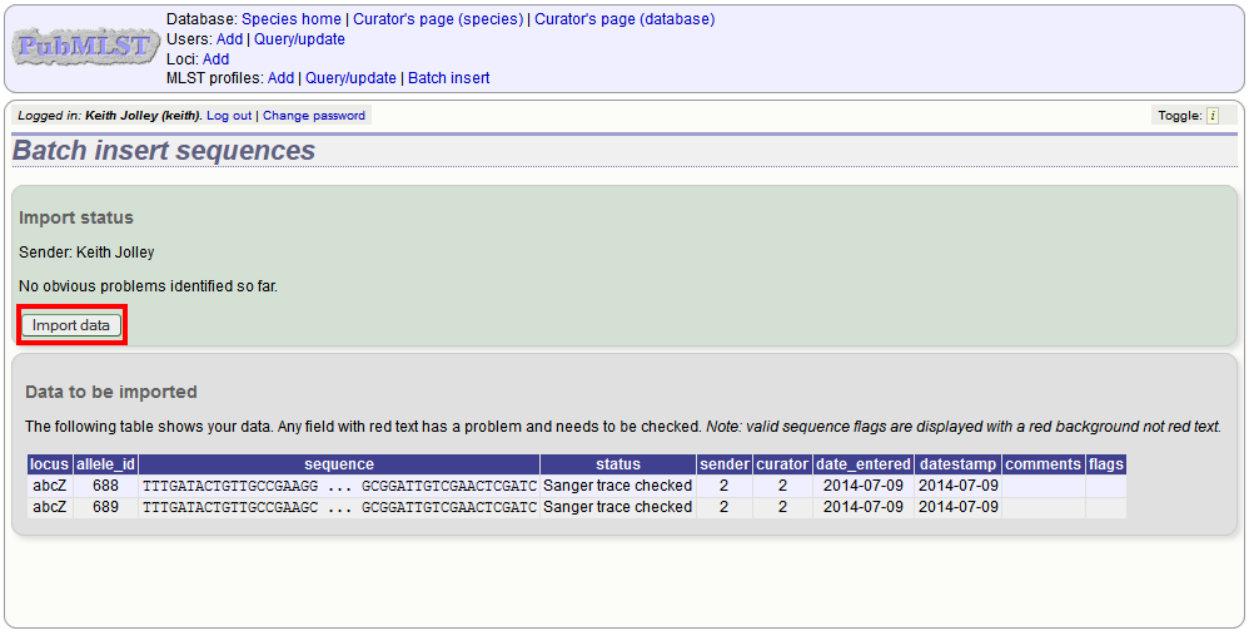
Fill in the spreadsheet. If the locus uses integer allele identifiers, the allele_id can be left blank and the next available number will be used automatically. Paste the entire sheet in to the web form and select the sender from the dropdown box.

Additionally, there are a number of options available. Some of these will ignore sequences if they don't match certain criteria - this is useful when sequence data has been extracted from genomes automatically. Available options are:

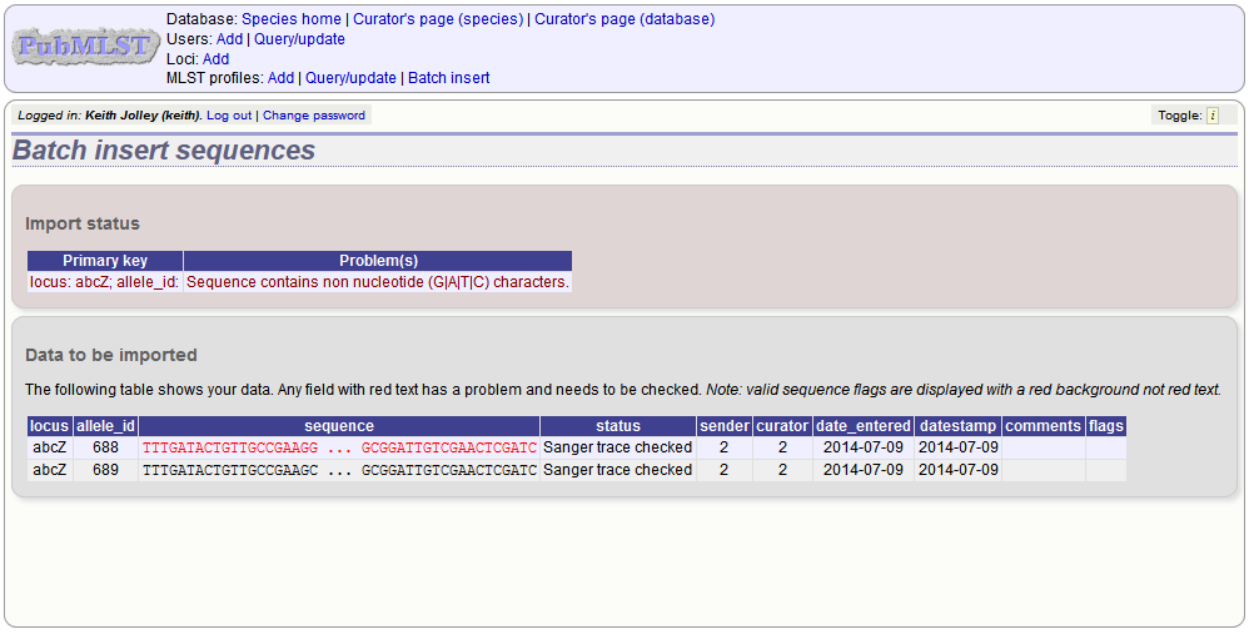
- Ignore existing or duplicate sequences.
- Ignore sequences containing non-nucleotide characters.
- Silently reject all sequences that are not complete reading frames - these must have a start and in-frame stop codon at the ends and no internal stop codons. Existing sequences are also ignored.
- Override sequence similarity check.



Press submit. You will be presented with a page indicating what data will be uploaded. This gives you a chance to back out of the upload. Click 'Import data'.



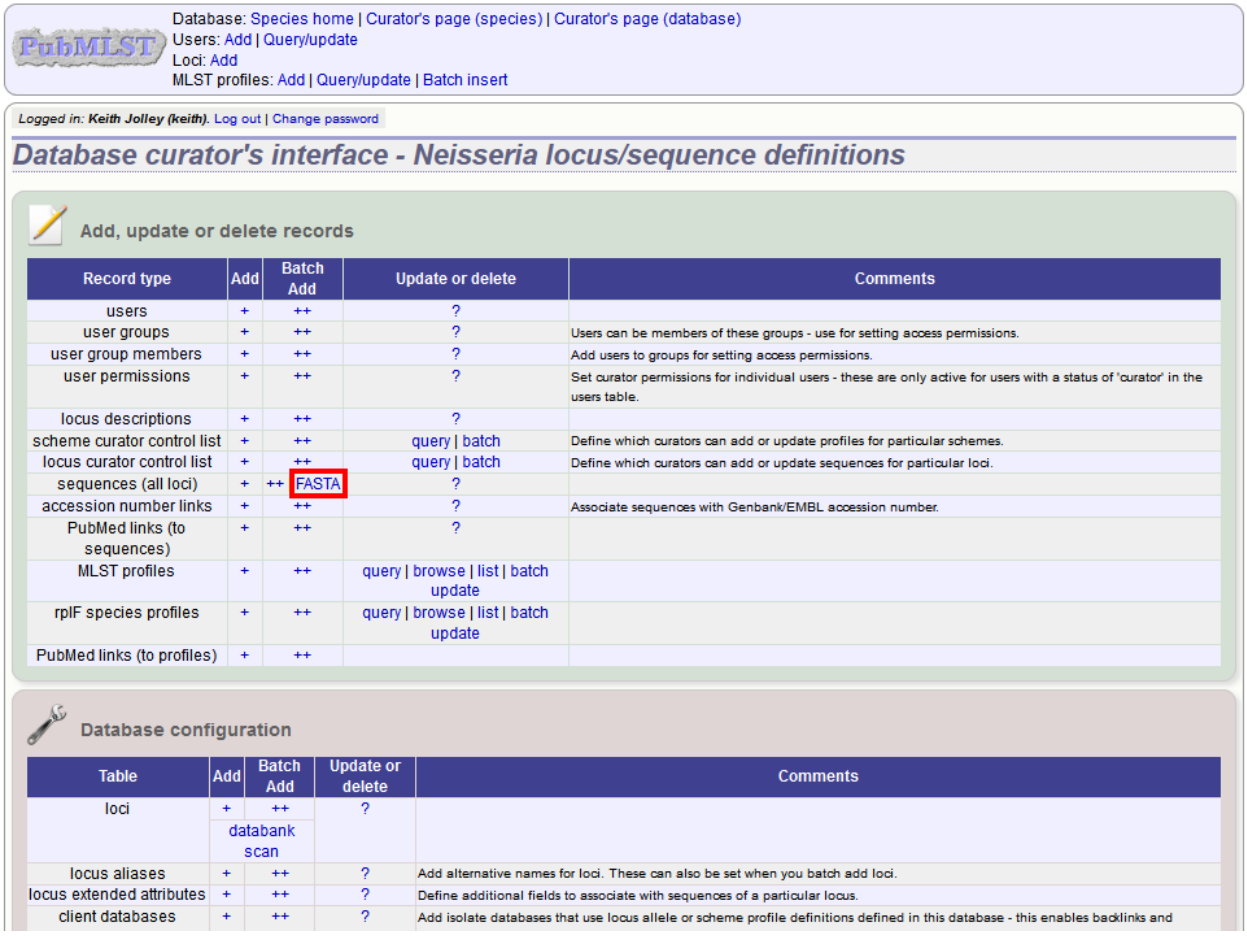
If there are any problems with the submission, these should be indicated at this stage, e.g.:



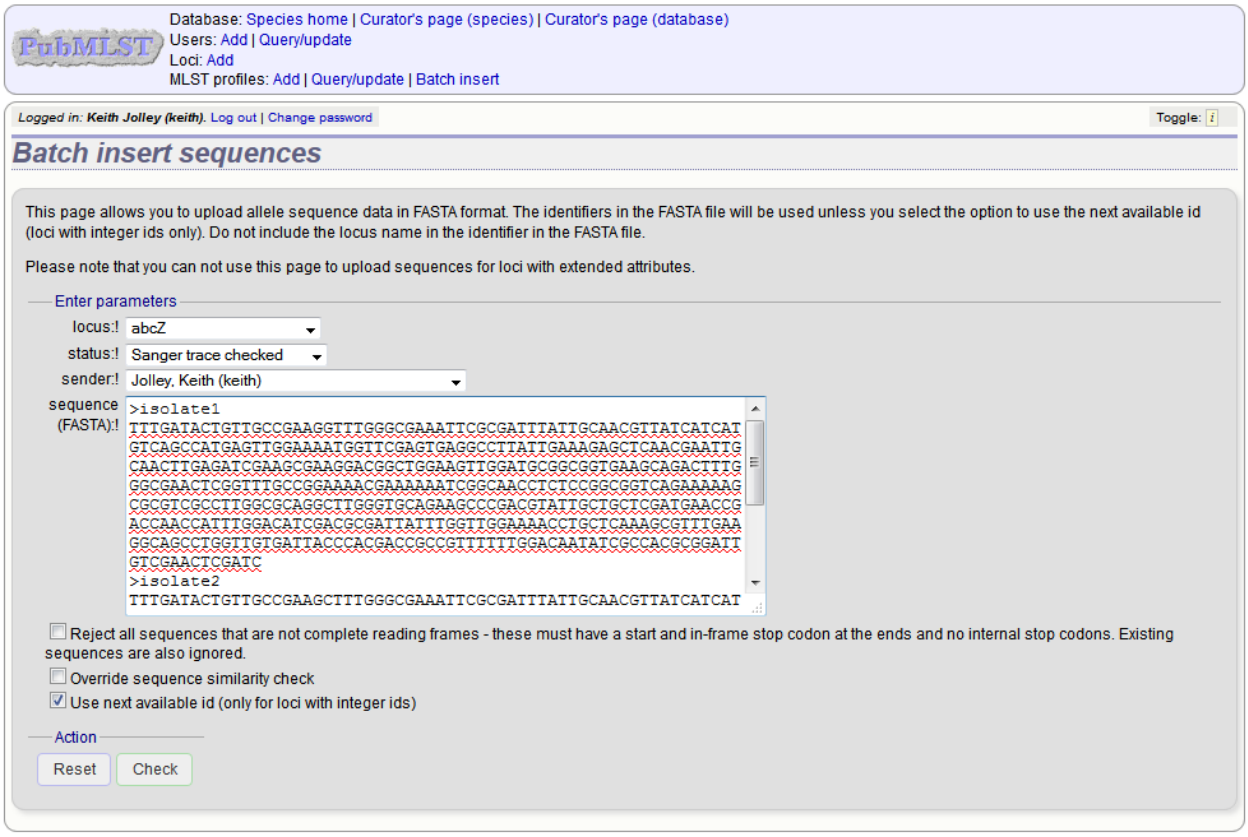
Upload using a FASTA file

Uploading new alleles from a FASTA file is usually more straightforward than generating an Excel sheet.

Click 'FASTA' upload on the curator's contents page.



Select the locus, status and sender from the dropdown boxes and paste in the new sequences in FASTA format.

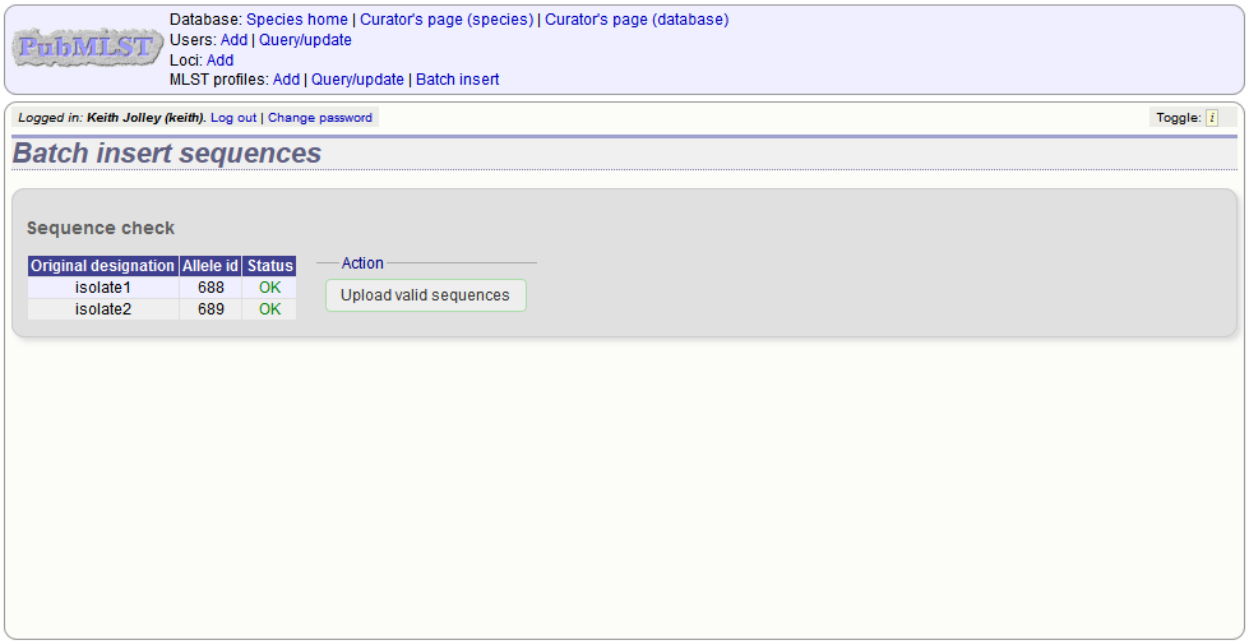


For loci with integer ids, the next available id number will be used by default (and the identifier in the FASTA file will be ignored). Alternatively, you can indicate the allele identifier within the FASTA file (do not include the locus name in this identifier).

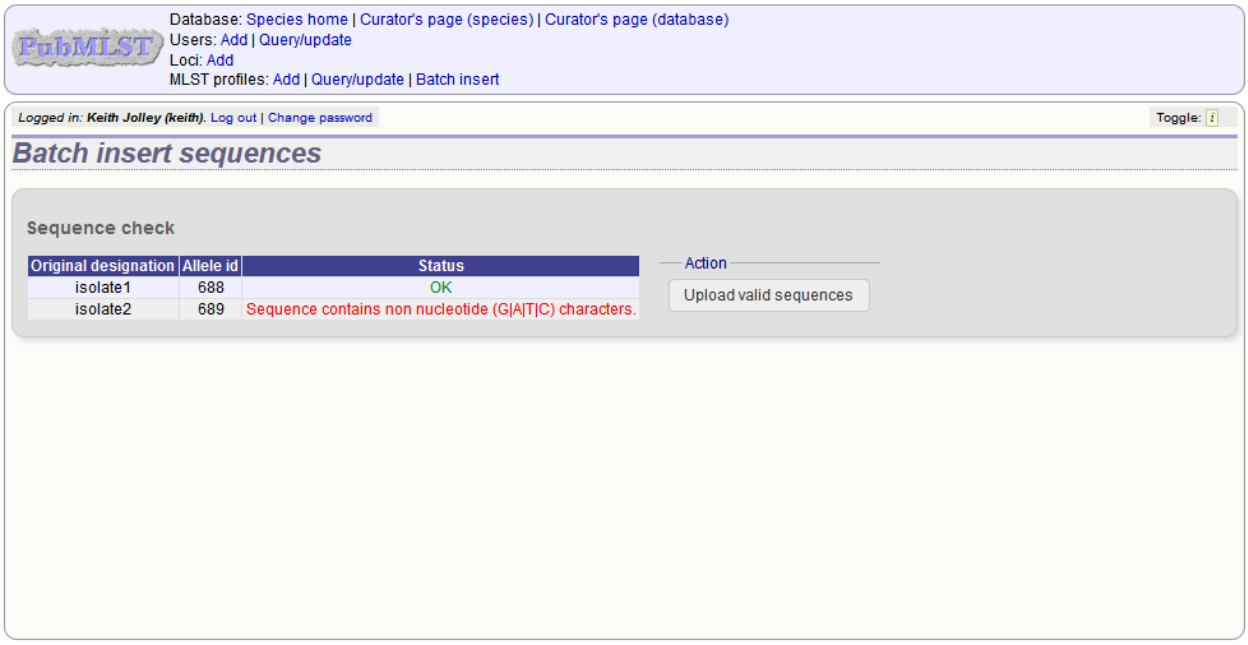
As with the spreadsheet upload, you can select options to ignore selected sequences if they don't match specific criteria.

Click 'Check'.

The sequences will be checked. You will be presented with a page indicating what data will be uploaded. This gives you a chance to back out of the upload. Click 'Upload valid sequences'.



Any invalid sequences will be indicated in this confirmation page and these will not be uploaded (you can still upload the others), e.g.

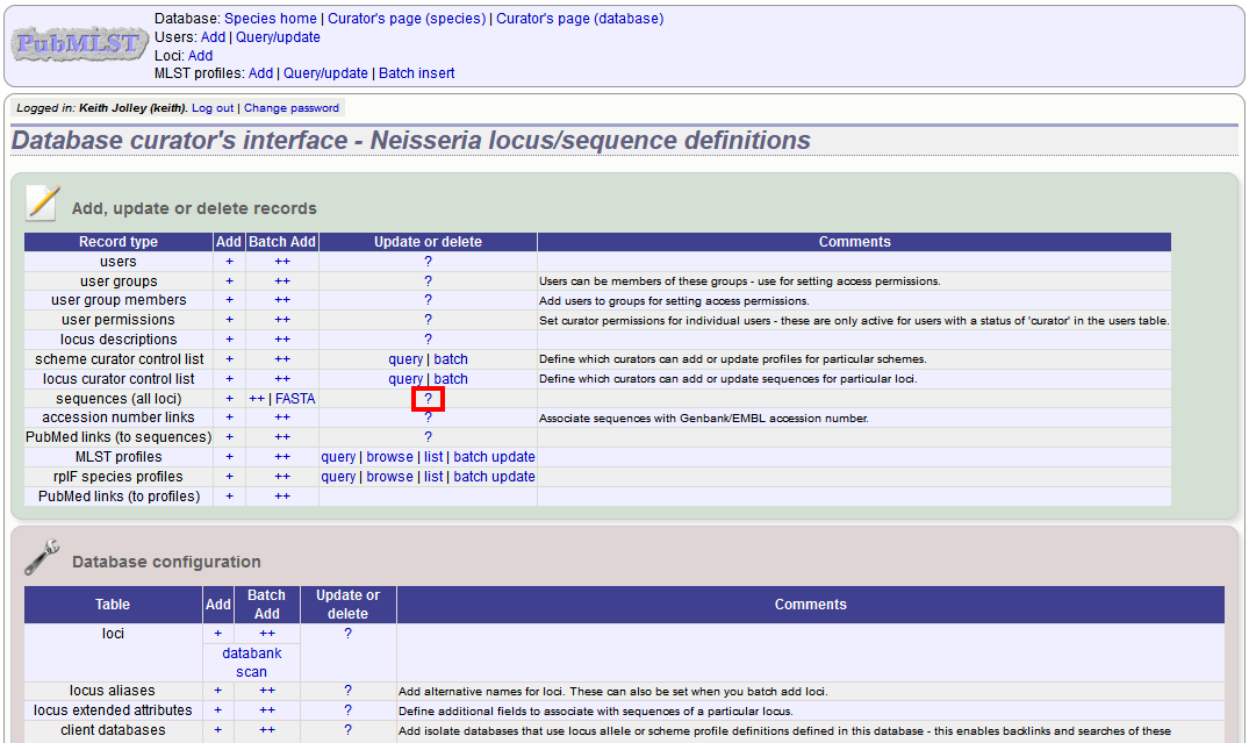


6.3 Updating and deleting allele sequence definitions

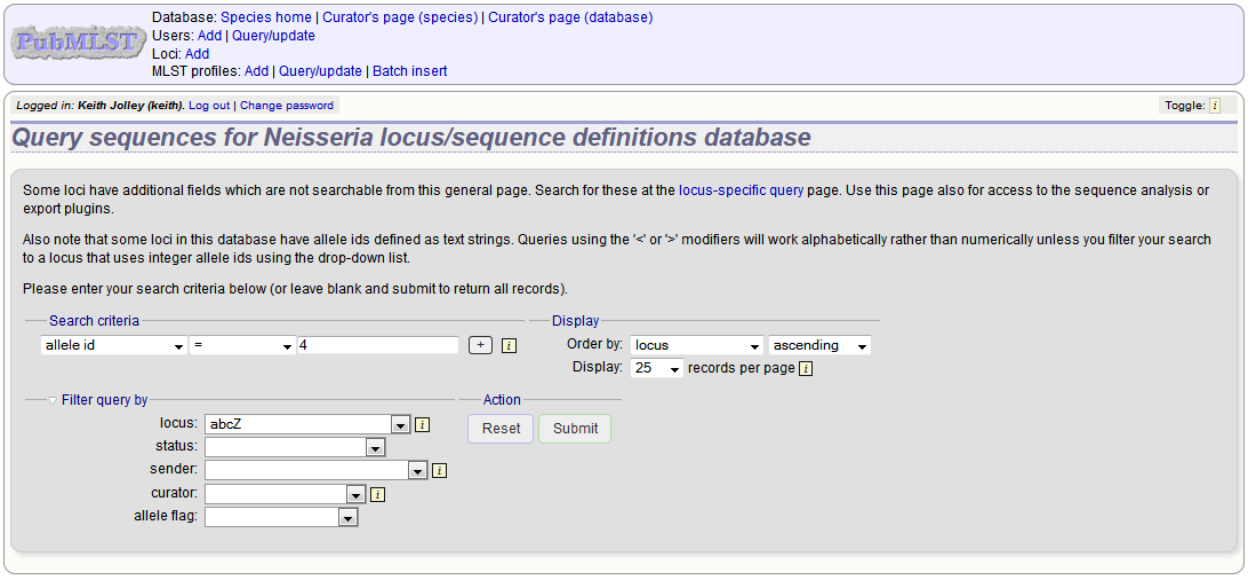
Note: You cannot update the sequence of an allele definition. This is for reasons of data integrity since an allele may form part of a scheme profile and be referred to in multiple databases. If you really need to change a sequence, you will have to remove the allele definition and then re-add it.

In order to update or delete an allele, first you must select it. Click the query (?) sequences (all loci) link - if only a

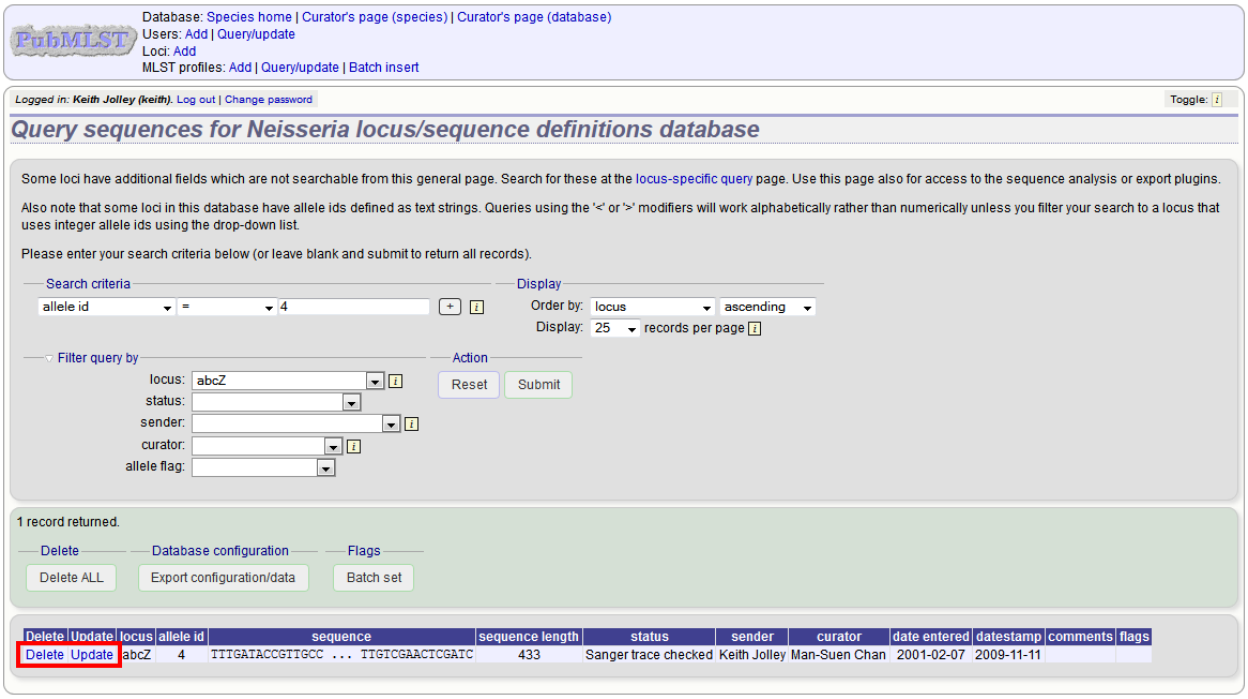
few loci are defined with permission for the current user to curate then they will be listed individually and the specific locus query links can also be used.



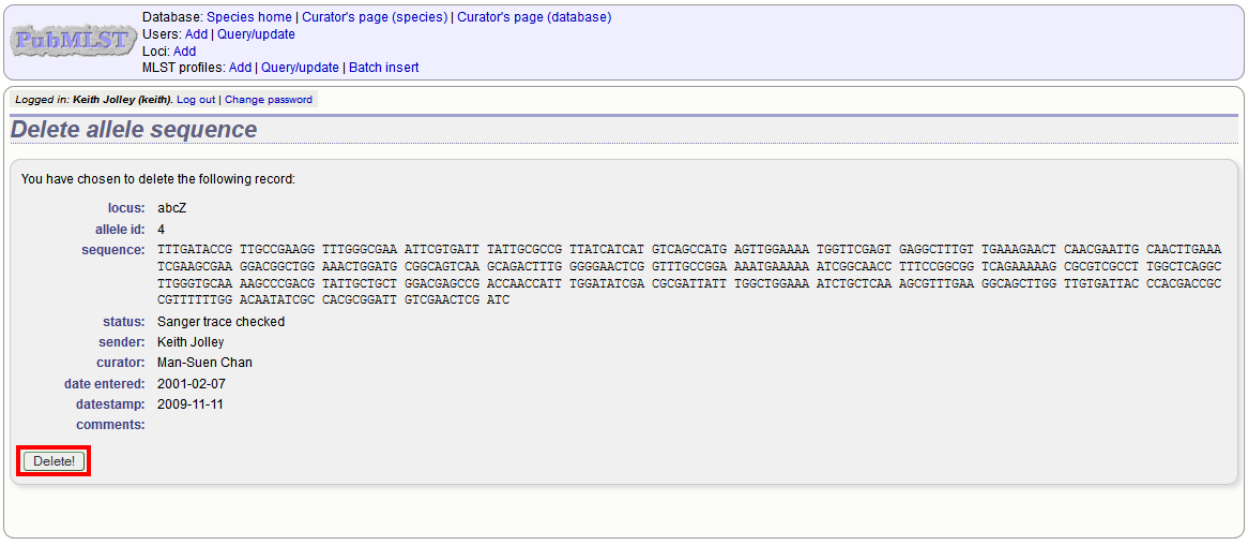
Either search for specific attributes in the search form, or leave it blank and click 'Submit' to return all alleles. For a specific allele, select the locus in the filter and enter the allele number in the allele_id field.



Click the appropriate link to either update the allele attributes or to delete it. If you have appropriate permissions, there may also be a link to 'Delete ALL'. This allows you to quickly delete all alleles returned from a search.

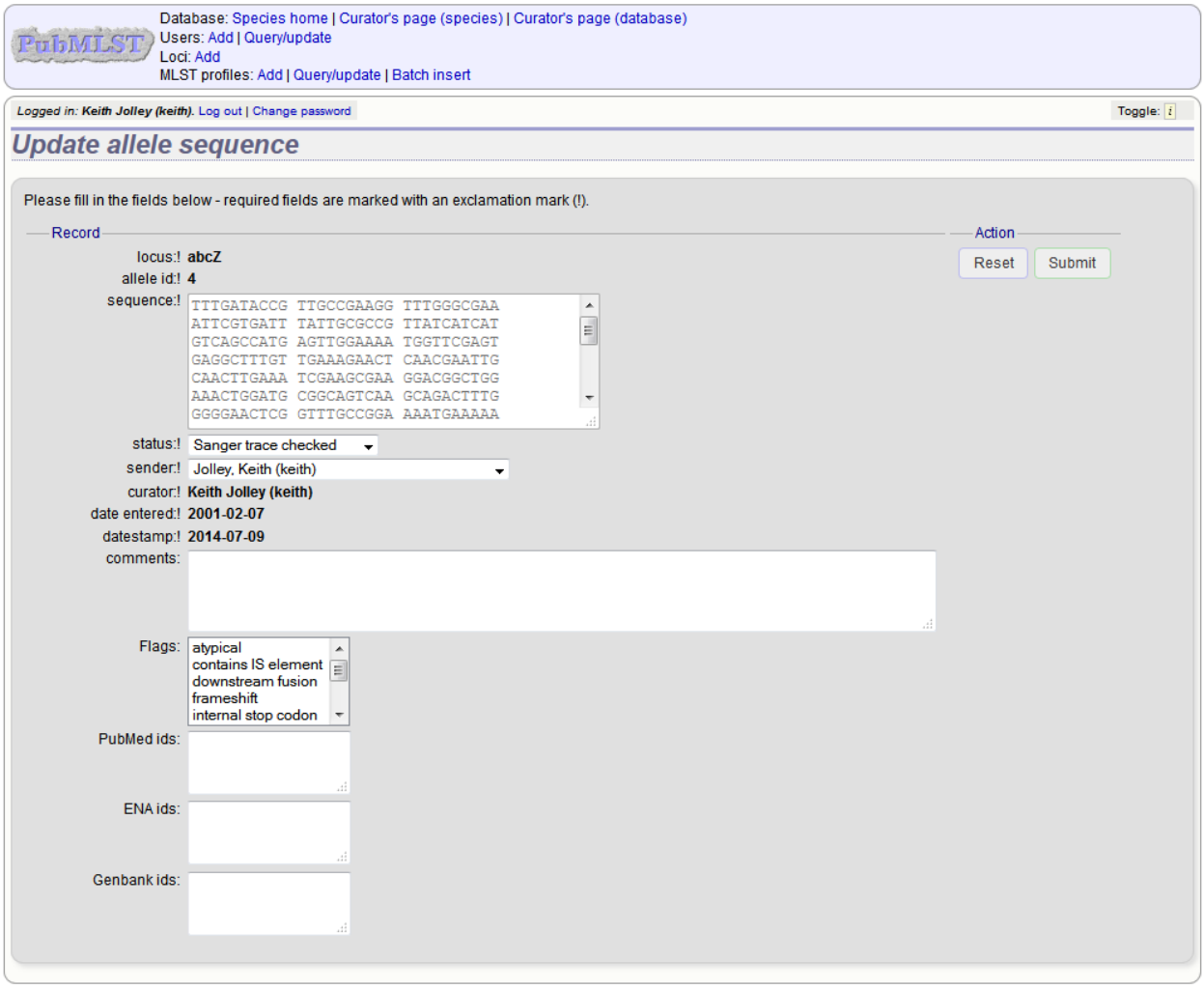


If you choose to delete, you will be presented with a final confirmation screen. To go ahead, click 'Delete!'. Deletion will not be possible if the allele is part of a scheme profile - if it is you will need to delete any profiles that it is a member of first.



If instead you clicked 'Update', you will be able to modify attributes of the sequence, or link PubMed, ENA or Genbank records to it. You will not be able to modify the sequence itself.

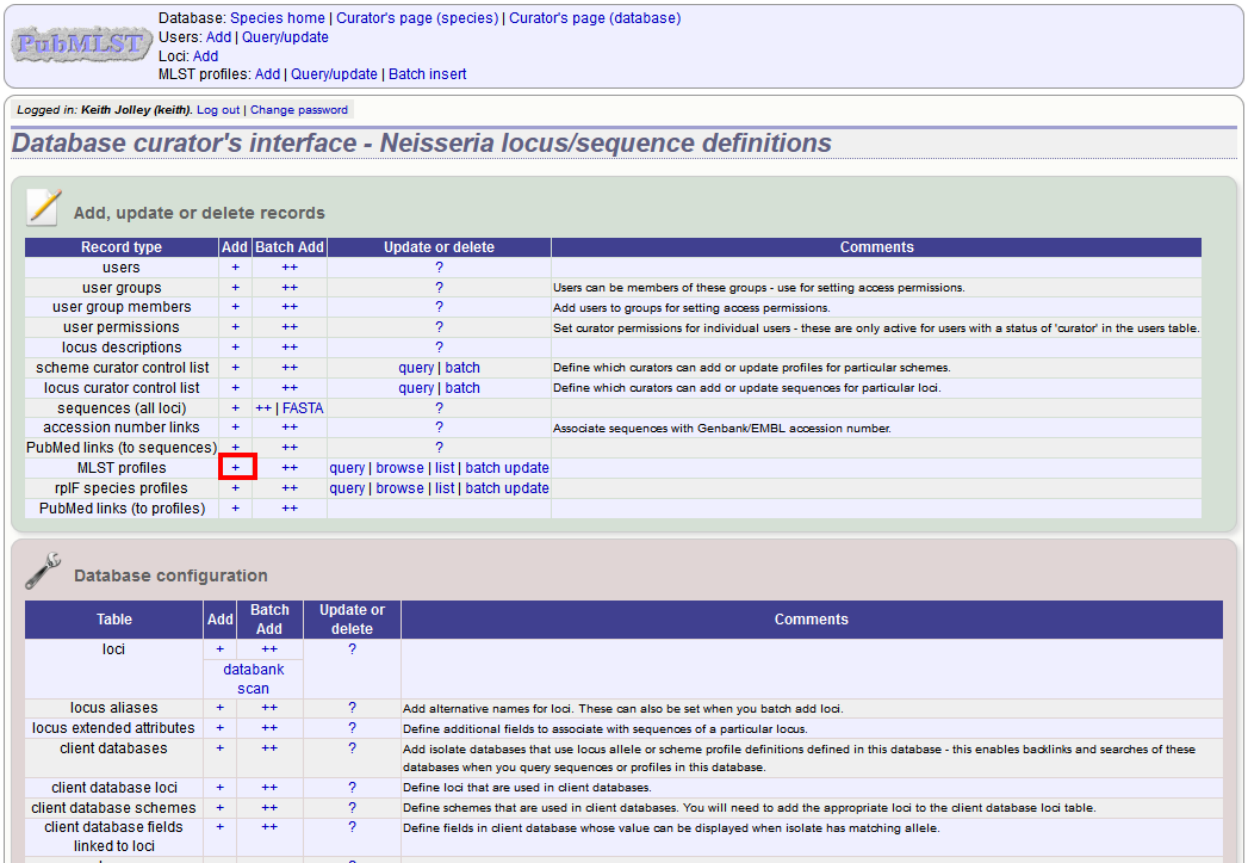
Note: Adding flags and comments to an allele record requires that this feature is enabled in the *database configuration*.



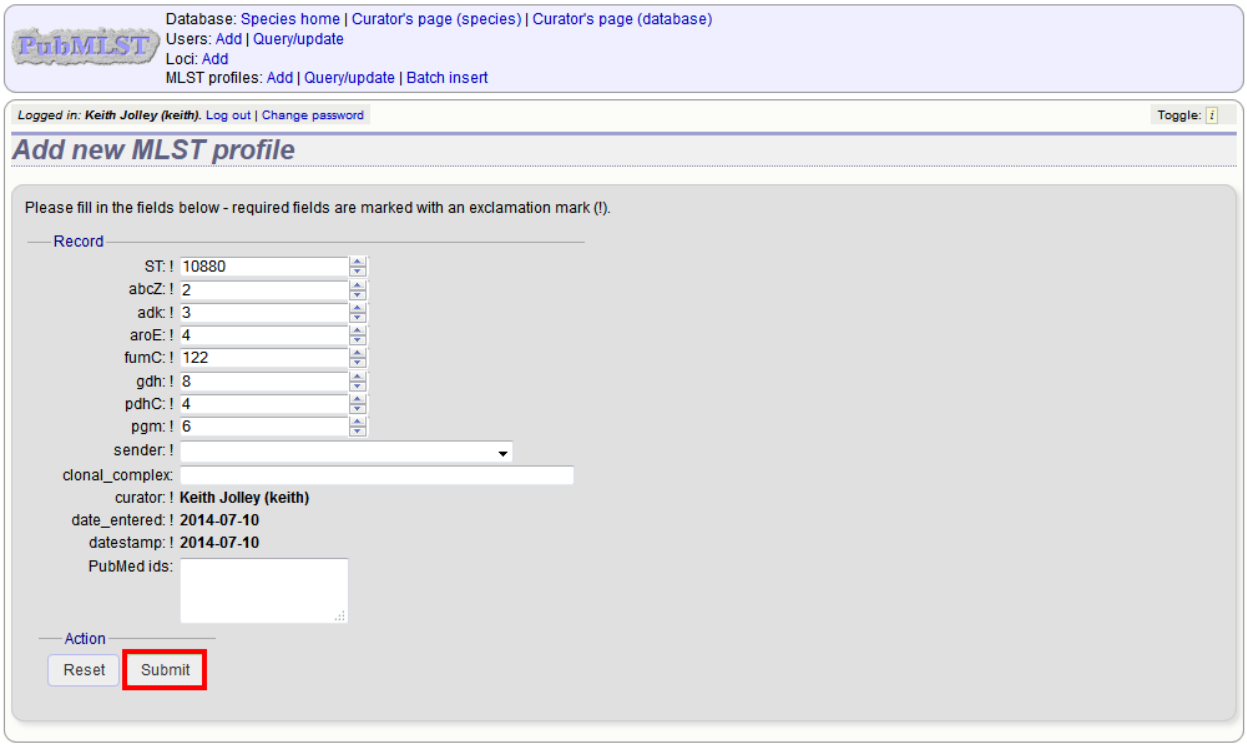
6.4 Adding new scheme profile definitions

Provided a scheme has been set up with at least one locus and a scheme field set as a primary key, there will be links on the curator's main page to add profiles for that scheme.

To add a single profile you can click the add (+) profiles link next to the scheme name (e.g. MLST):

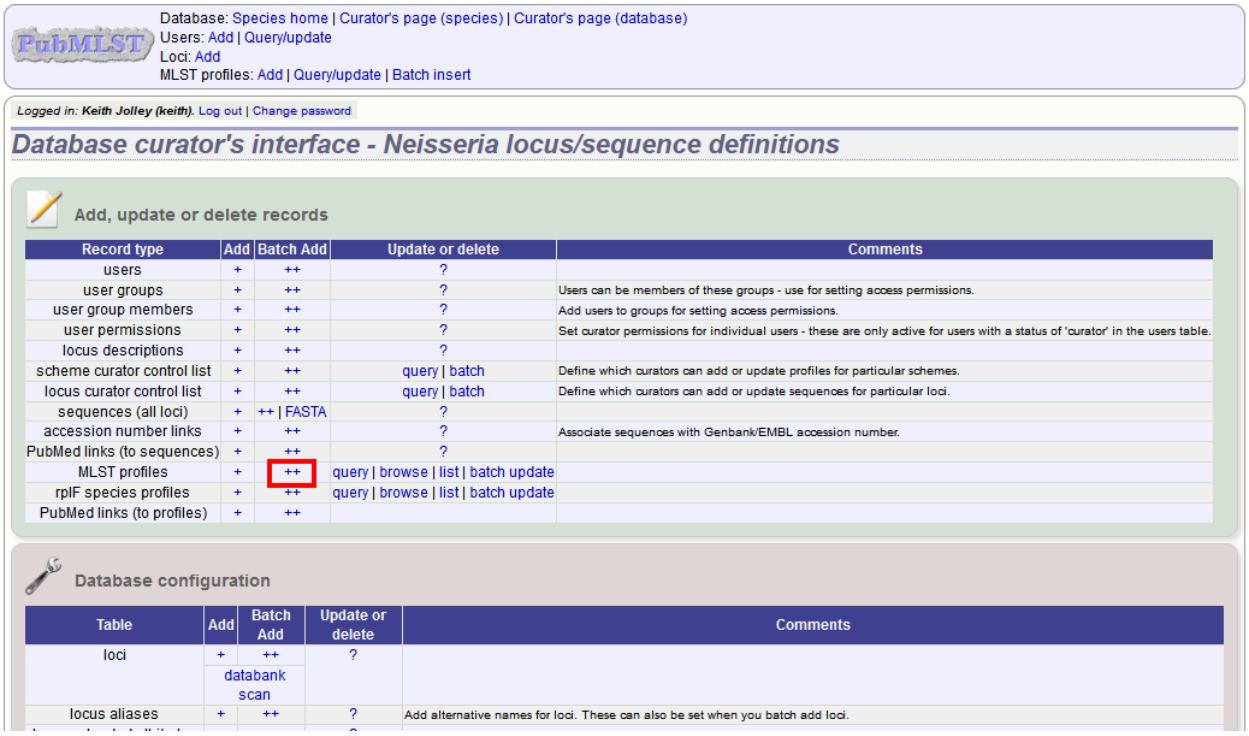


A form will be displayed with the next available primary key number already entered (provided integers are used for the primary key format). Enter the new profile, associated scheme fields, and the sender, then click 'Submit'. The new profile will be added provided the primary key or the profile has not previously been entered.

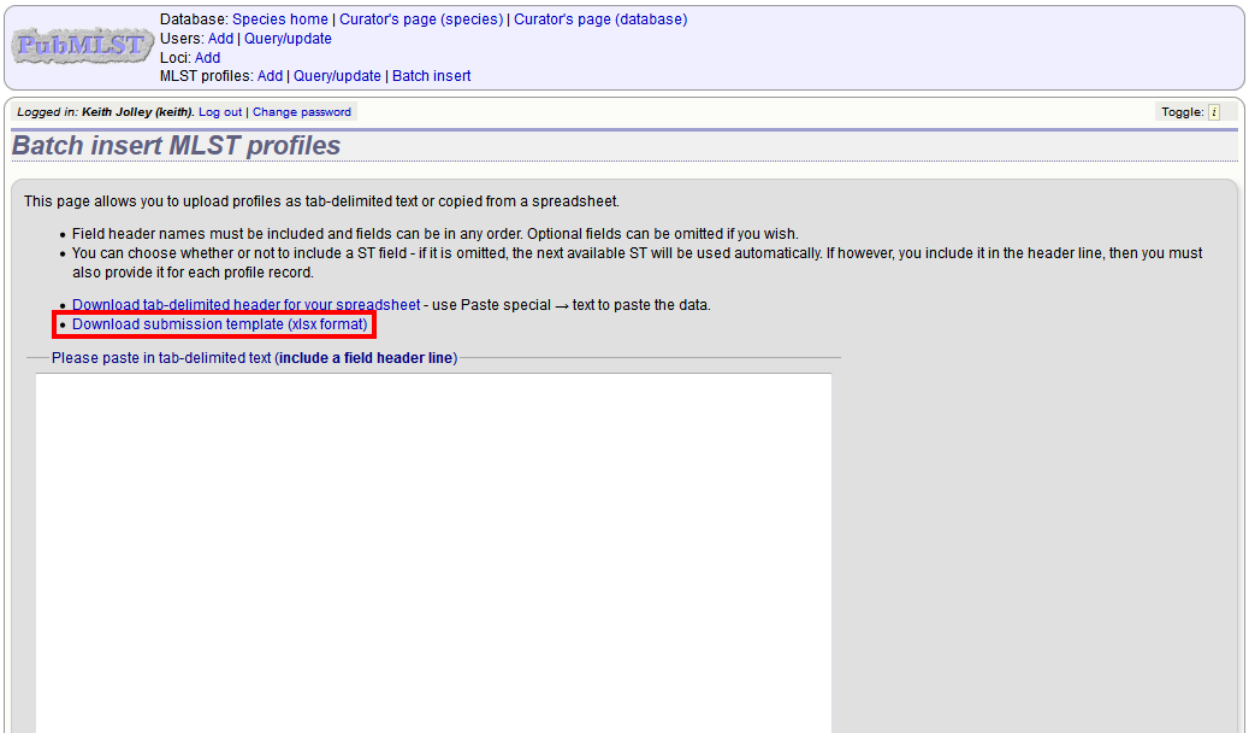


More usually, profiles are added in a batch mode. It is often easier to do this even for a single profile since it allows copying and pasting data from a spreadsheet.

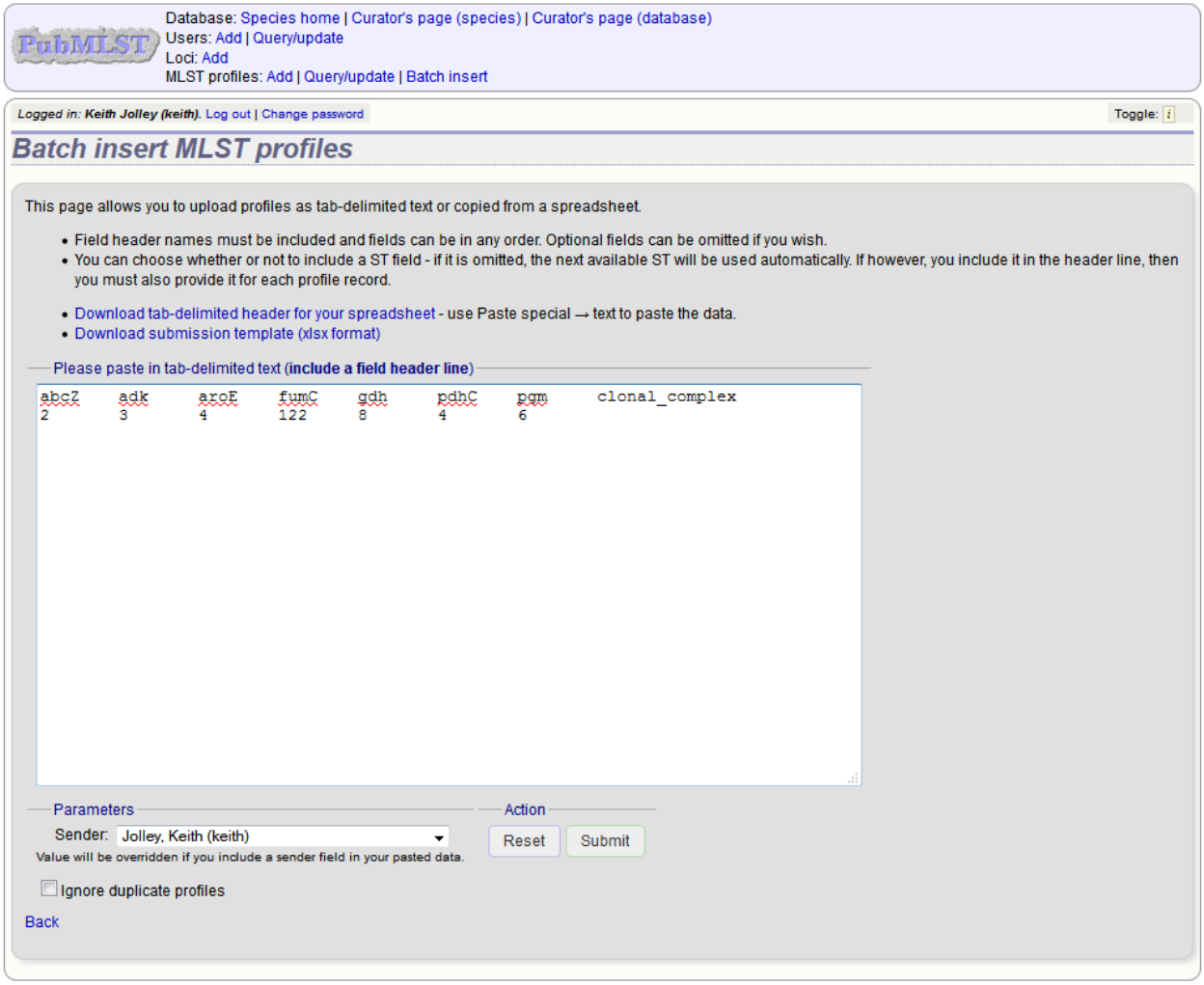
Click the batch add (++) profiles link next to the scheme name:



Click the 'Download submission template (xlsx format)' link to download an Excel submission template.



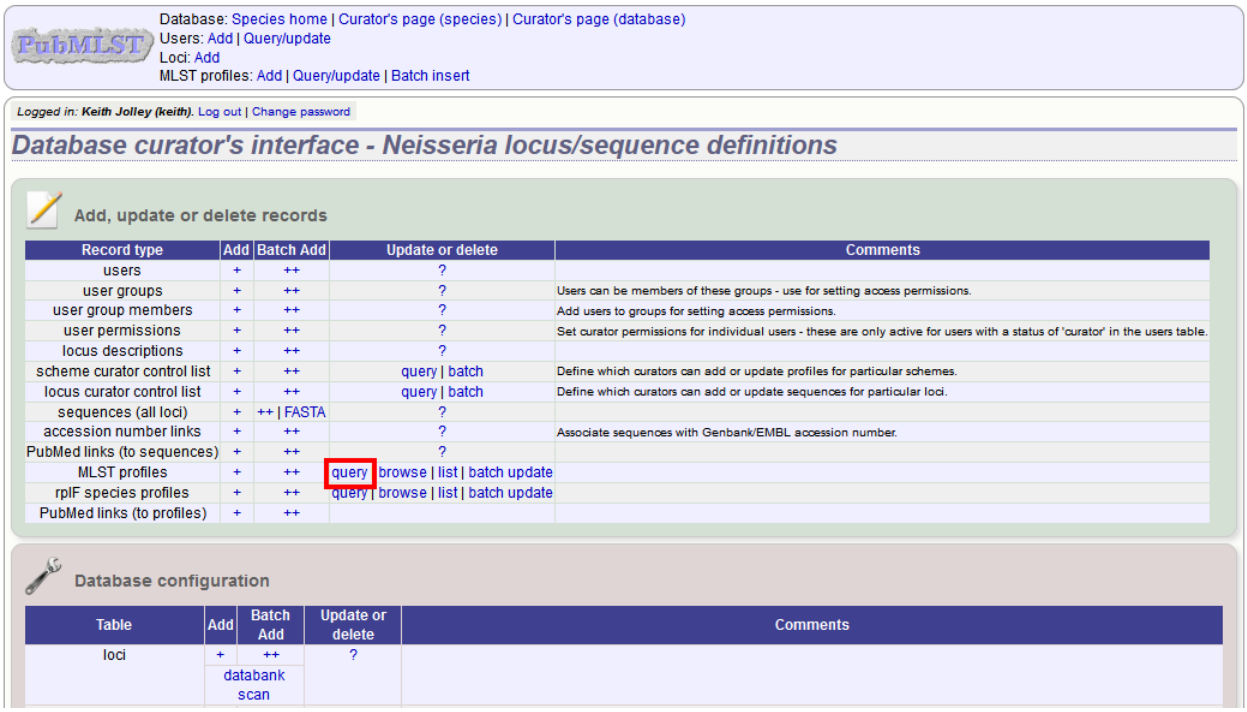
Fill in the spreadsheet using the copied template, then copy and paste the whole spreadsheet in to the large form on the upload page. If the primary key has an integer format, you can exclude this column and the next available number will be used automatically. If the column is included, however, a value must be set. Select the sender from the dropdown list box and then click 'Submit'.



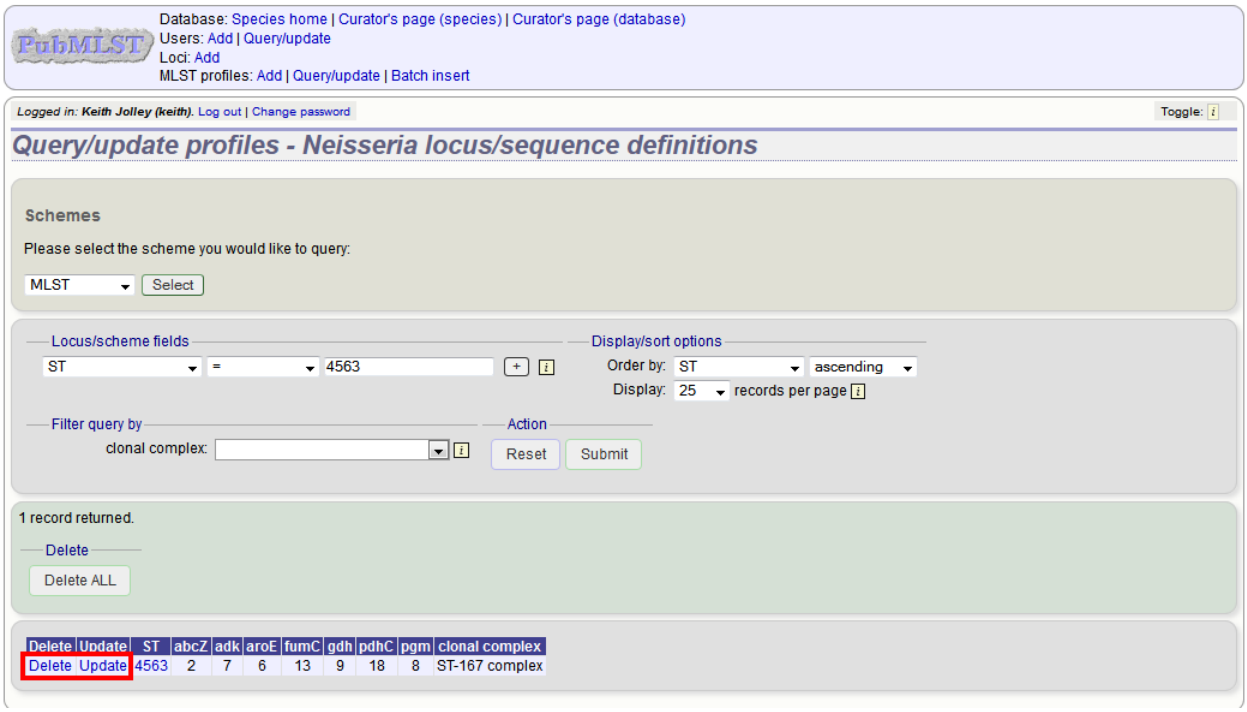
You will be given a final confirmation page stating what will be uploaded. If you wish to proceed with the submission, click 'Import data'.

6.5 Updating and deleting scheme profile definitions

In order to update or delete a scheme profile, first you must select it. Click the query (?) profiles link next to the scheme name (e.g. MLST):

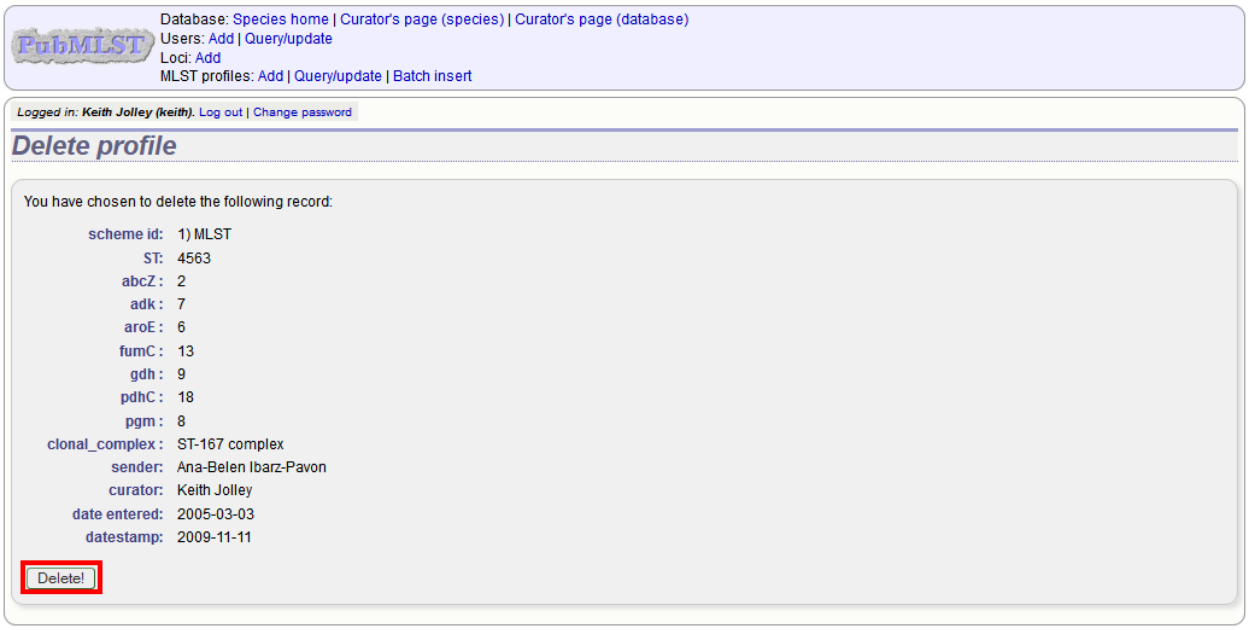


Search for your profile by entering search criteria (alternatively you can use the browse or list query functions).

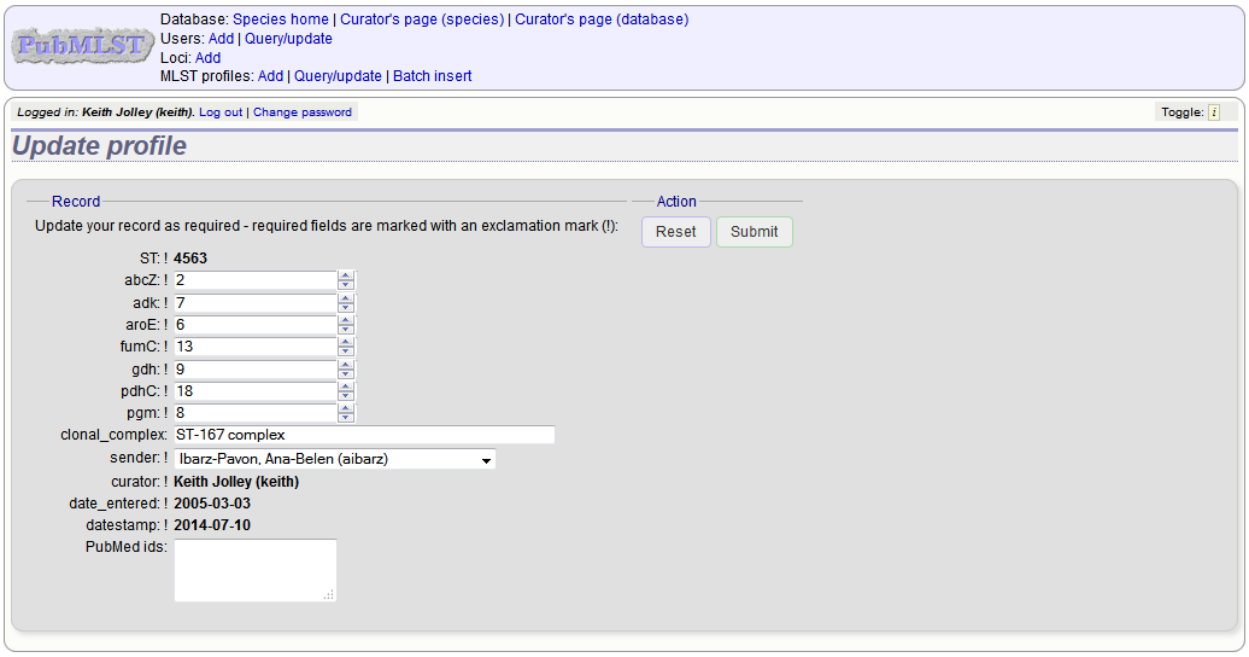


To delete the profile, click the 'Delete' link next to the profile. Alternatively, if your account has permission, you may be able to 'Delete ALL' records retrieved from the search.

For deletion of a single record, the full record will be displayed. Confirm deletion by clicking 'Delete!'.

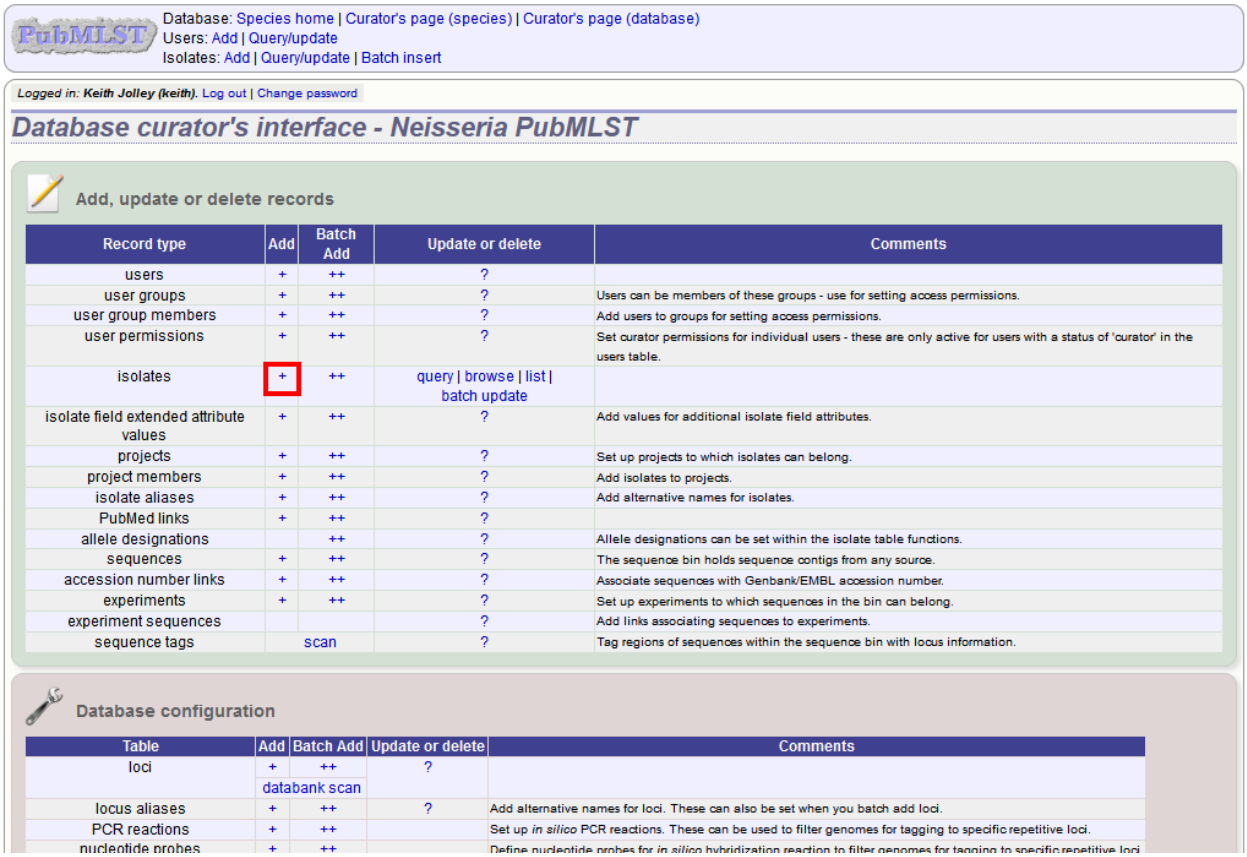


To modify the profile, click the 'Update' link next to the profile following the query. A form will be displayed - make any changes and then click 'Update'.

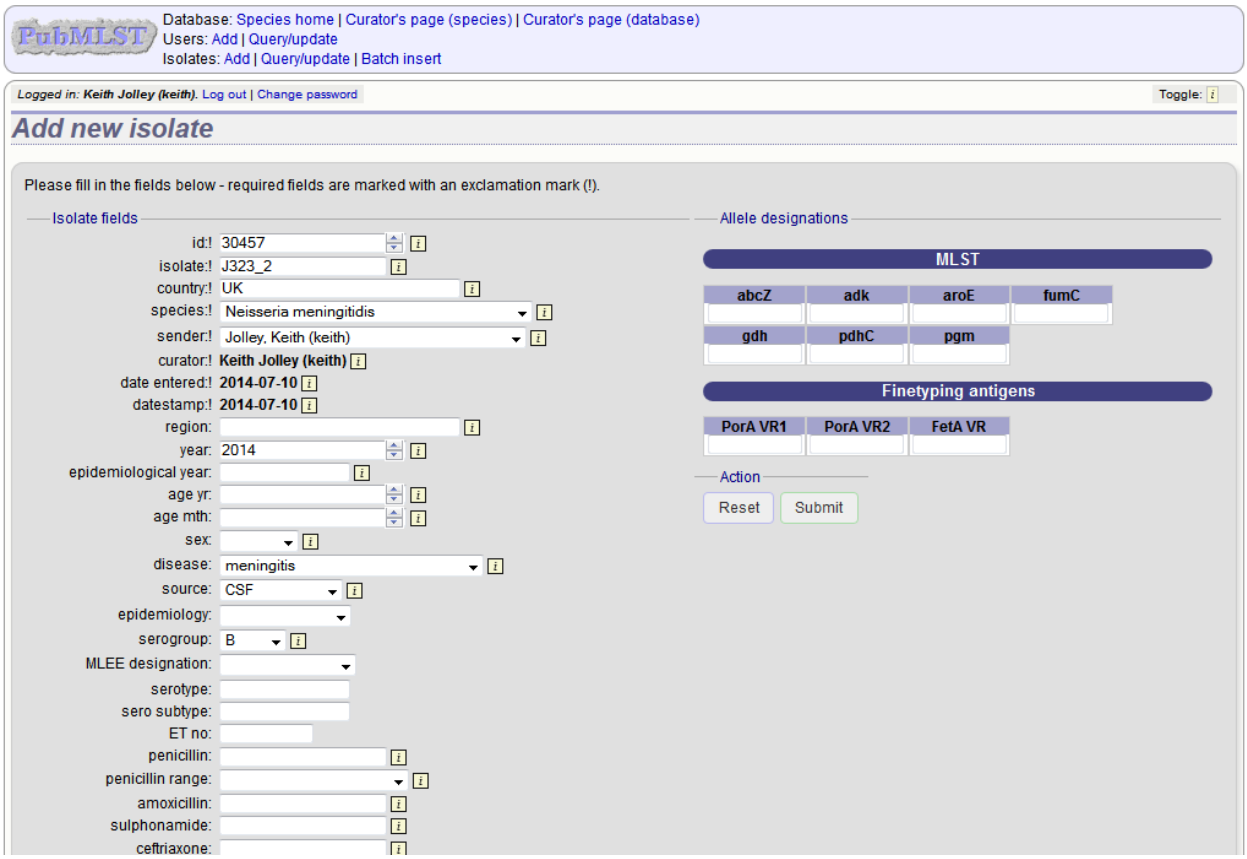


6.6 Adding isolate records

To add a single record, click the add (+) isolates link on the curator's index page.



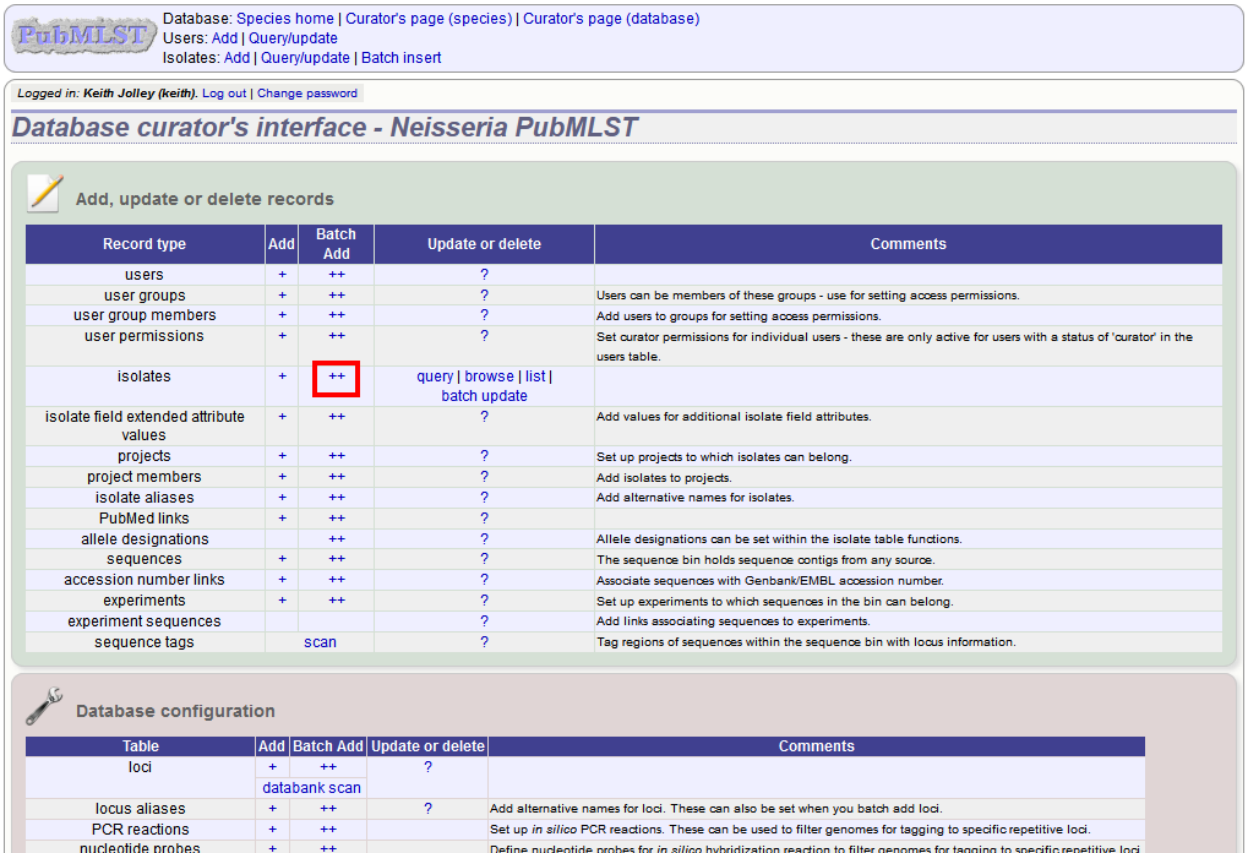
The next available id will be filled in automatically but you are free to change this. Fill in the individual fields. Required fields are listed first and are marked with an exclamation mark (!). Some fields may have drop-down list boxes of allowed values. You can also enter allele designations for any loci that have been defined.



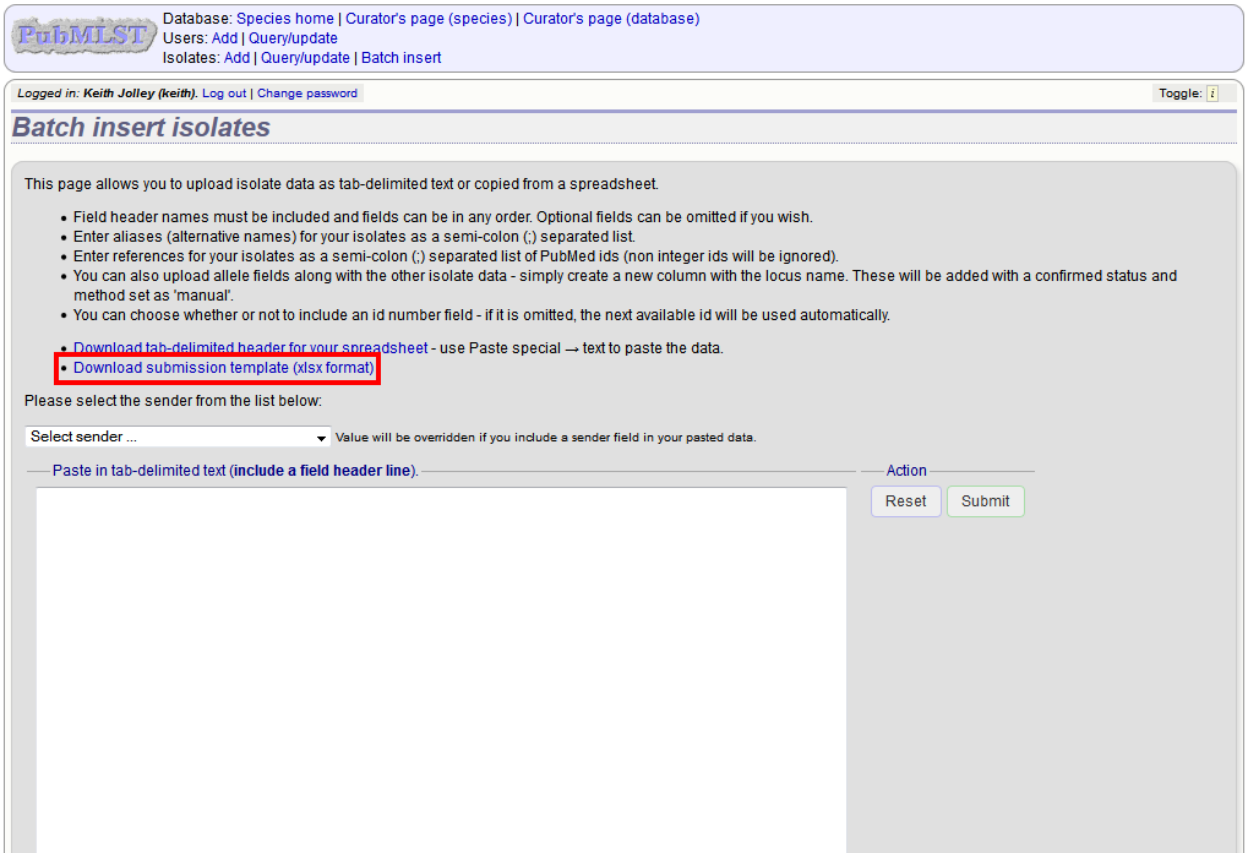
Press submit when finished.

More usually, isolate records are added in batch mode, even when only a single record is added, since the submission can be prepared in a spreadsheet and copied and pasted.

Select batch add (++) isolates link on the curator's index page.

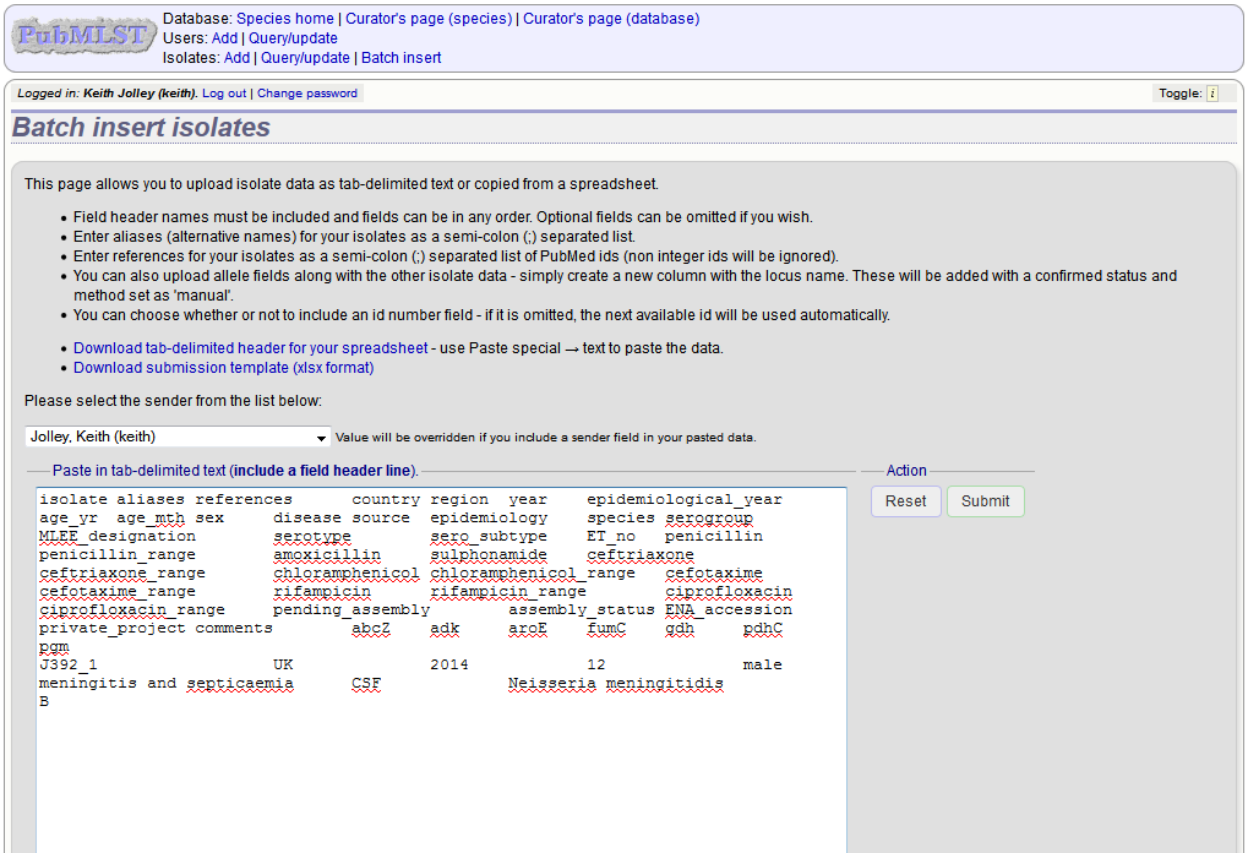


Download a submission template in Excel format from the link.

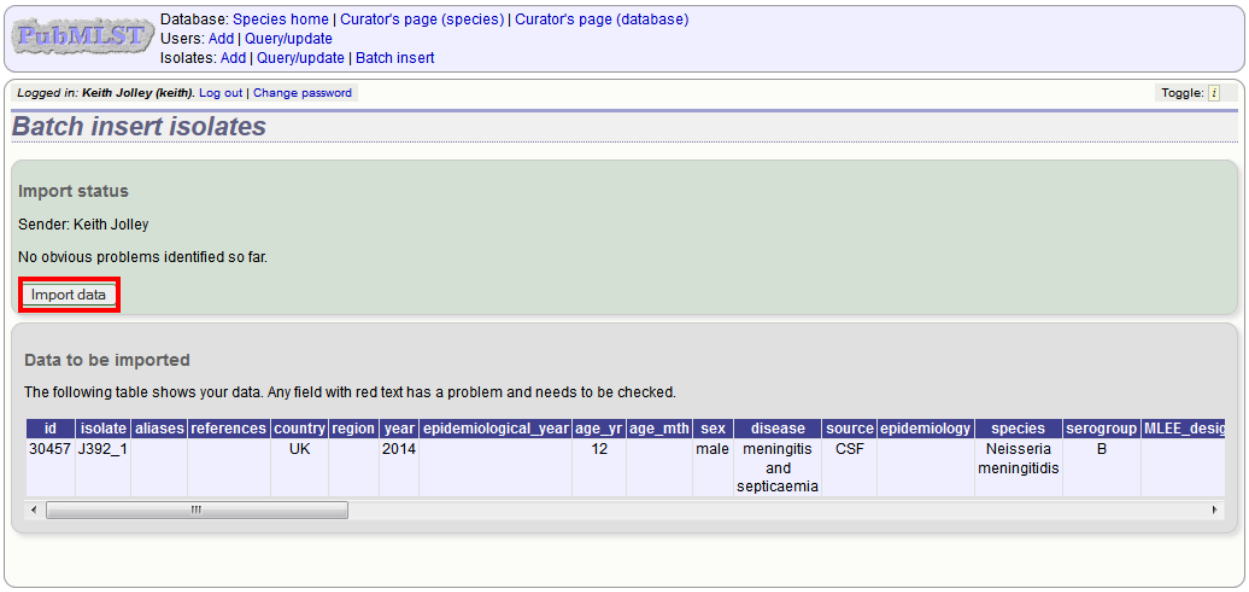


Prepare your data in the spreadsheet - the column headings must match the database fields. In databases with large numbers of loci, there won't be columns for each of these. You can, however, manually add locus columns.

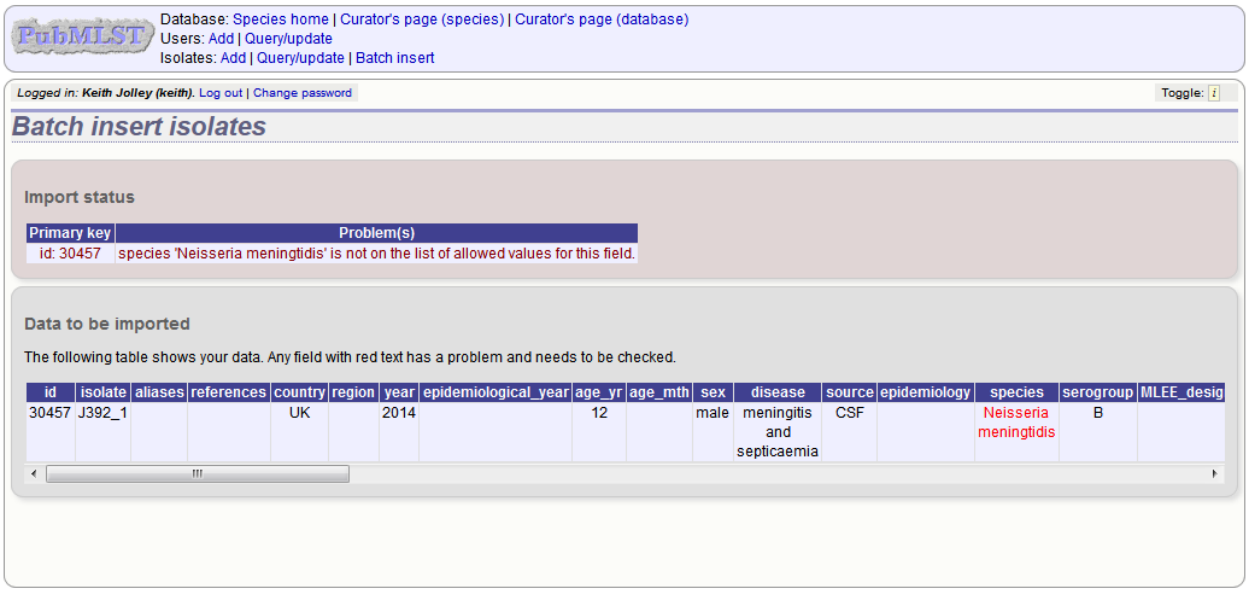
Pick a sender from the drop-down list box and paste the data from your spreadsheet in to the web form. The next available isolate id number will be used automatically (this can be overridden if you manually add an id column).



Press submit. Data are checked for consistency and if there are no problems you can then confirm the submission.

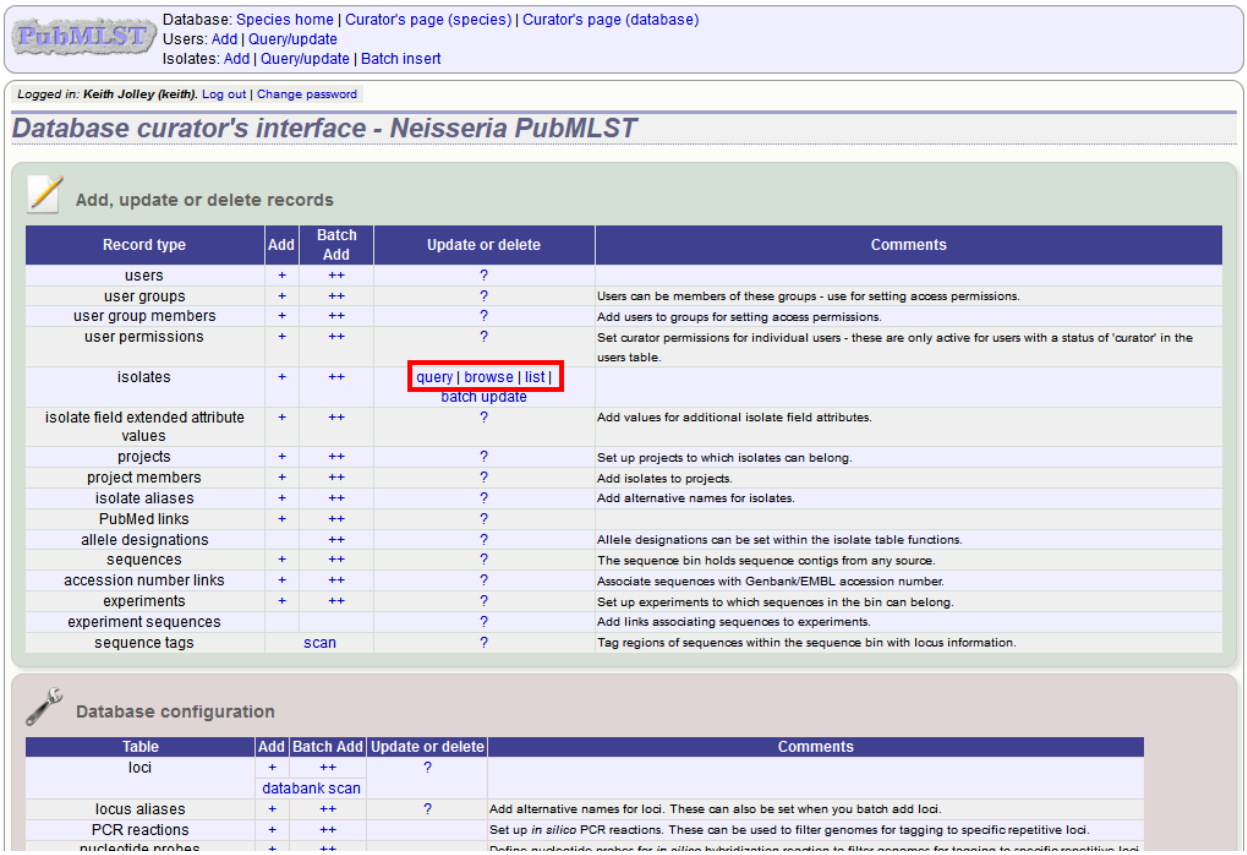


Any problems with the data will be listed and highlighted within the table. Fix the data and resubmit if this happens.

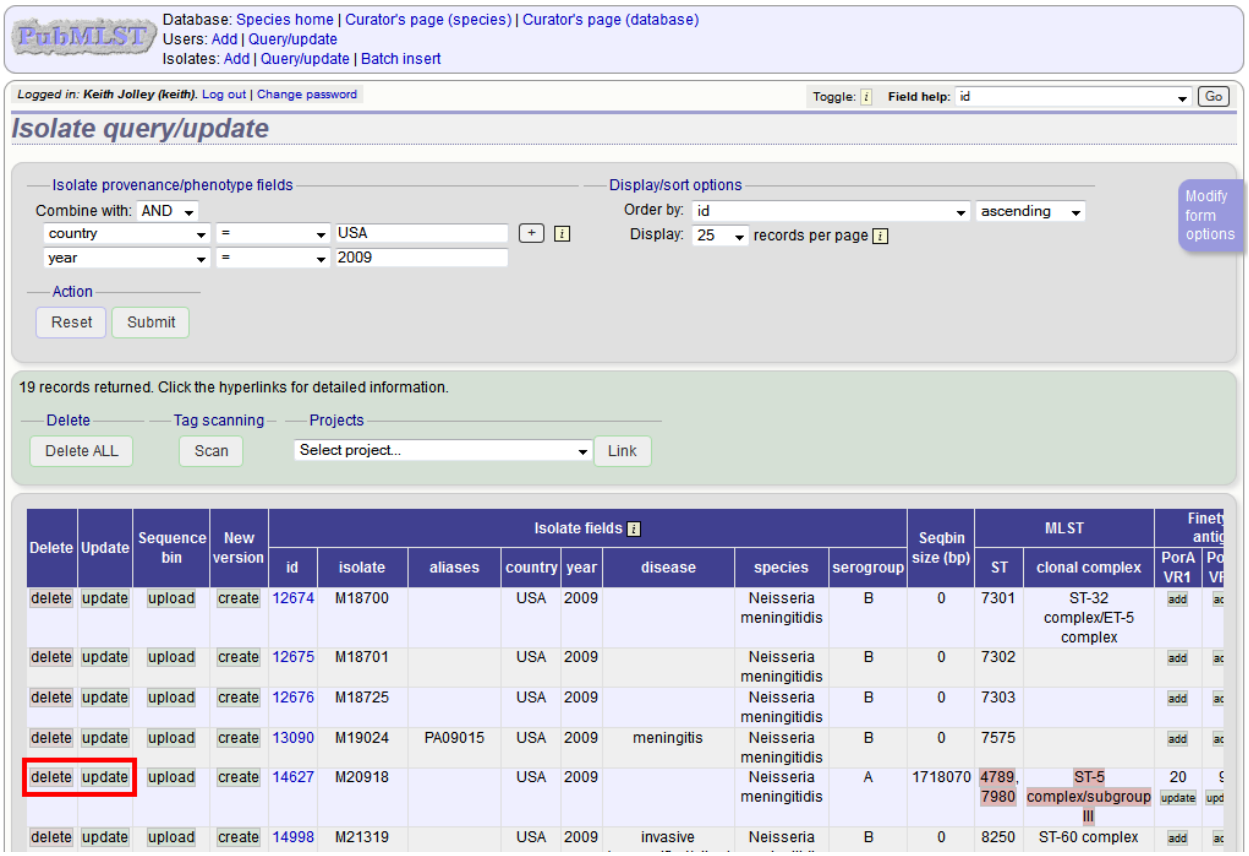


6.7 Updating and deleting single isolate records

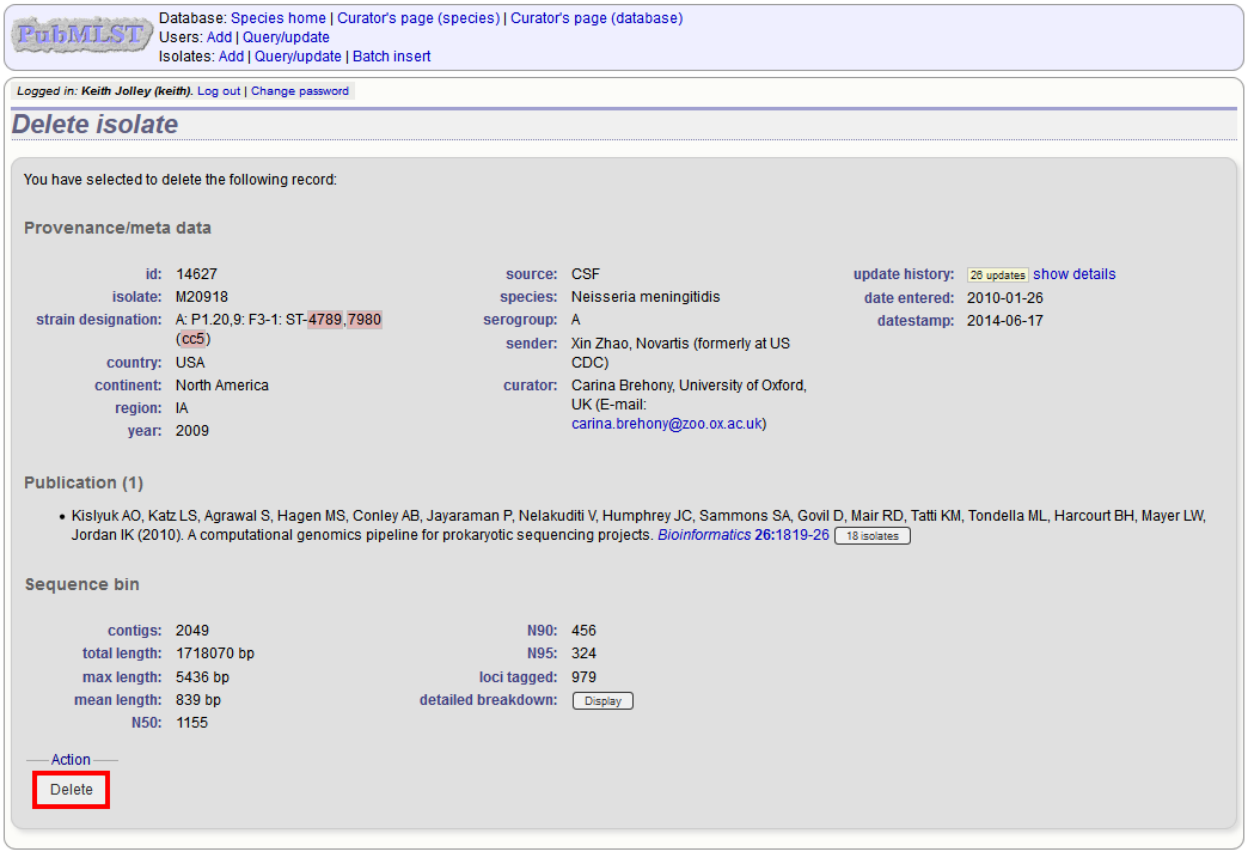
First you need to locate the isolate record. You can either browse or use a search or list query.



The query interface is the same as the *public query interface*. Following a query, a results table of isolates will be displayed. There will be delete and update links for each record.

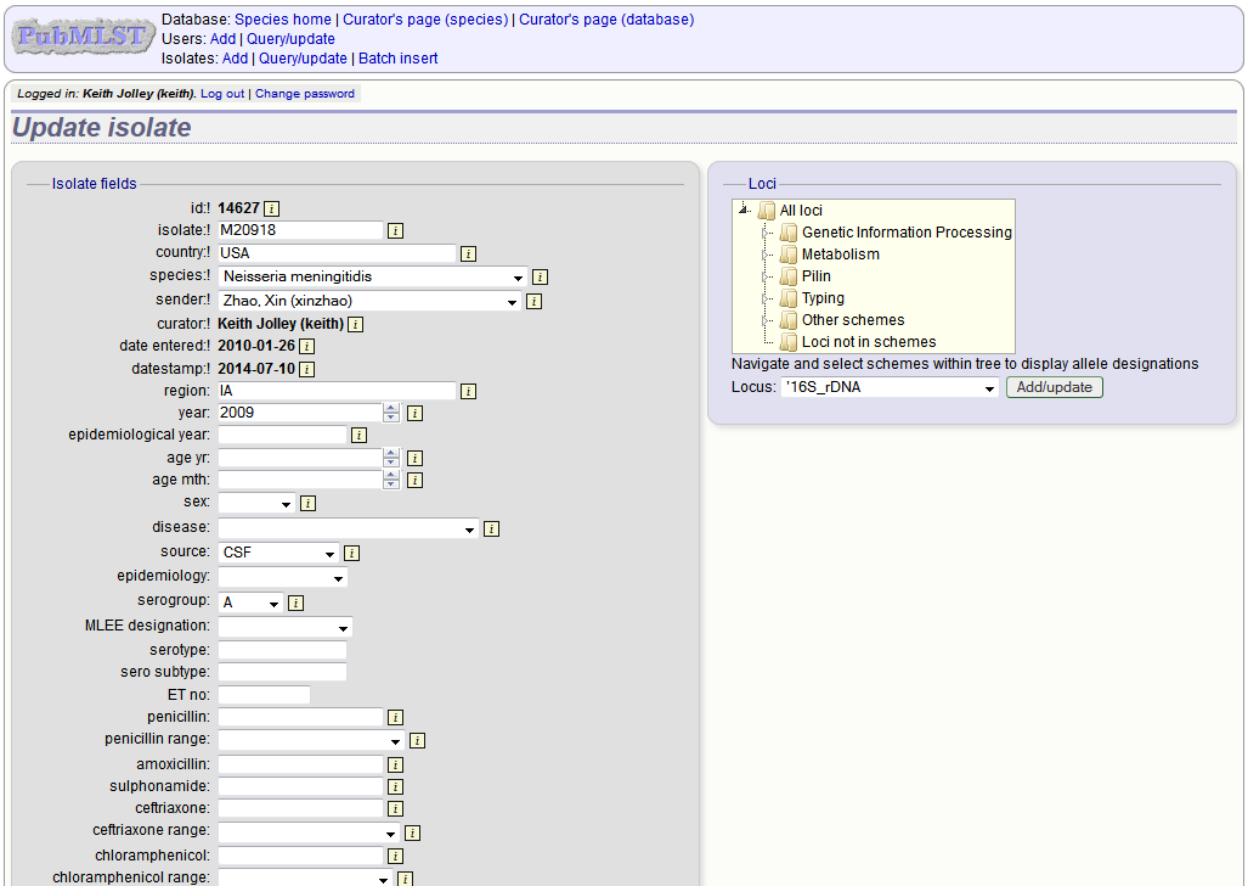


Clicking the 'Delete' link takes you to a page displaying the full isolate record.

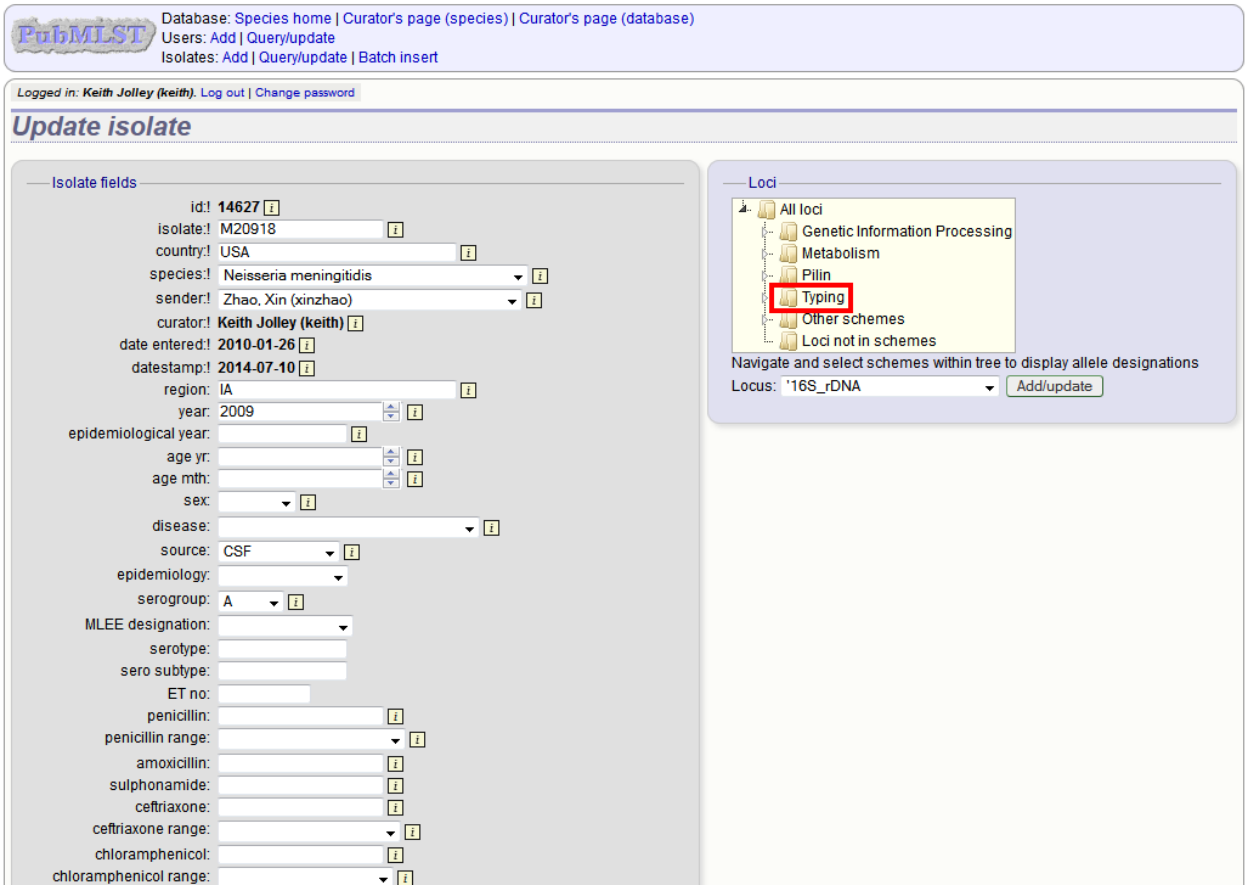


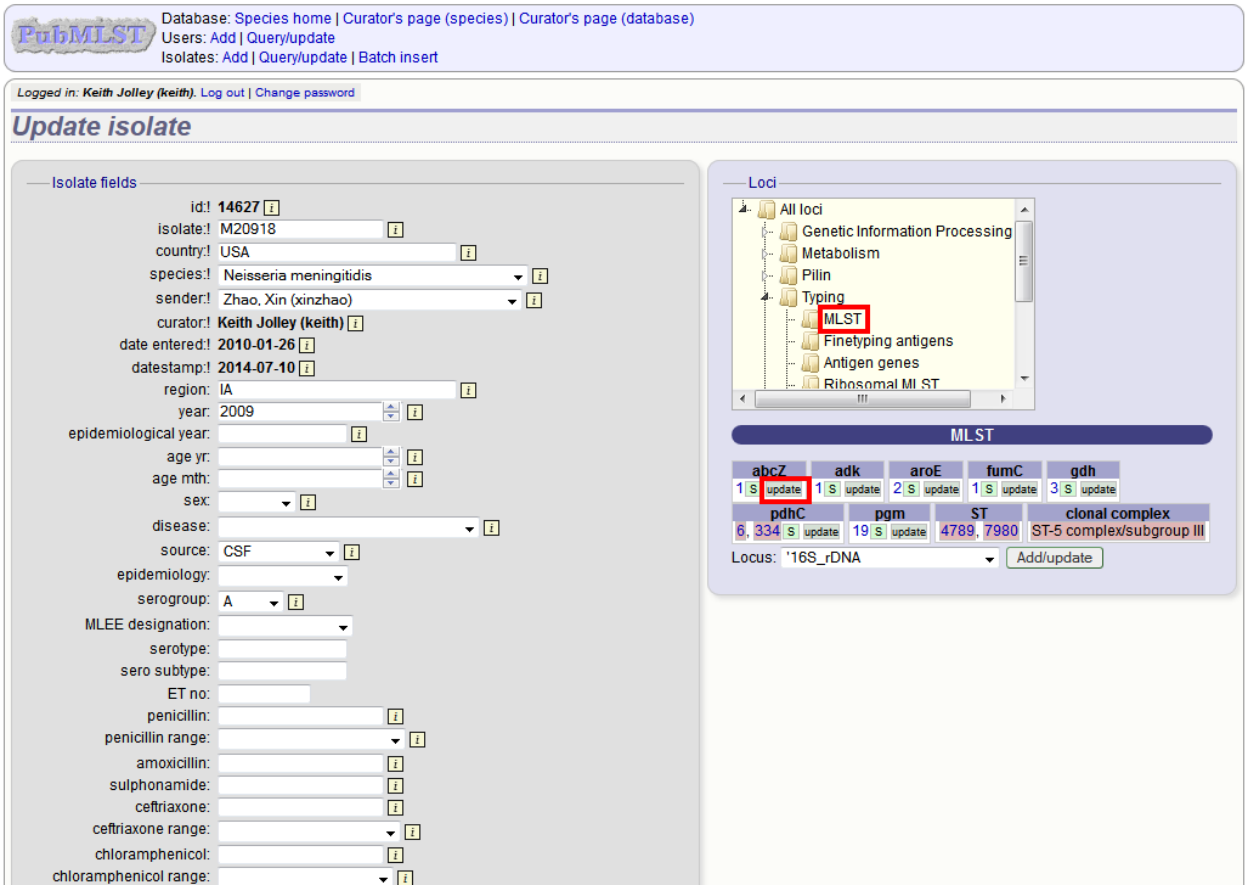
Pressing 'Delete' from this record page confirms the deletion.

Clicking the 'Update' link for an isolate takes you to an update form. Make the required changes and click 'Update'.

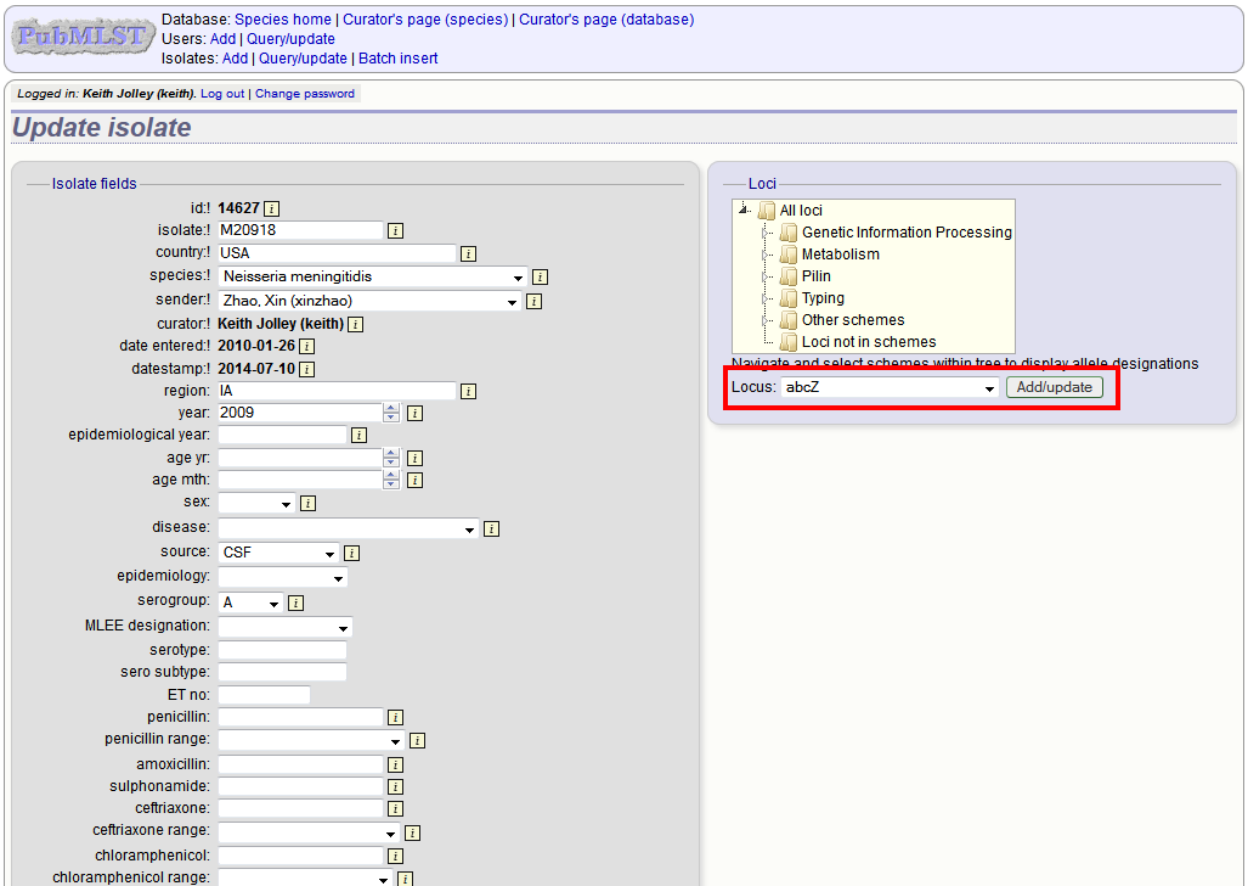


Allele designations can also be updated by clicking within the scheme tree and selecting the 'Add' or 'Update' link next to a displayed locus.

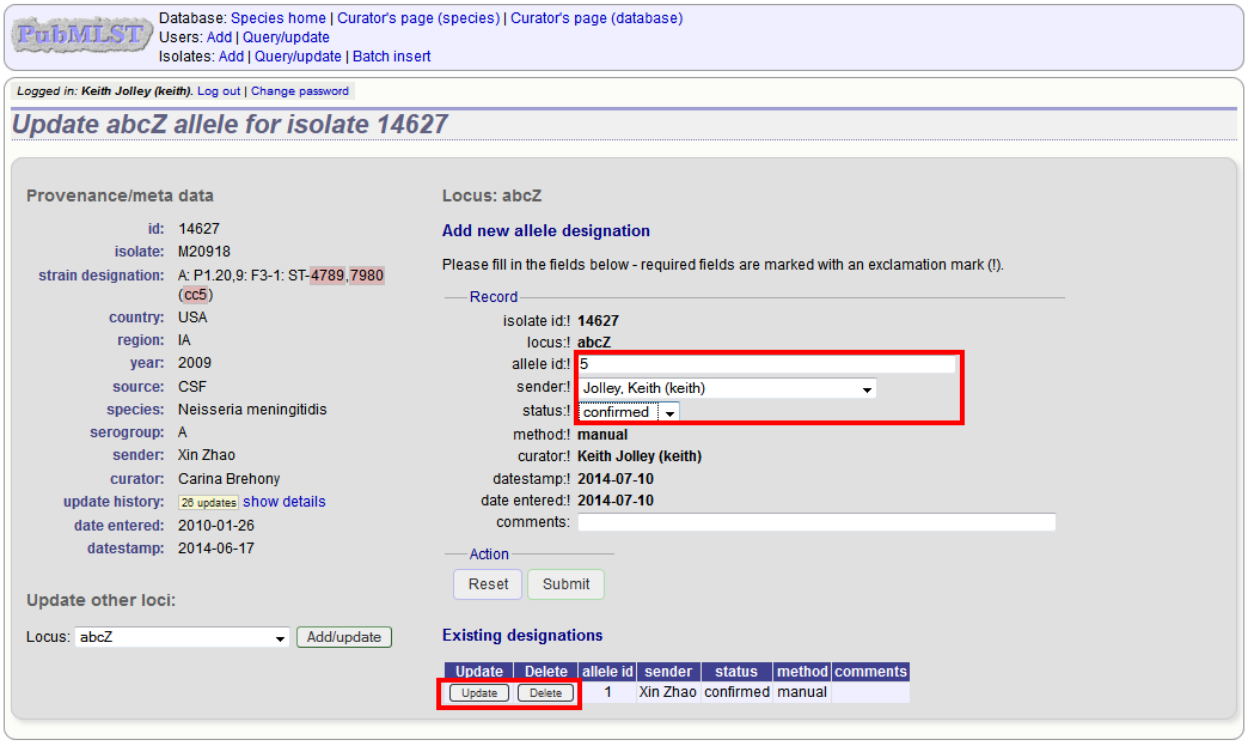

PubMLST
Database: Species home | Curator's page (species) | Curator's page (database)
Users: Add | Query/update
Isolates: Add | Query/update | Batch insert
Logged in: Keith Jolley (keith). Log out | Change password
Update isolate
Isolate fields
id:! 14627
isolate:! M20918
country:! USA
species:! Neisseria meningitidis
sender:! Zhao, Xin (xinzhao)
curator:! Keith Jolley (keith)
date entered:! 2010-01-26
datestamp:! 2014-07-10
region: IA
year: 2009
epidemiological year:
age yr:
age mth:
sex:
disease:
source: CSF
epidemiology:
serogroup: A
MLEE designation:
serotype:
sero subtype:
ET no:
penicillin:
penicillin range:
amoxicillin:
sulphonamide:
ceftriaxone:
ceftriaxone range:
chloramphenicol:
chloramphenicol range:
Loci
All loci
Genetic Information Processing
Metabolism
Pilin
Typing
Other schemes
Loci not in schemes
Navigate and select schemes within tree to display allele designations
Locus: '16S_rDNA
Add/update



Schemes will only appear in the tree if data for at least one of the loci within the scheme has been added. You can additionally add or update allelic designations for a locus by choosing a locus in the drop-down list box and clicking 'Add/update'.

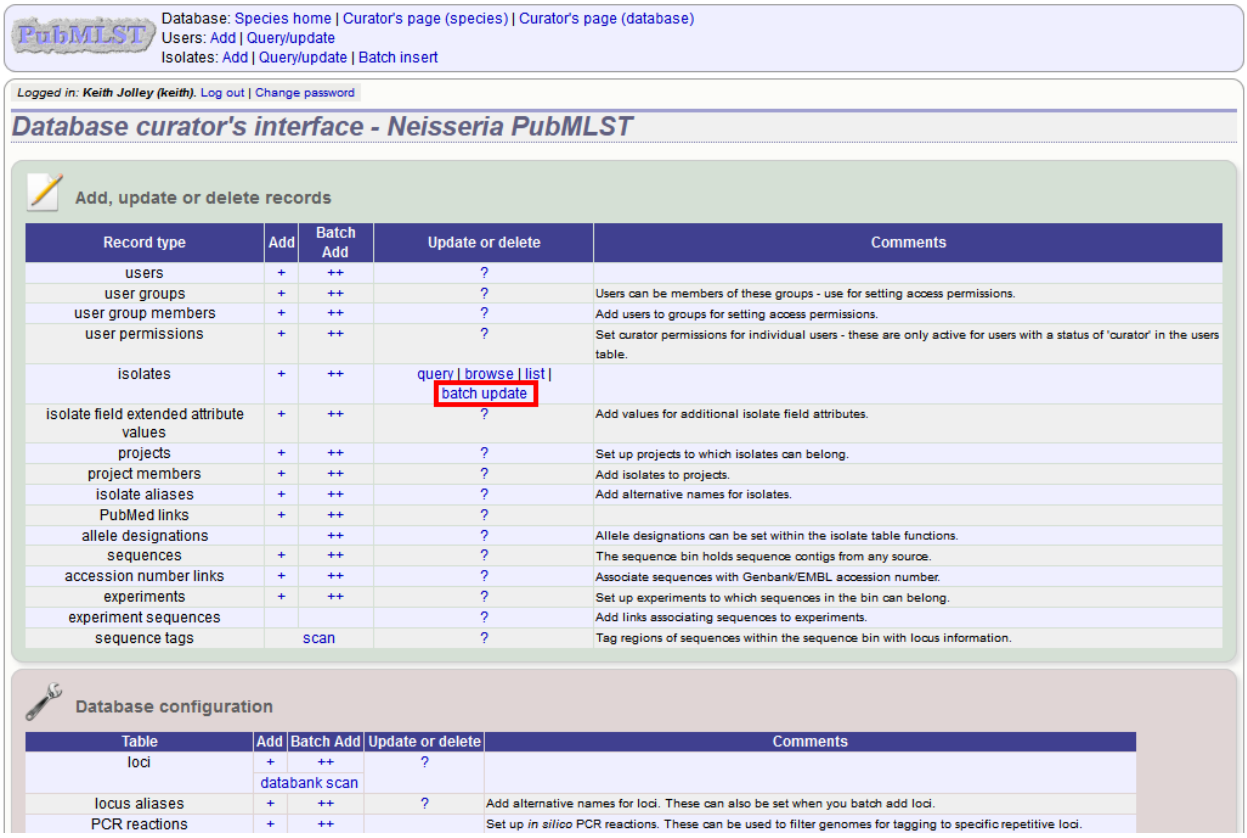


The allele designation update page allows you to modify an existing designation, or alternatively add additional designations. The sender, status (confirmed/provisional) and method (manual/automatic) needs to be set for each designation (all pending designations have a provisional status). The method is used to differentiate designations that have been determined manually from those determined by an automated algorithm.



6.8 Batch updating multiple isolate records

Select 'batch update' isolates link on the curator's index page.



Prepare your update data in 3 columns in a spreadsheet:

1. Unique identifier field
2. Field to be updated
3. New value for field

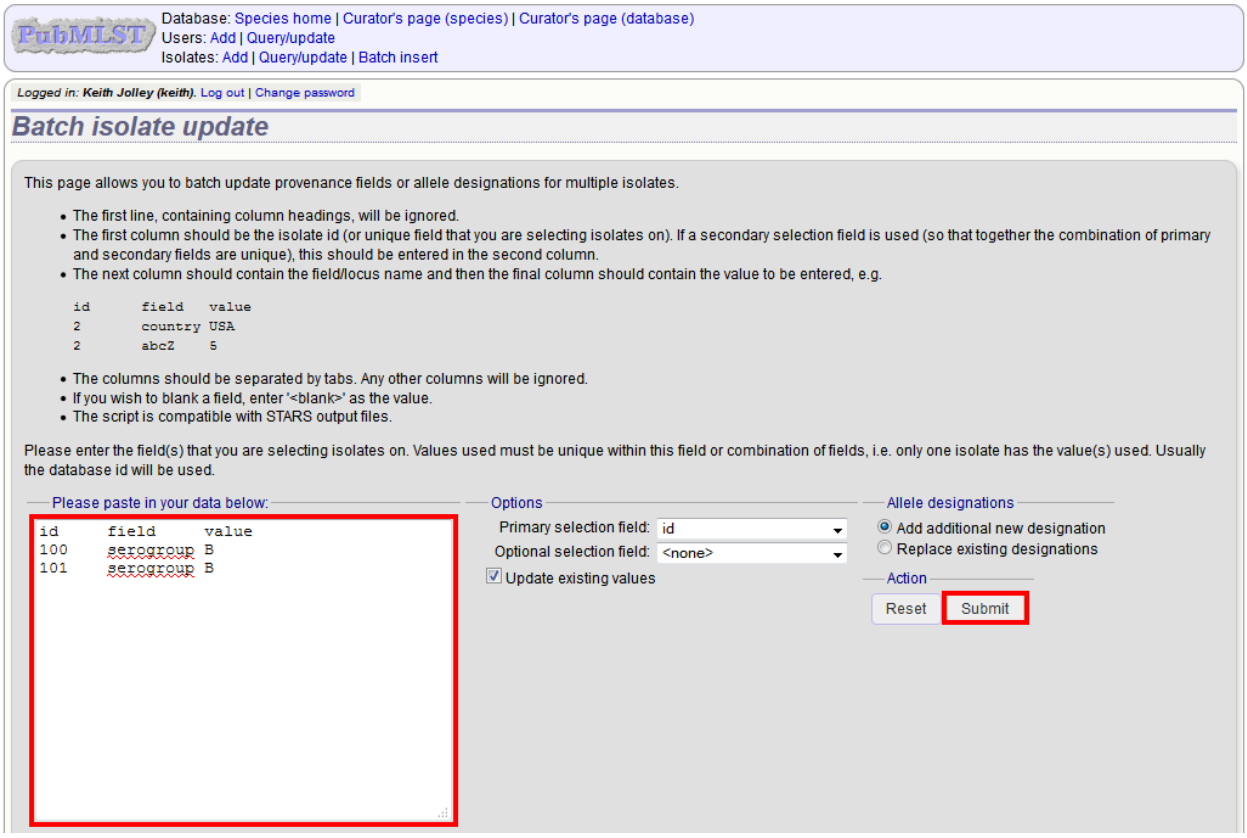
You should also include a header line at the top - this isn't used so can contain anything but it should be present.

Columns must be tab-delimited which they will be if you copy and paste directly from the spreadsheet.

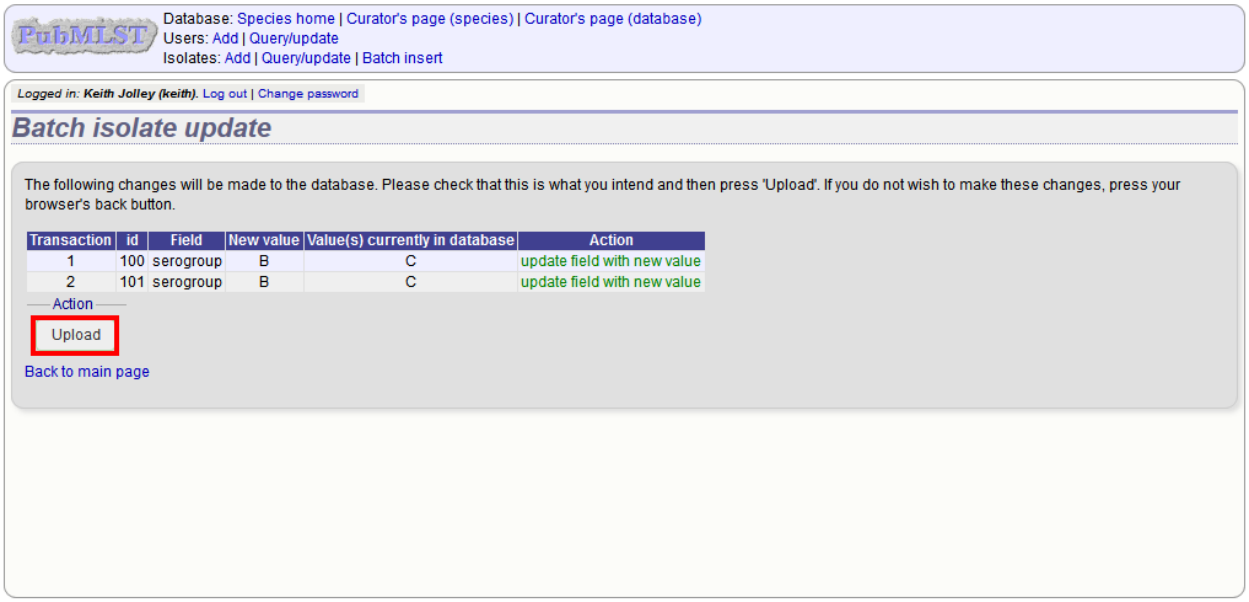
So, to update isolate id-100 and id-101 to serogroup B you would prepare the following:

```
id      field      value
100     serogroup  B
101     serogroup  B
```

Select the field you are using as a unique identifier, in this case id, from the drop-down list box, and paste in the data. If the fields already have values set, you should also check the 'Overwrite existing data' checkbox. Press 'submit'.



A confirmation page will be displayed if there are no problems. If there are problems, these will be listed. Press 'Upload' to upload the changes.



You can also use a secondary selection field such that a combination of two fields uniquely defines the isolate, for example using country and isolate name.

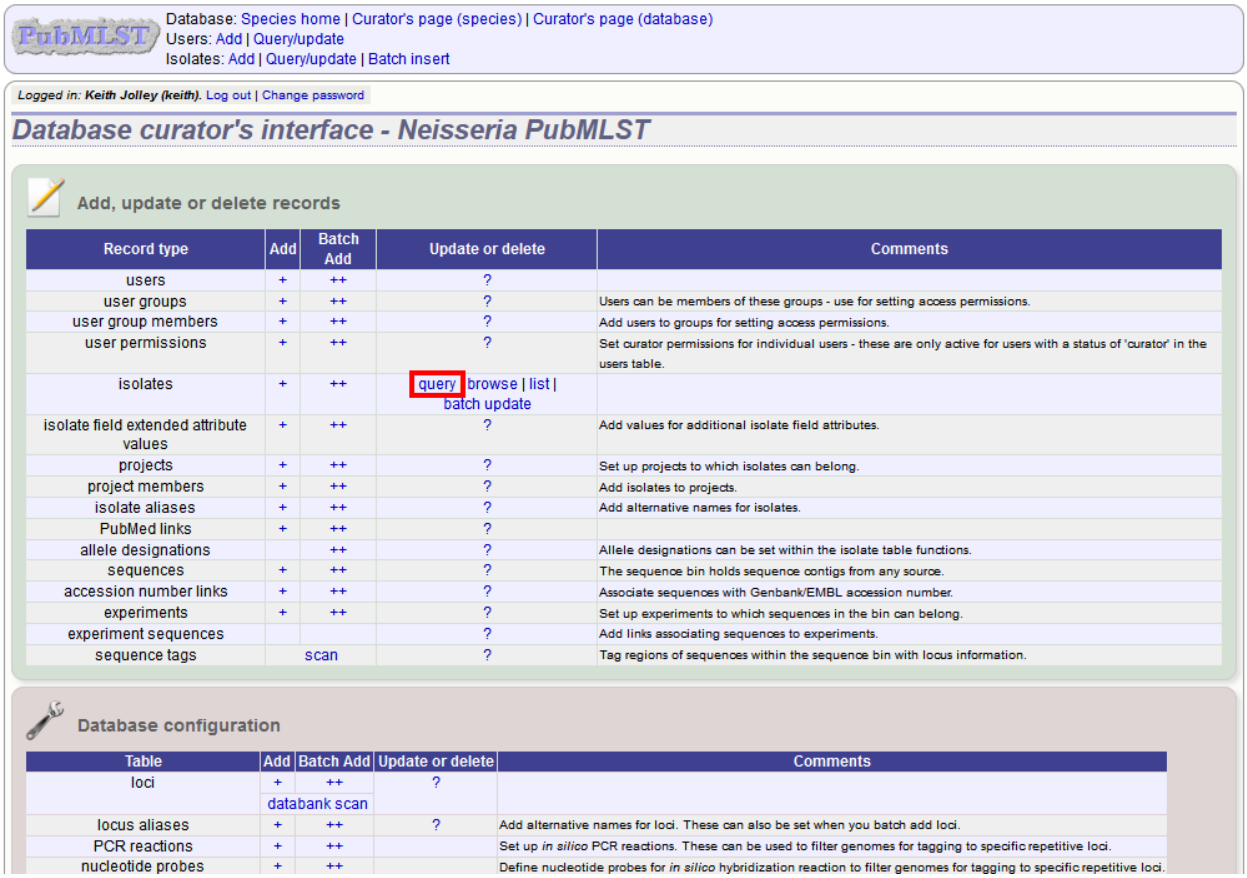
So, for example, to update the serogroups of isolates CN100 and CN103, both from the UK, select the appropriate primary and secondary fields and prepare the data as follows:

```
isolate     country     field       value
CN100       UK          serogroup   B
CN103       UK          serogroup   B
```

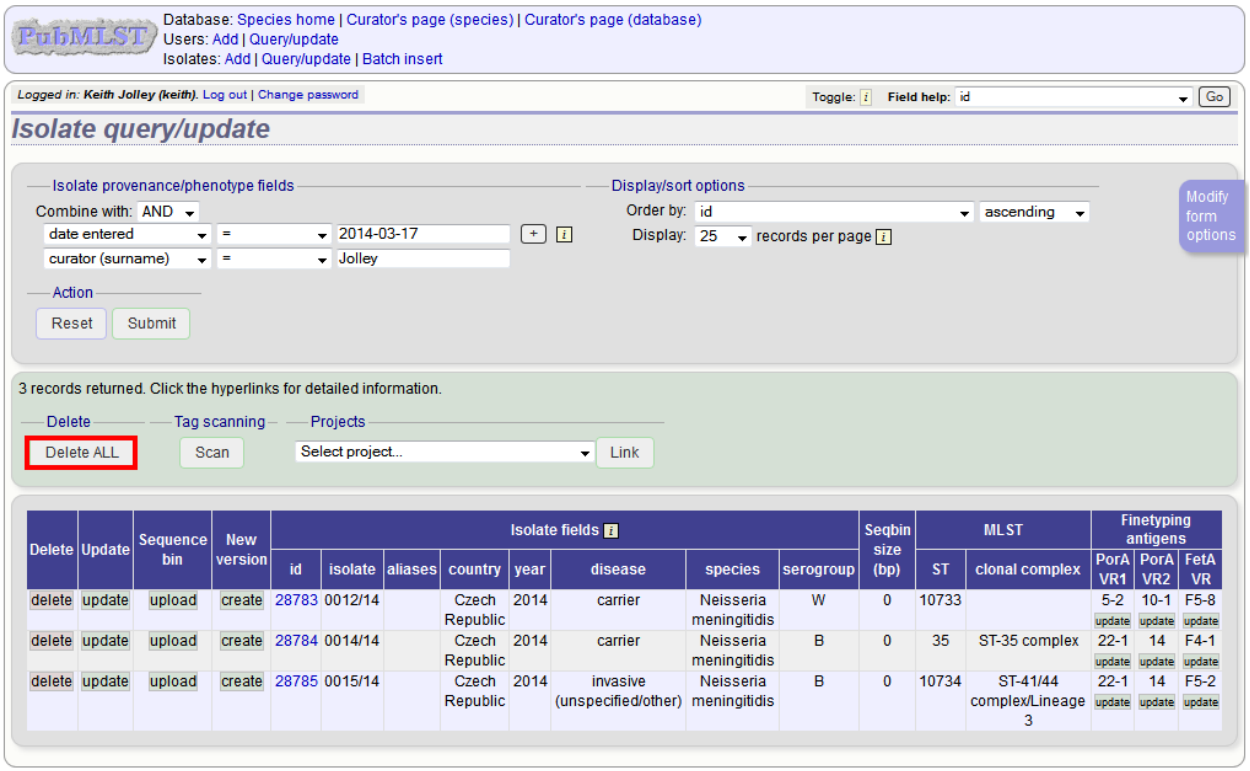
6.9 Deleting multiple isolate records

Note: Please note that standard curator accounts may not have permission to delete multiple isolates. Administrator accounts are always able to do this.

Before you can delete multiple records, you need to search for them. From the curator's main page, click the Query isolates link:



Enter search criteria that specifically return the isolates you wish to delete. Click 'Delete ALL'.



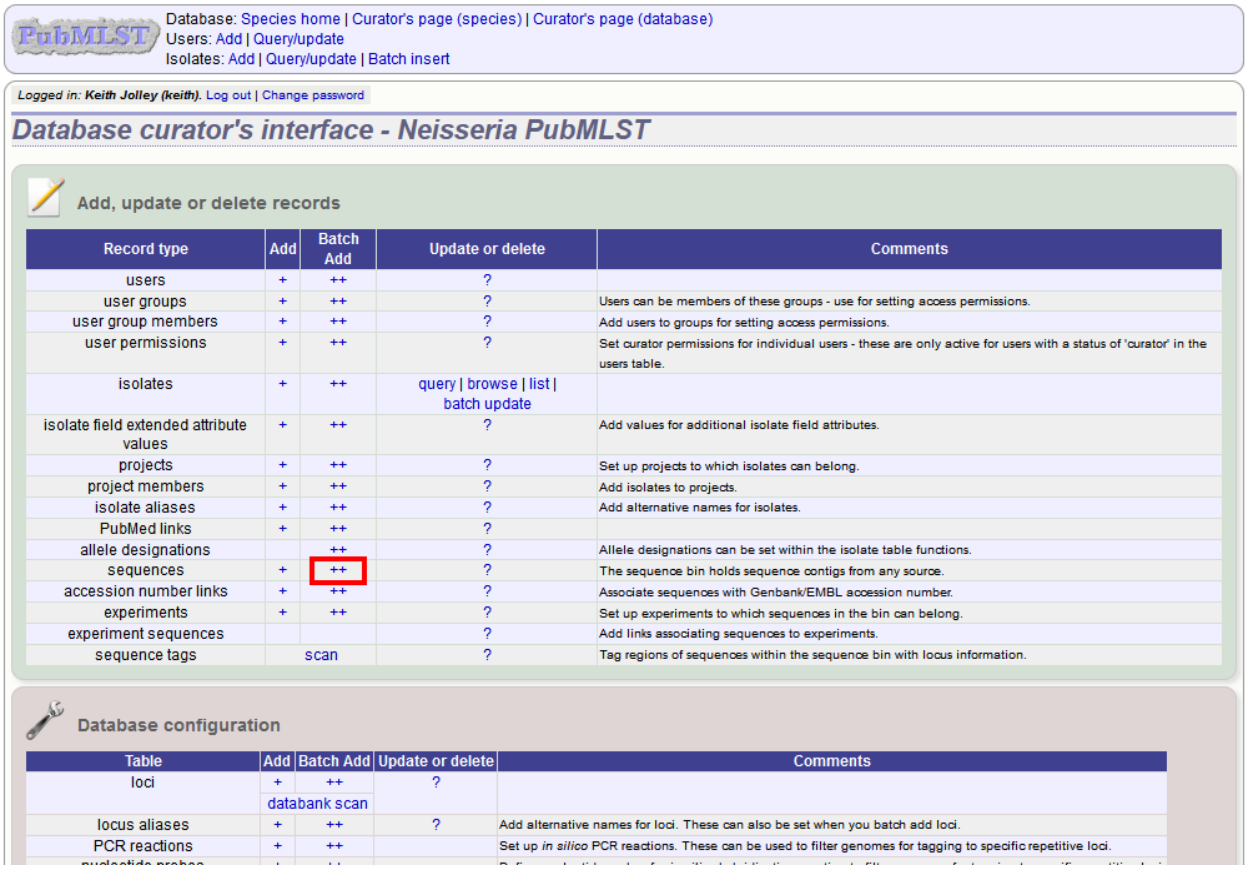
You will have a final chance to change your mind:

Click 'Confirm deletion!'.

6.10 Uploading sequence contigs linked to isolate records

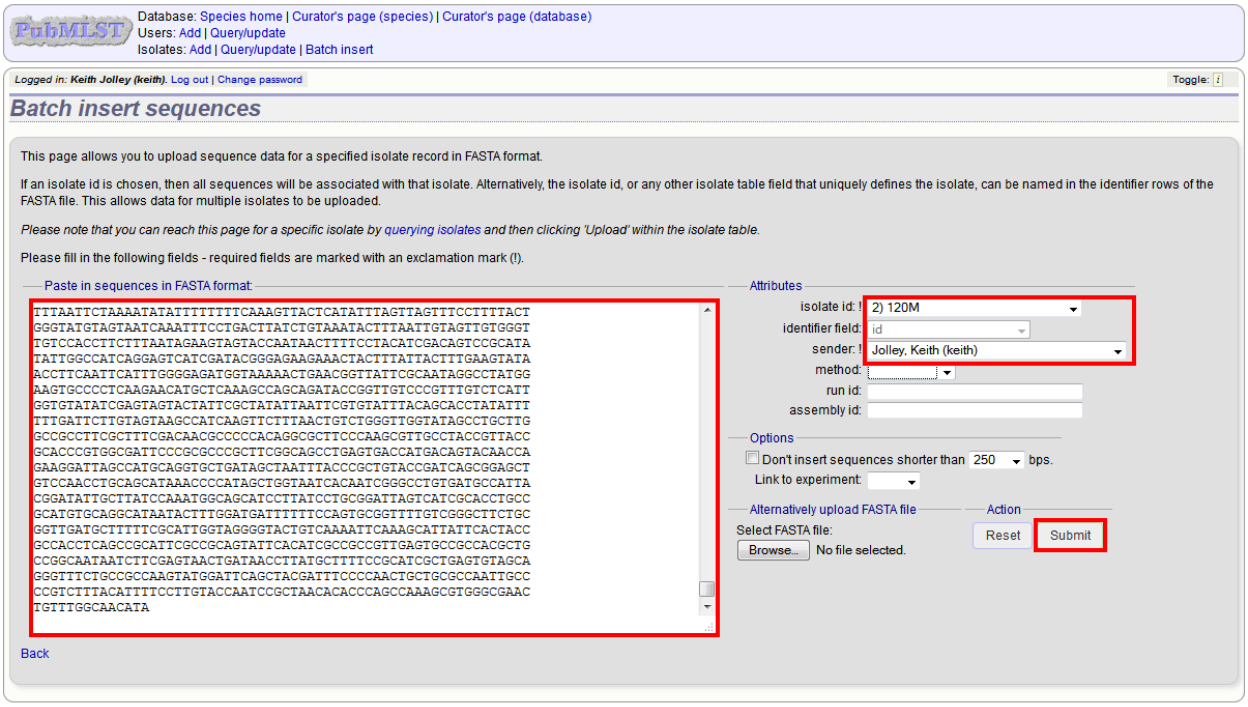
6.10.1 Select isolate from drop-down list

To upload sequence data, click the sequences batch add (++) link on the curator's main page.

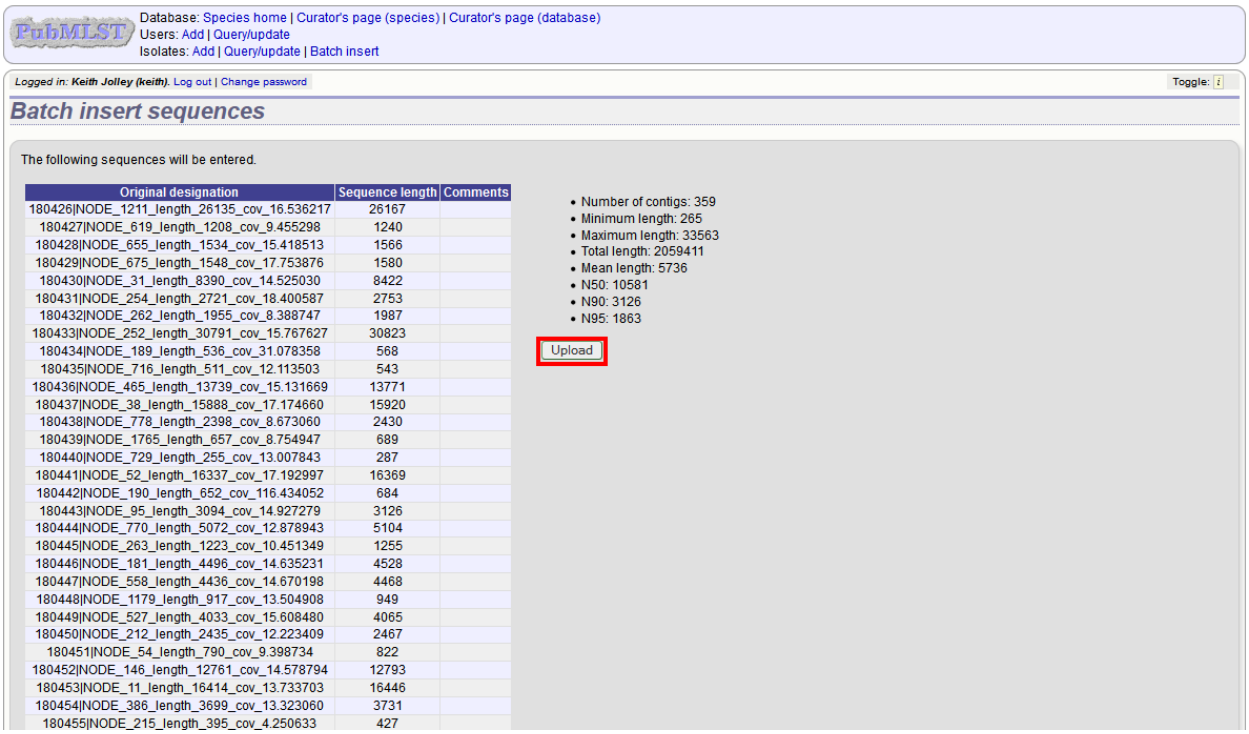


Select the isolate that you wish to link the sequence to from the dropdown list box. You also need to enter the person who sent the data. Optionally, you can add the sequencing method used.

Paste sequence contigs in FASTA format in to the form.

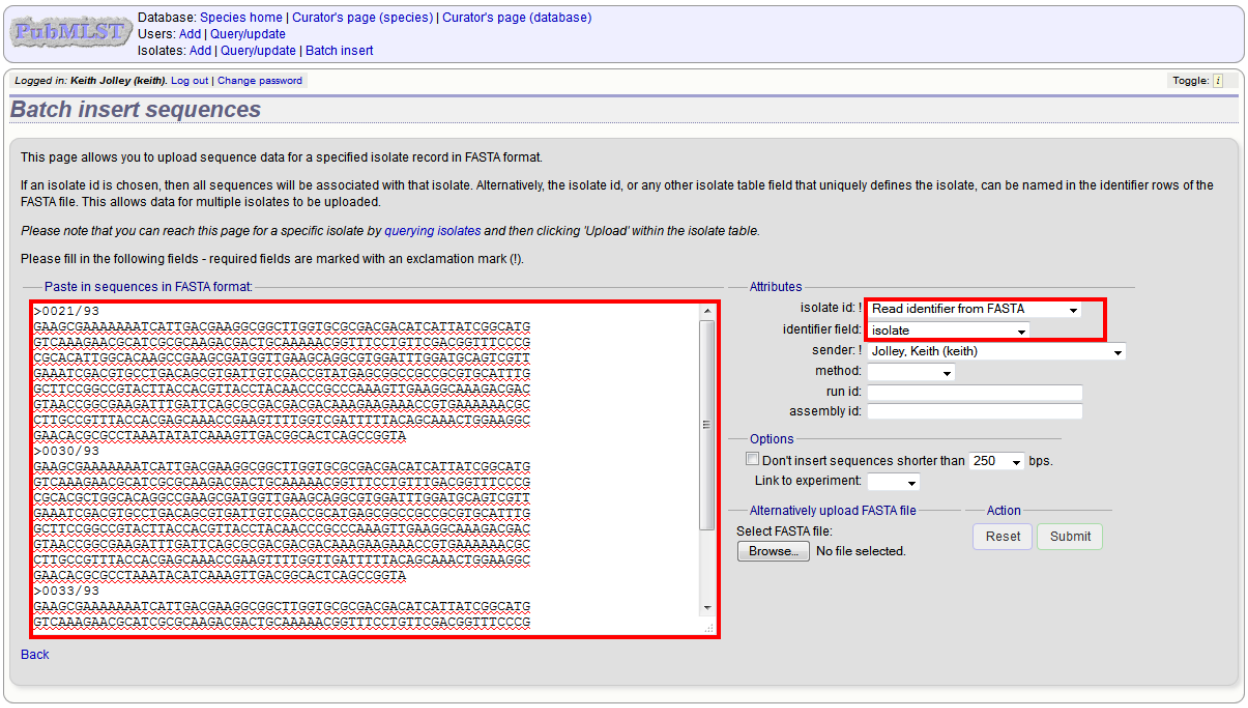


Click 'Submit'. A summary of the number of isolates and their lengths will be displayed. To confirm upload, click 'Upload'.

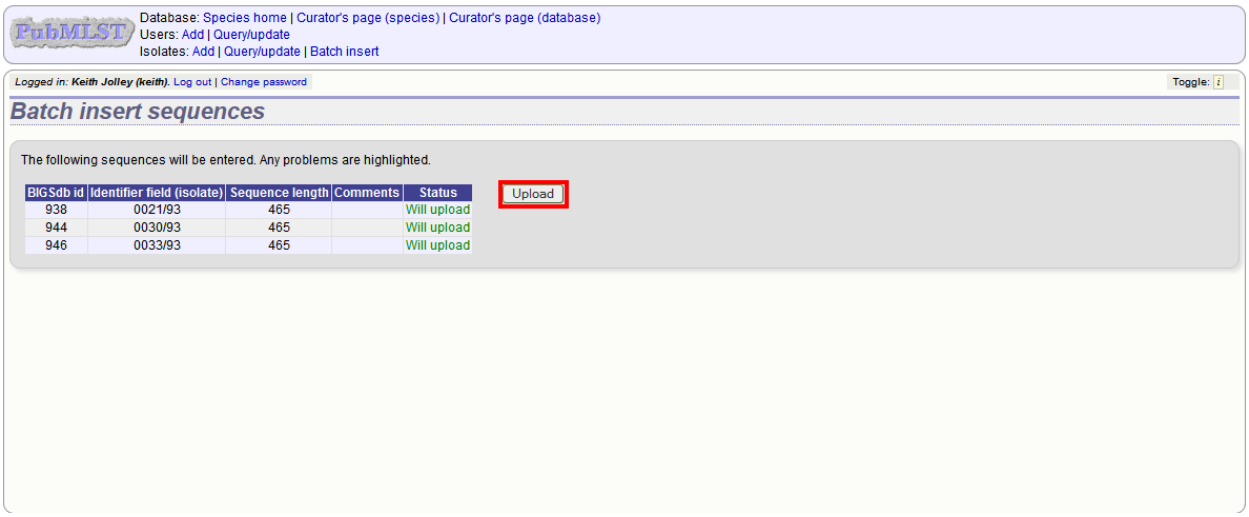


Original designation	Sequence length	Comments
180426|NODE_1211_length_26135_cov_16.536217	26167	
180427|NODE_619_length_1208_cov_9.455298	1240	
180428|NODE_655_length_1534_cov_15.418513	1566	
180429|NODE_675_length_1548_cov_17.753876	1580	
180430|NODE_31_length_8390_cov_14.525030	8422	
180431|NODE_254_length_2721_cov_18.400587	2753	
180432|NODE_262_length_1955_cov_8.388747	1987	
180433|NODE_252_length_30791_cov_15.767627	30823	
180434|NODE_189_length_536_cov_31.078358	568	
180435|NODE_716_length_511_cov_12.113503	543	
180436|NODE_465_length_13739_cov_15.131669	13771	
180437|NODE_38_length_15888_cov_17.174660	15920	
180438|NODE_778_length_2398_cov_8.673060	2430	
180439|NODE_1765_length_657_cov_8.754947	689	
180440|NODE_729_length_255_cov_13.007843	287	
180441|NODE_52_length_16337_cov_17.192997	16369	
180442|NODE_190_length_652_cov_116.434052	684	
180443|NODE_95_length_3094_cov_14.927279	3126	
180444|NODE_770_length_5072_cov_12.878943	5104	
180445|NODE_263_length_1223_cov_10.451349	1255	
180446|NODE_181_length_4496_cov_14.635231	4528	
180447|NODE_558_length_4436_cov_14.670198	4468	
180448|NODE_1179_length_917_cov_13.504908	949	
180449|NODE_527_length_4033_cov_15.608480	4065	
180450|NODE_212_length_2435_cov_12.223409	2467	
180451|NODE_54_length_790_cov_9.398734	822	
180452|NODE_146_length_12761_cov_14.578794	12793	
180453|NODE_11_length_16414_cov_13.733703	16446	
180454|NODE_386_length_3699_cov_13.323060	3731	
180455|NODE_215_length_395_cov_4.250633	427	

It is also possible to upload data for multiple isolates at the same time, but these must exist as single contigs for each isolate. To do this, select 'Read identifier from FASTA' in the isolate id field and select the field that you wish to use as the identifier in the 'identifier field', e.g. to use isolate names select 'isolate' here.



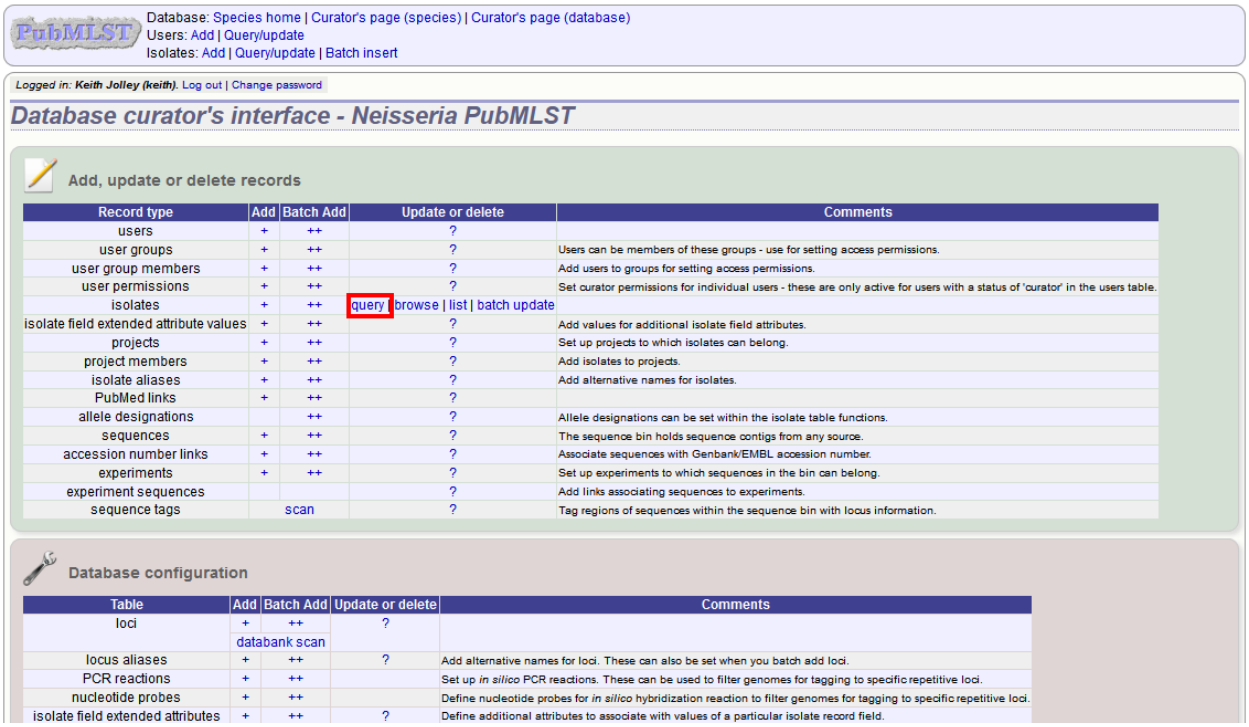
Provided the identifier used uniquely identifies the isolate you will get a confirmation screen. If the isolate name does not do this you'll probably have to use the database id number instead. Click 'Upload' to confirm.



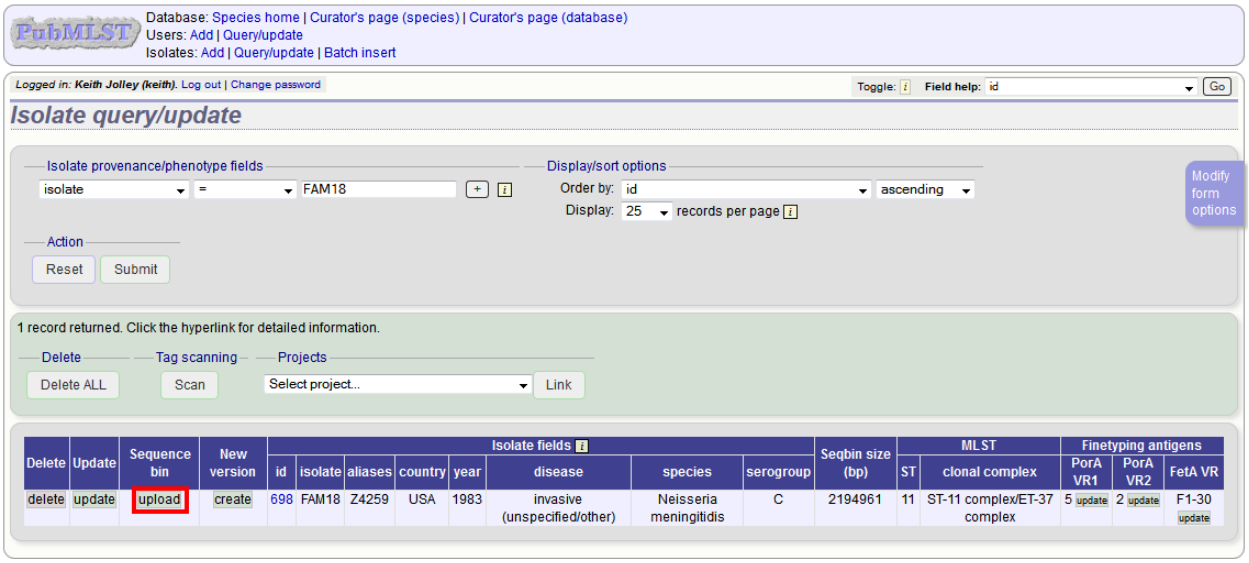
6.10.2 Select from isolate query

As an alternative to selecting the isolate from a dropdown list (which can become unwieldy for large databases), it is also possible to upload sequence data following an isolate query.

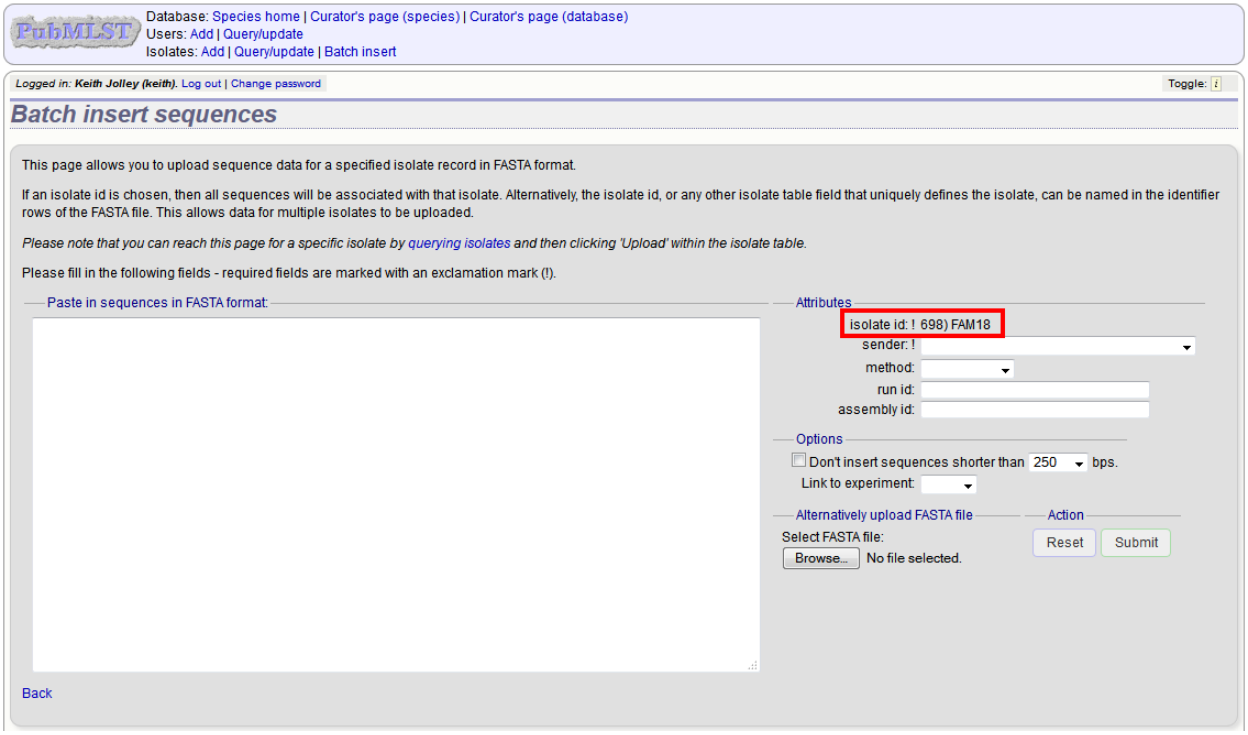
Click the isolate query link from the curator's main page.



Enter your search criteria. From the list of isolates displayed, click the 'Upload' link in the sequence bin column of the appropriate isolate record.



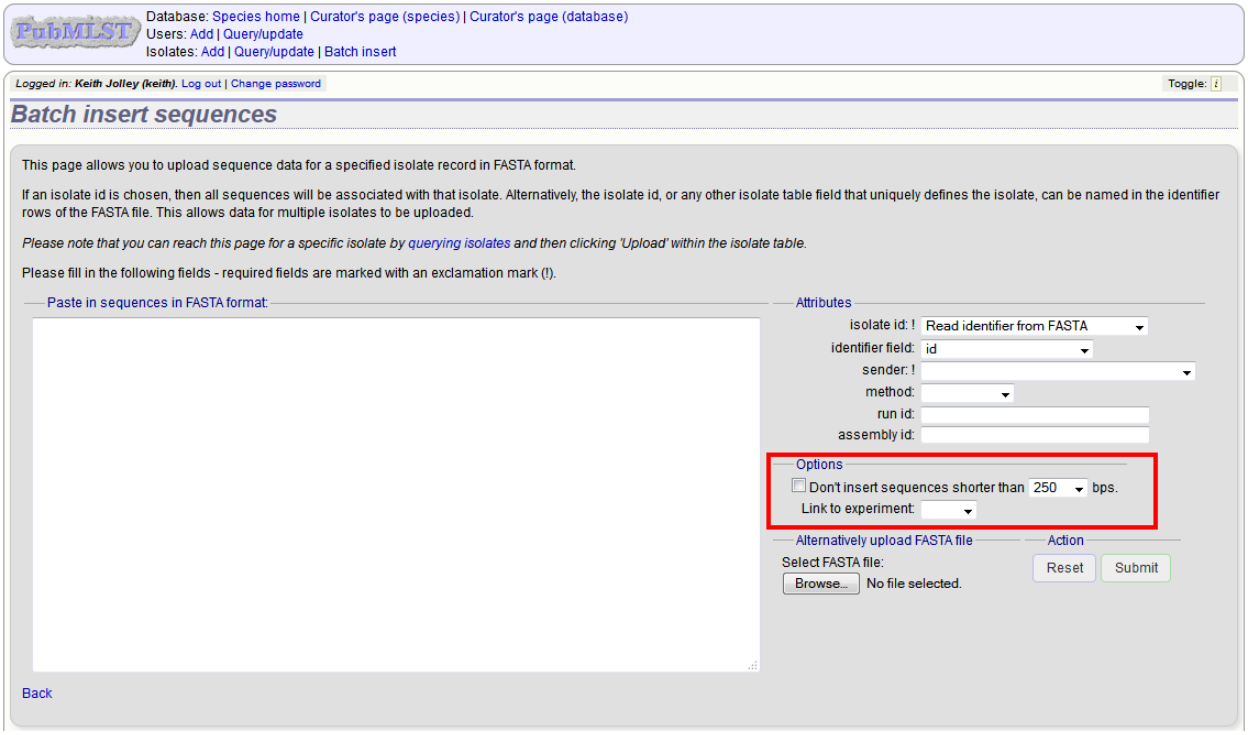
The same upload form as detailed above is shown. Instead of a dropdown list for isolate selection, however, the chosen isolate will be pre-selected.



6.10.3 Upload options

On the upload form, you can select to filter out short sequences from your contig list.

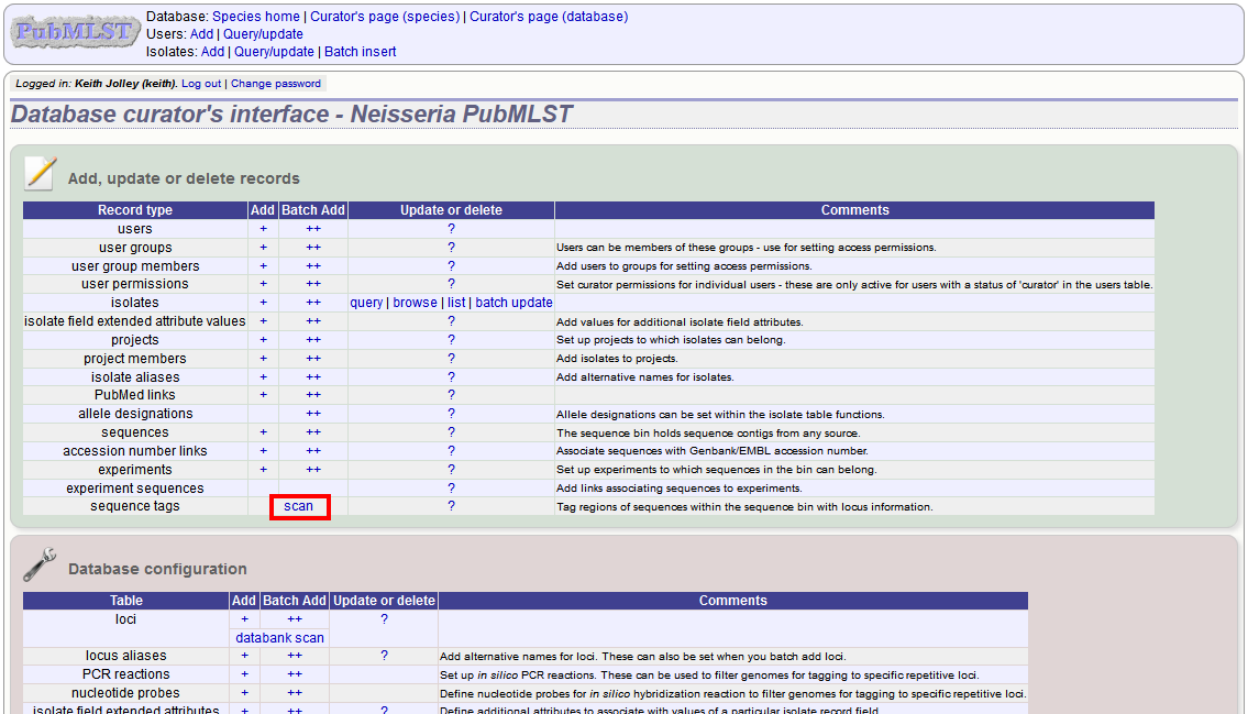
If your database has experiments defined (experiments are used for grouping sequences and can be used to filter the sequences used in *tag scanning*), you can also choose to upload your contigs as part of an experiment. To do this, select the experiment from the dropdown list box.



6.11 Automated web-based sequence tagging

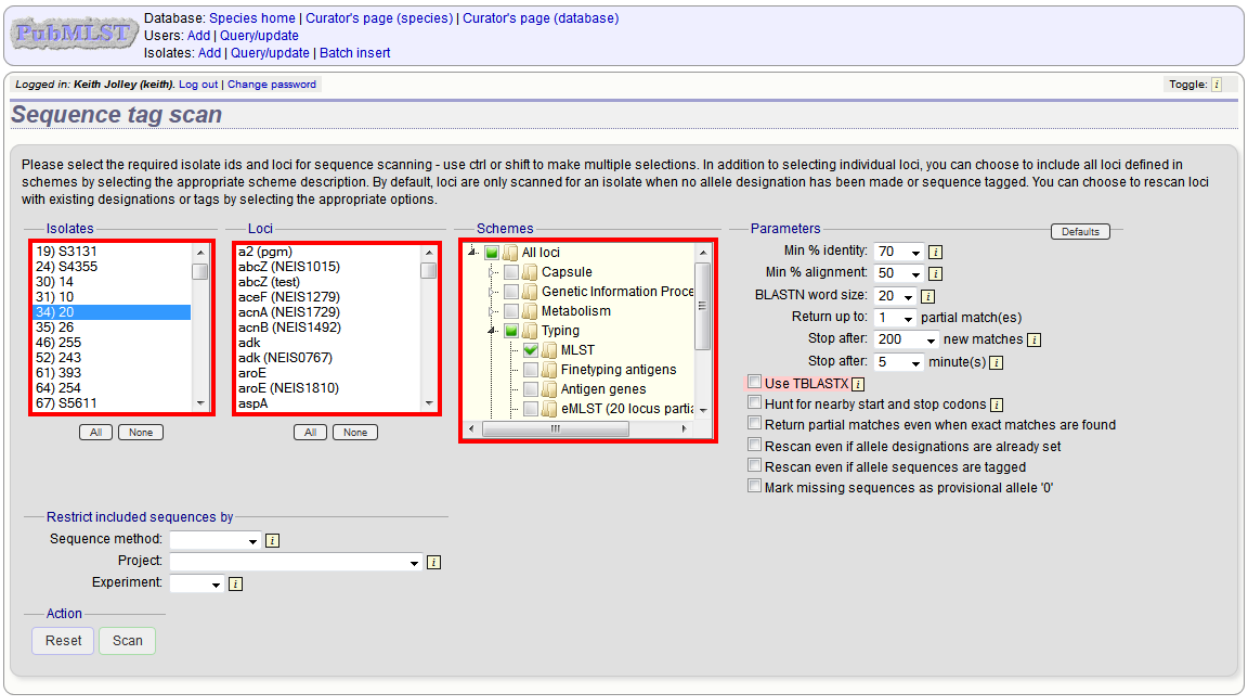
Sequence tagging, or tag-scanning, is the process of identifying alleles by scanning the sequence bin linked to an isolate record. Defined loci can either have a single reference sequence, that is defined in the locus table, or they can be linked to an external database that contains the sequences for known alleles. The tagging function uses BLAST to identify sequences and will tag the specific sequence region with locus information and an allele designation if a matching allele is identified by reference to an external database.

Select 'scan' sequence tags on the curator's index page.



Next, select the isolates whose sequences you wish to scan against. Multiple isolates can be selected by holding down the Ctrl key. All isolates can be selected by clicking the 'All' button under the isolate selection list.

Select either individual loci or schemes (collections of loci) to scan against. Again, multiple selections can be made.

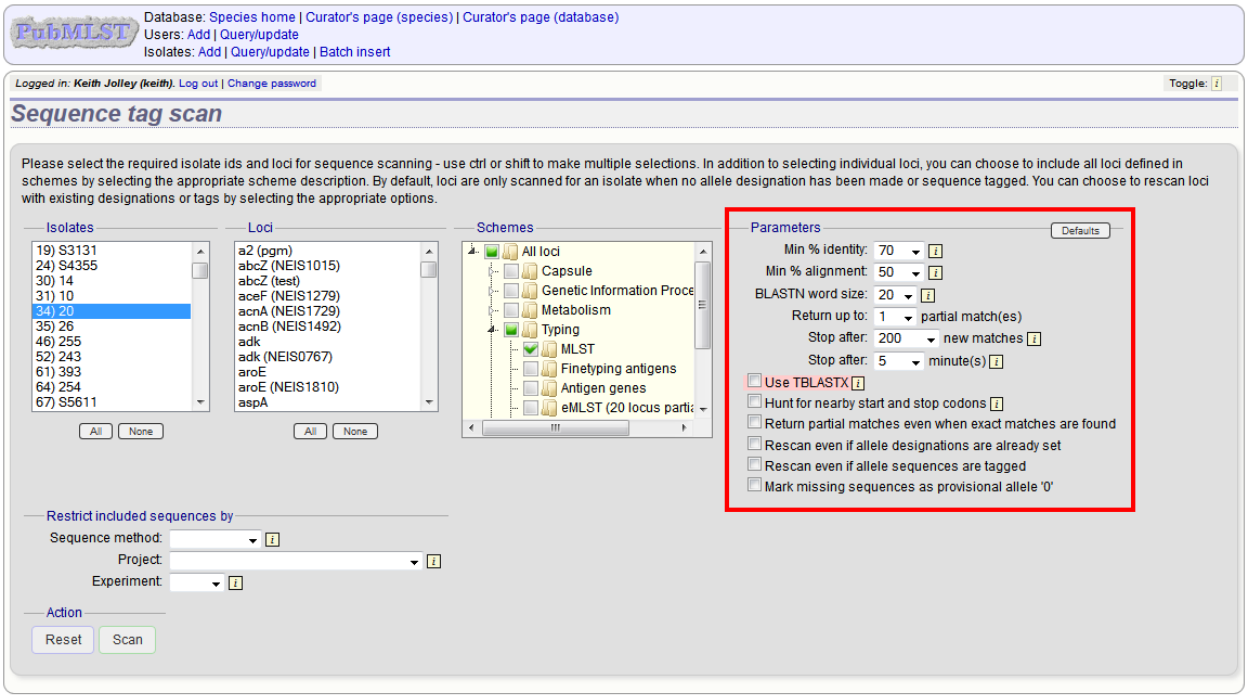


Choose your scan parameters. Lowering the value for BLASTN word size will increase the sensitivity of the search at the expense of time. Using TBLASTX is more sensitive but also much slower. TBLASTX can only be used to identify the sequence region rather than a specific allele (since it will only match the translated sequence and there may be multiple alleles that encode a particular peptide sequence).

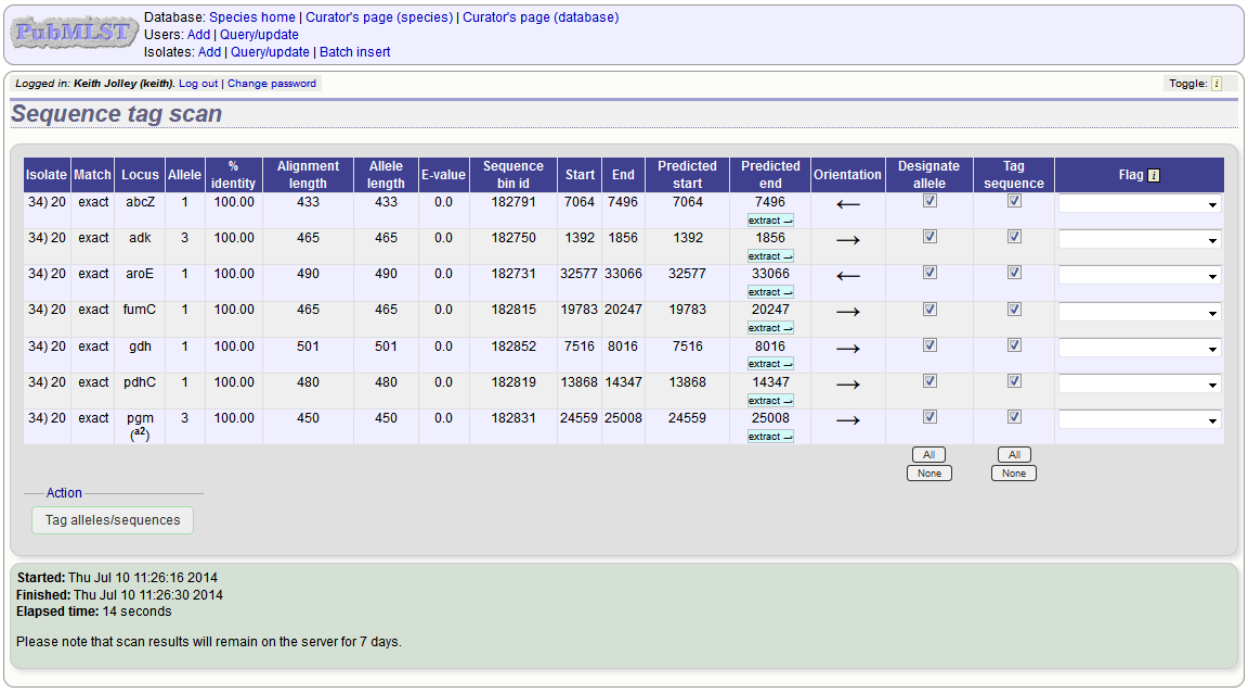
By default, for each isolate only loci that have not had either an allele designation made or a sequence region scanned will be scanned again. To rescan in these cases, select either or both the following:

- Rescan even if allele designations are already set
- Rescan even if allele sequences are tagged

Options can be returned to their default setting by clicking the 'Defaults' button.



Press 'Scan'. The system takes approximately 1-2 seconds to identify each sequence (depending on machine speed and size of definitions databases). Any identified sequences will be listed in a table, with checkboxes indicating whether allele sequences or sequence regions are to be tagged.



Individual sequences can be extracted for inspection by clicking the 'extract →' link. The sequence (along with flanking regions) will be opened in another browser window or tab.

Checkboxes are enabled against any new sequence region or allele designation. You can also set a flag for a particular sequence to mark an attribute. These will be set automatically if these have been defined within the sequence definition database for an identified allele.

See also:

Sequence tag flags

Ensure any sequences you want to tag are selected, then press 'Tag alleles/sequences'.

If any new alleles are found, a link at the bottom will display these in a format suitable for automatic allele assignment by *batch uploading to sequence definition* database.

See also:

Offline curation tools

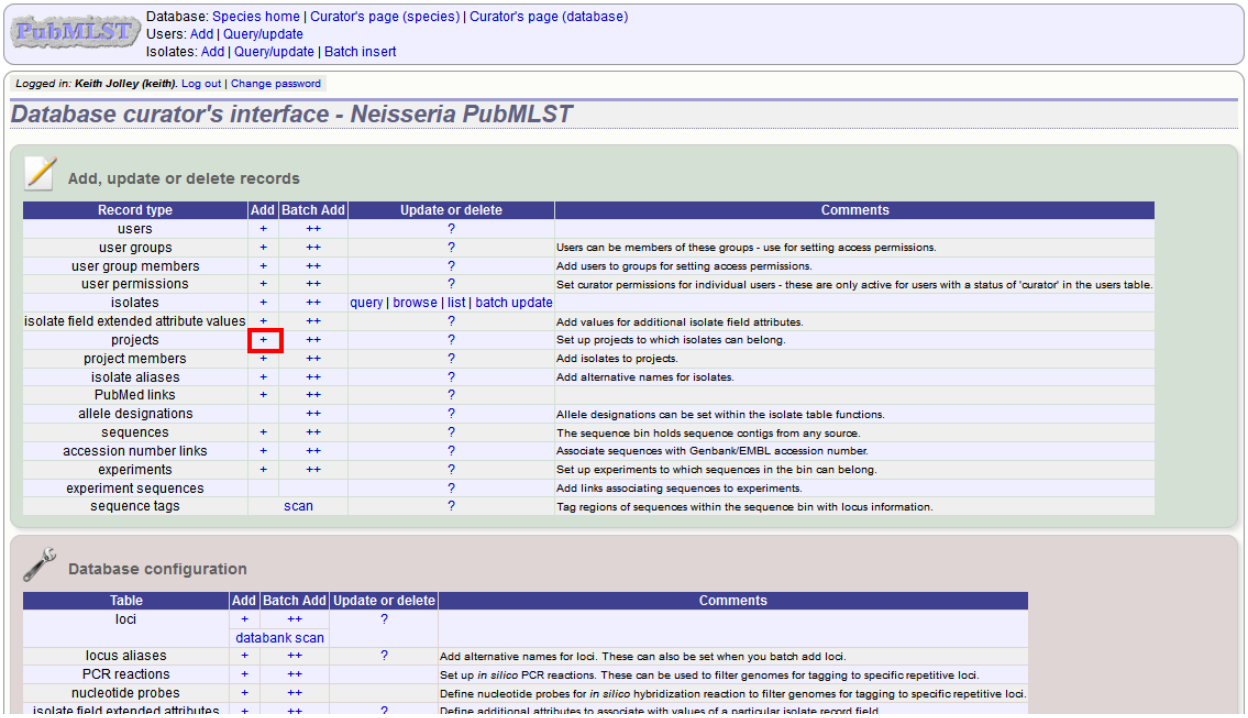
Automated offline sequence tagging

6.12 Projects

6.12.1 Creating the project

The first step in grouping by project is to set up a project.

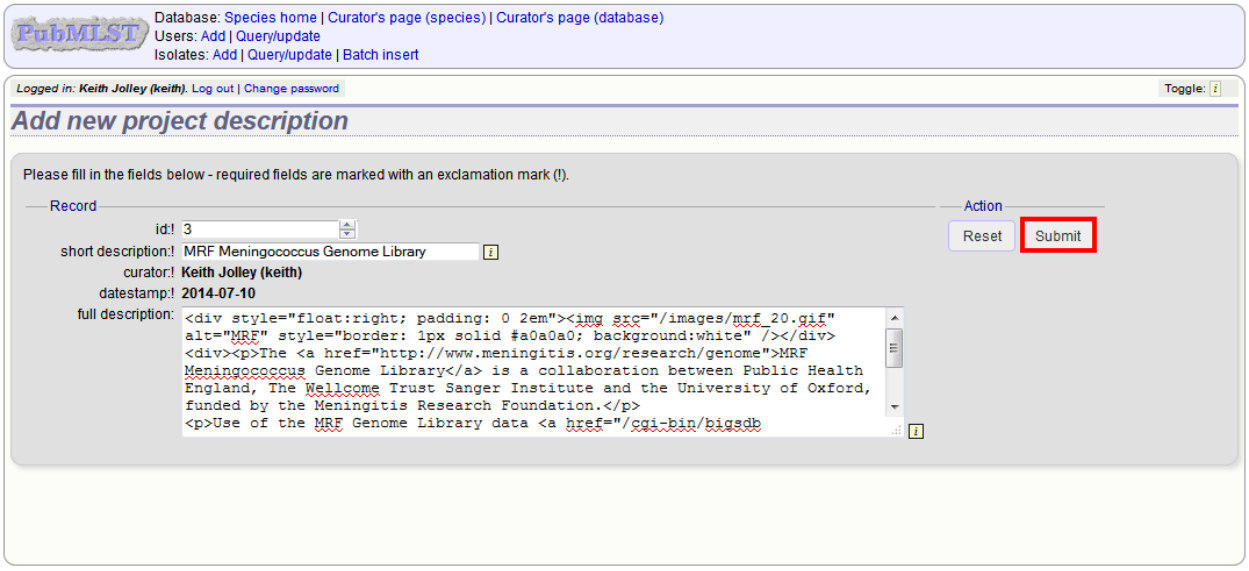
Click the add (+) project link on the curator's main page.



Enter a short description for the project. This is used in drop-down list boxes within the query interfaces, so make sure it is not too long.

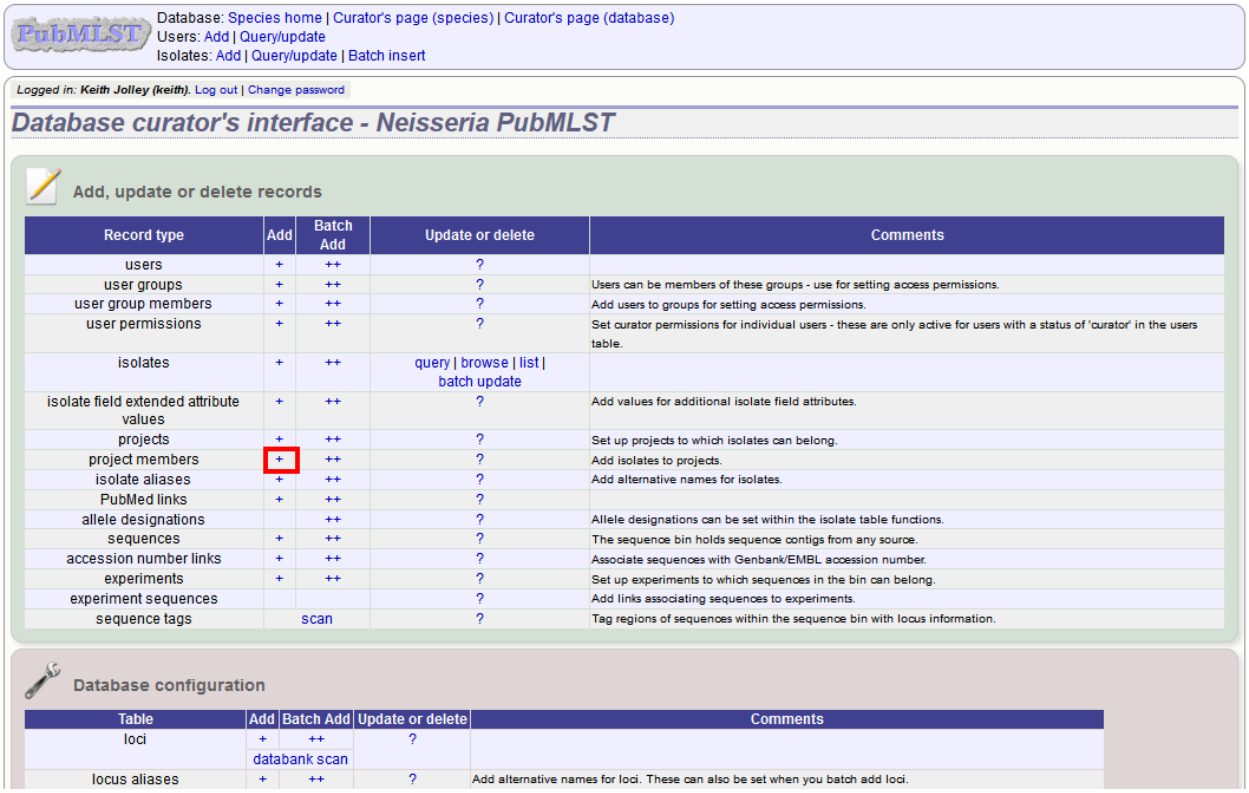
You can also enter a full description. If this is added, the project description is displayed at the top of an isolate information page. The full description can include HTML formatting, including image links.

Click 'Submit'.

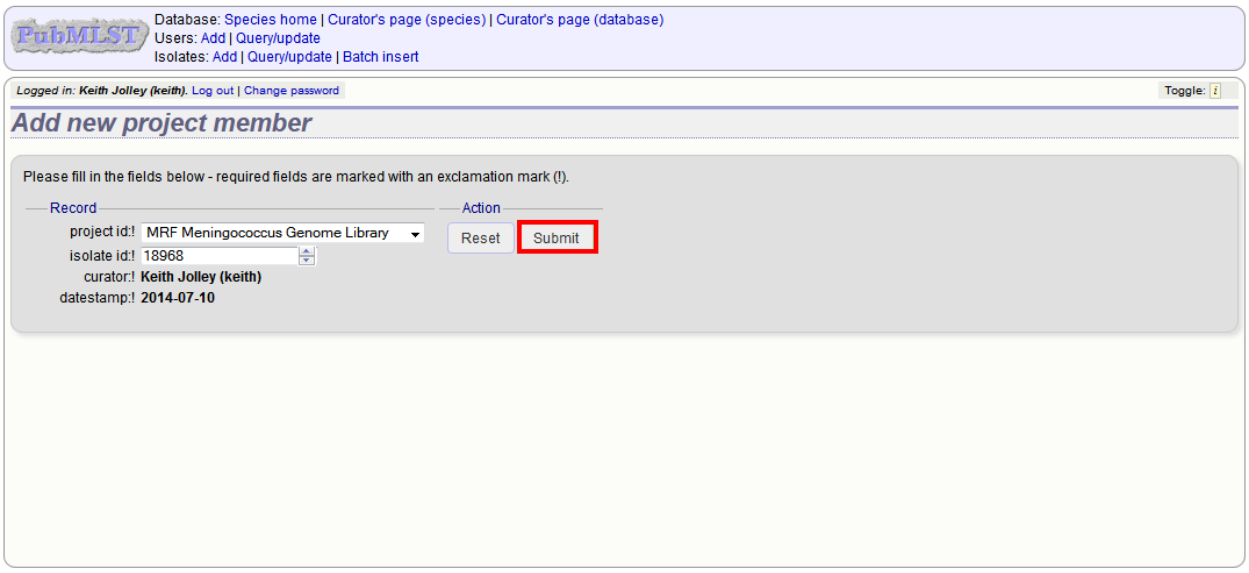


6.12.2 Explicitly adding isolates to a project

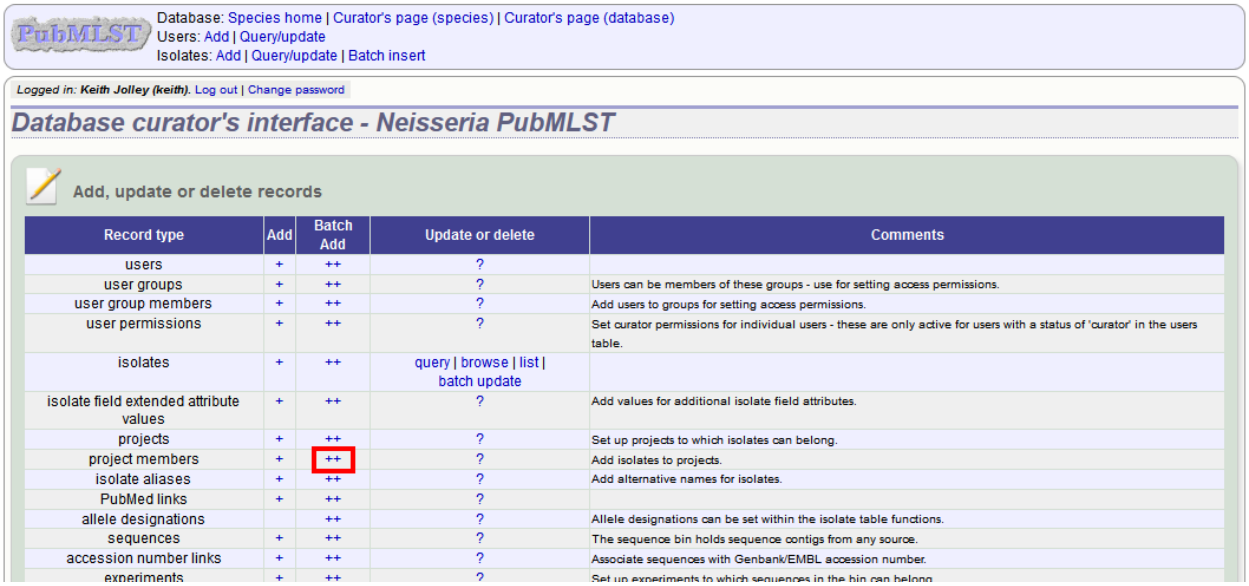
Explicitly adding isolates to the project can be done individually or in batch mode. To add individually, click the add (+) project member link on the curator's main page.



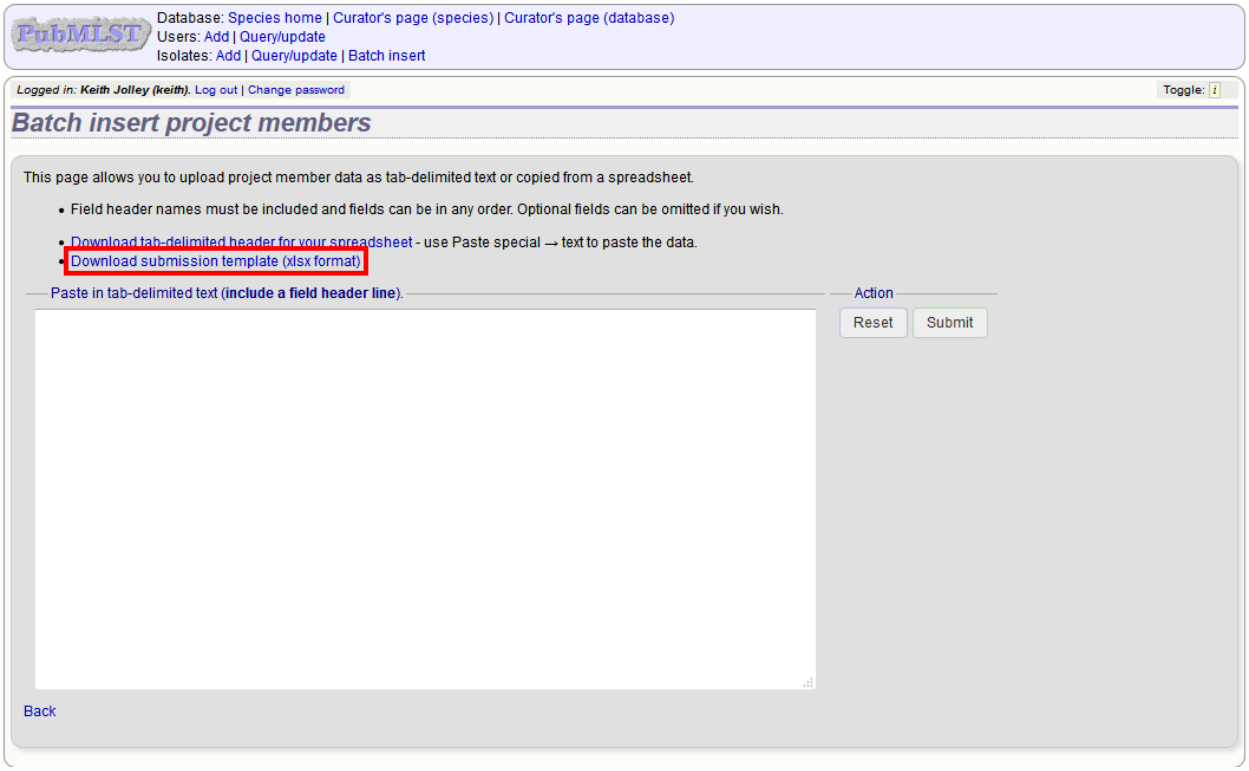
Select the project from the dropdown list box and enter the id of the isolate that you wish to add to the project. Click 'Submit'.



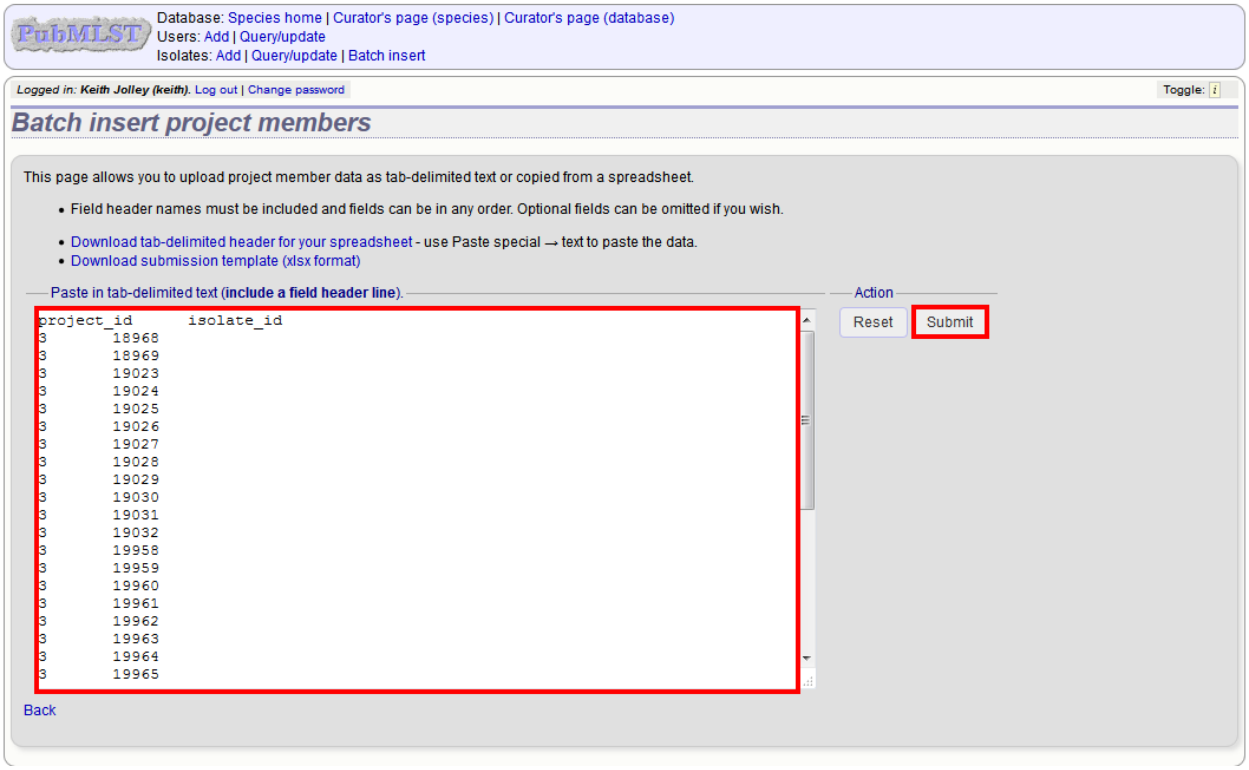
To add isolates in batch mode. Click the batch add (++) project members link on the curator's main page.



Download an Excel submission template:



You will need to know the id number of the project - this is the id that was used when you created the project. Fill in the spreadsheet, listing the project and isolate ids. Copy and paste this to the web upload form. press 'Submit'.



6.13 Isolate record versioning

New in version 1.9.0.

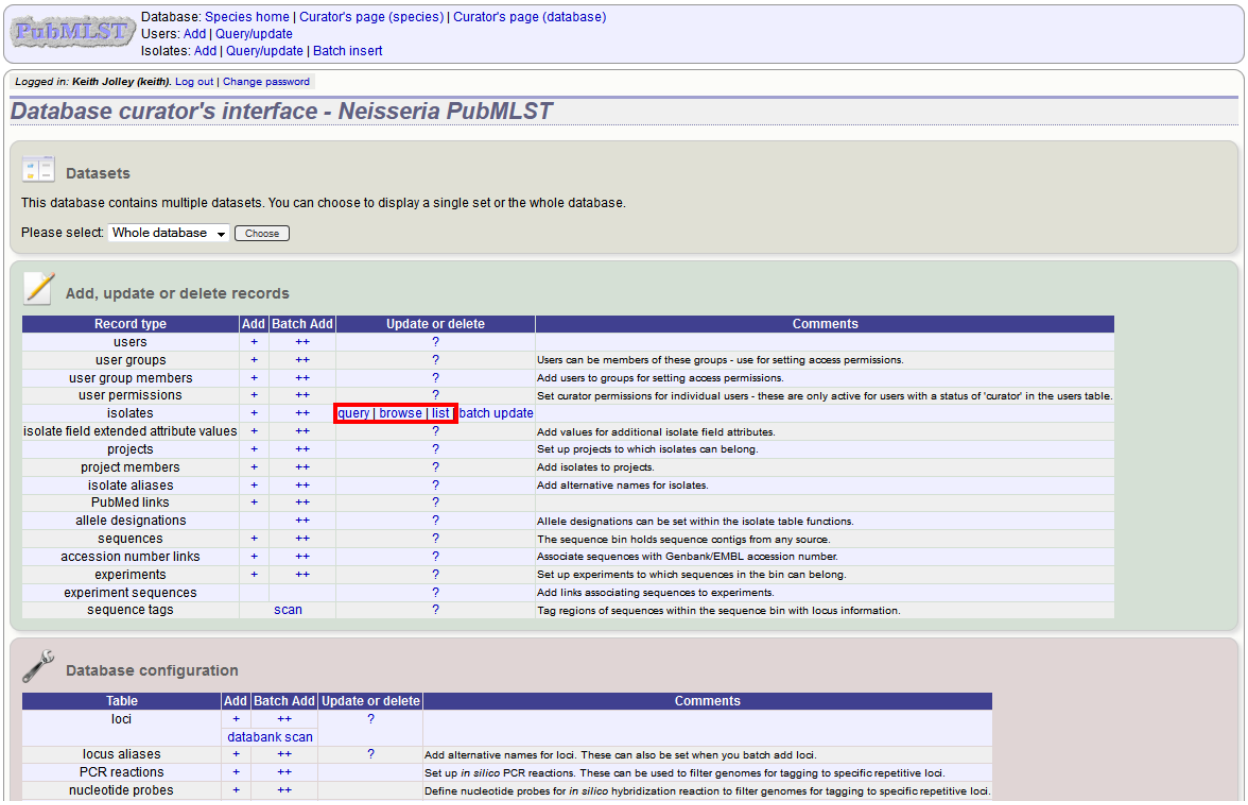
Versioning enables multiple versions of genomes to be uploaded to the database and be analysed separately. When a new version is created, a copy of the provenance metadata, and publication links are created in a new isolate record. The sequence bin and allele designations are not copied.

By default, old versions of the record are not returned from queries. Most query pages have a checkbox to 'Include old record versions' to override this.

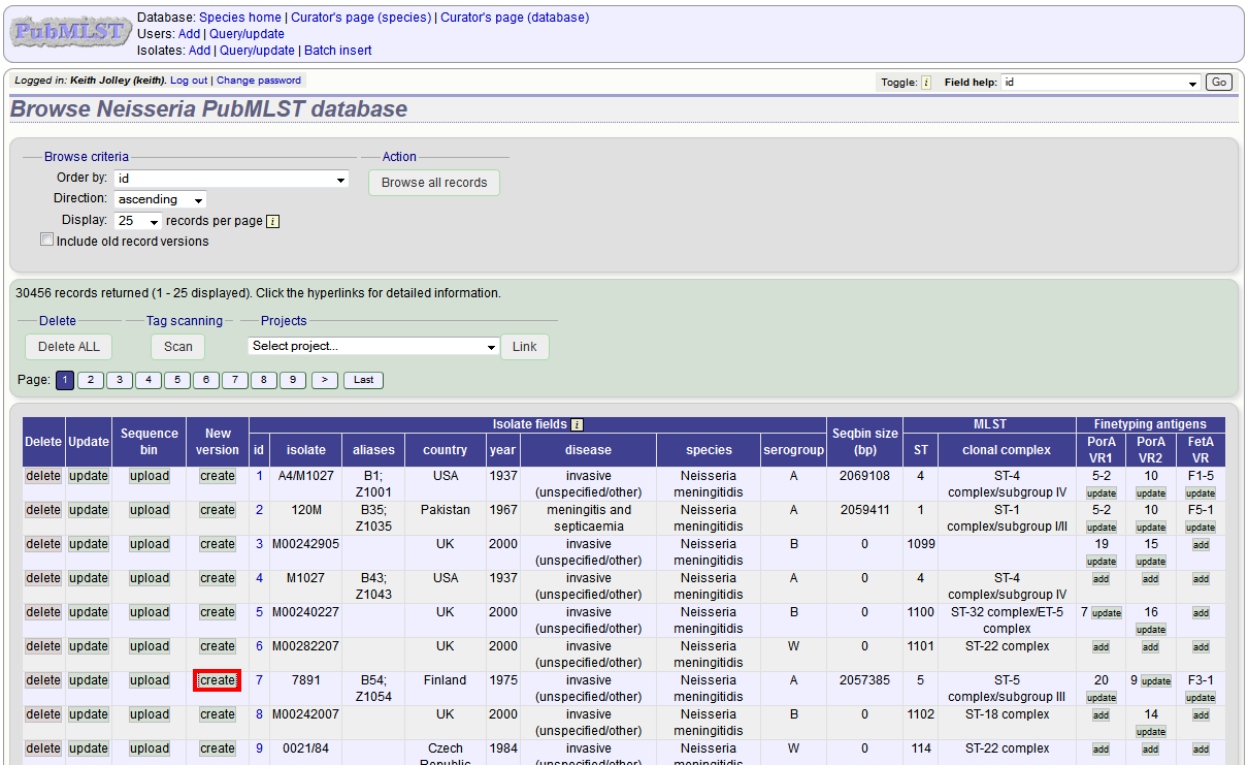
Links to different versions are displayed within an isolate record:

The different versions will also be listed in analysis plugins, with old versions identified with an [old version] designation after their name.

To create a new version of an isolate record, query or browse for the isolate:

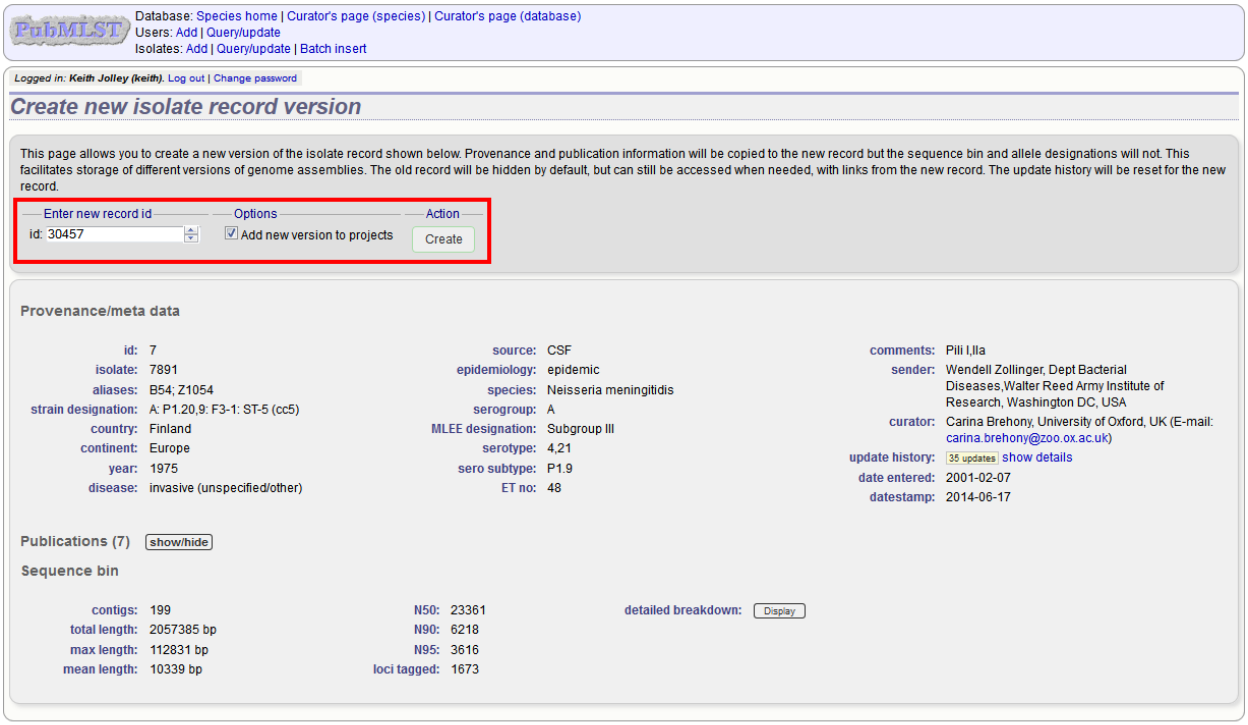


Click the 'create' new version link next to the isolate record:



The isolate record will be displayed. The suggested id number for the new record will be displayed - you can change this. By default, the new record will also be added to any projects that the old record is a member of. Uncheck the 'Add new version to projects' checkbox to prevent this.

Click the 'Create' button.



CHAPTER 7

Offline curation tools

7.1 Automated offline sequence tagging

Sequence tagging is the process of identifying alleles by scanning the sequence bin linked to an isolate record. Loci need to be defined in an external sequence definition database that contains the sequences for known alleles. The tagging function uses BLAST to identify sequences and will tag the specific sequence region with locus information and an allele designation if a matching allele is identified by reference to an external database.

There is a script called 'autotag.pl' in the BIGSdb package. This can be used to tag genome sequences from the command line.

Before autotag.pl can be run for the first time, a log file needs to be created. This can be created if it doesn't already exist with the following:

```
sudo touch /var/log/bigsdb_scripts.log
sudo chown bigsdb /var/log/bigsdb_scripts.log
```

The autotag.pl script should be installed in /usr/local/bin. It is run as follows:

```
autotag.pl --database <database configuration>
```

where <database configuration> is the name used for the argument 'db' when using the BIGSdb application.

If you have multiple processor cores available, use the –threads option to set the number of jobs to run in parallel. Isolates for scanning will be split among the threads.

The script must be run by a user that can both write to the log file and access the databases, e.g. the 'bigsdb' user (see 'Setting up the offline job manager').

A full list of options can be found by typing:

```
autotag.pl --help

NAME
    autotag.pl - BIGSdb automated allele tagger

SYNOPSIS
    autotag.pl --database NAME [options]

OPTIONS
-0, --missing
   Marks missing loci as provisional allele 0. Sets default word size to 15.

-d, --database NAME
```

```
    Database configuration name.

-h, --help
    This help page.

-i, --isolates LIST
    Comma-separated list of isolate ids to scan (ignored if -p used).

-I, --exclude_isolates LIST
    Comma-separated list of isolate ids to ignore.

-l, --loci LIST
    Comma-separated list of loci to scan (ignored if -s used).

-L, --exclude_loci LIST
    Comma-separated list of loci to exclude

-m, --min_size SIZE
    Minimum size of seqbin (bp) - limit search to isolates with at least this
    much sequence.

-n, --new_only
    New (previously untagged) isolates only.

-o, --order
    Order so that isolates last tagged the longest time ago get scanned first
    (ignored if -r used).

-p, --projects LIST
    Comma-separated list of project isolates to scan.

-P, --exclude_projects LIST
    Comma-separated list of projects whose isolates will be excluded.

-q, --quiet
    Only error messages displayed.

-r, --random
    Shuffle order of isolate ids to scan.

-R, --locus_regex REGEX
    Regex for locus names.

-s, --schemes LIST
    Comma-separated list of scheme loci to scan.

-t, --time MINS
    Stop after t minutes.

--threads THREADS
    Maximum number of threads to use.

-T, --already_tagged
    Scan even when sequence tagged (no designation).

-w, --word_size SIZE
    BLASTN word size.
```

```
-x, --min ID
    Minimum isolate id.

-y, --max ID
    Maximum isolate id.
```

7.2 Automated offline allele definition

There is a script called 'scannew.pl' in the BIGSdb scripts/automation directory. This can be used to identify new alleles from the command line. This can (optionally) upload these to a sequence definition database.

Before scannew.pl can be run for the first time, a log file needs to be created. This can be created if it doesn't already exist with the following:

```
sudo touch /var/log/bigsdb_scripts.log
sudo chown bigsdb /var/log/bigsdb_scripts.log
```

The autotag.pl script should be installed in /usr/local/bin. It is run as follows:

```
scannew.pl --database <database configuration>
```

where <database configuration> is the name used for the argument 'db' when using the BIGSdb application.

If you have multiple processor cores available, use the –threads option to set the number of jobs to run in parallel. Loci for scanning will be split among the threads.

The script must be run by a user that can both write to the log file and access the databases, e.g. the 'bigsdb' user (see 'Setting up the offline job manager').

A full list of options can be found by typing:

```
scannew.pl --help

NAME
  scannew.pl - BIGSdb automated allele definer

SYNOPSIS
  scannew.pl --database NAME [options]

OPTIONS
-a, --assign
     Assign new alleles in definitions database.

-A, --alignment INT
    Percentage alignment (default: 100).

-B, --identity INT
    Percentage identity (default: 99).

-c, --coding_sequences
    Only return complete coding sequences.

-d, --database NAME
    Database configuration name.

-h, --help
    This help page.
```

```
-i, --isolates LIST
    Comma-separated list of isolate ids to scan (ignored if -p used).

-I, --exclude_isolates LIST
    Comma-separated list of isolate ids to ignore.

-l, --loci LIST
    Comma-separated list of loci to scan (ignored if -s used).

-L, --exclude_loci LIST
    Comma-separated list of loci to exclude.

-m, --min_size SIZE
    Minimum size of seqbin (bp) - limit search to isolates with at least this
    much sequence.

-n, --new_only
    New (previously untagged) isolates only.

-o, --order
    Order so that isolates last tagged the longest time ago get scanned first
    (ignored if -r used).

-p, --projects LIST
    Comma-separated list of project isolates to scan.

-P, --exclude_projects LIST
    Comma-separated list of projects whose isolates will be excluded.

-r, --random
    Shuffle order of isolate ids to scan.

-R, --locus_regex REGEX
    Regex for locus names.

-s, --schemes LIST
    Comma-separated list of scheme loci to scan.

-t, --time MINS
    Stop after t minutes.

--threads THREADS
    Maximum number of threads to use.

-T, --already_tagged
    Scan even when sequence tagged (no designation).

-w, --word_size SIZE
    BLASTN word size.

-x, --min ID
    Minimum isolate id.

-y, --max ID
    Maximum isolate id.
```

7.3 Cleanly interrupting offline curation

Sometimes you may wish to stop running autotagger or allele autodefiner jobs as they can be run for a long time and as CRON jobs. If these are running in single threaded mode, the easiest way is to simply send a kill signal to the process, i.e. identify the process id using 'top', e.g. 23232 and then

```
kill 23232
```

The scripts should respond to this signal within a couple of seconds, clean up all their temporary files and write the history log (where appropriate). Do not use 'kill -9' as this will terminate the processes immediately and not allow them to clean up.

If these scripts are running using multiple threads, then you need to cleanly kill each of these. The simplest way to terminte all autotagger jobs is to, type

```
pkill autotag
```

The parent process will wait for all forked processes to cleanly terminate and then exit itself.

Similarly, to terminate all allele autodefiner jobs, type

```
pkill scannew
```

CHAPTER 8

Definition downloads

The sequence definition database defines alleles, i.e. links an allele identifier to a sequence. It also defines scheme, e.g. MLST, profiles.

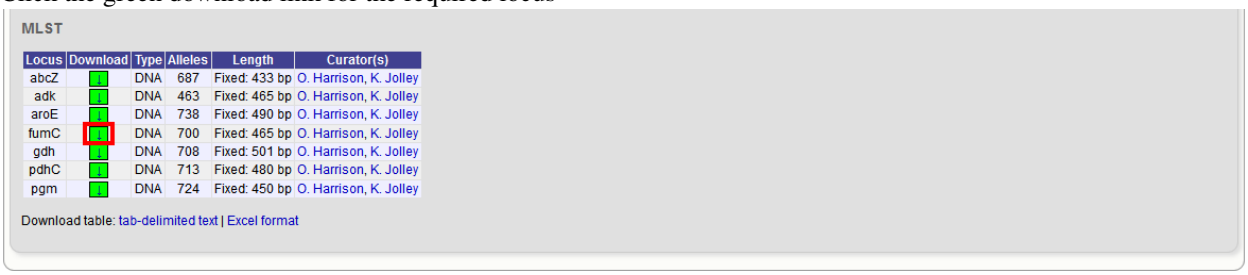
8.1 Allele sequence definitions

Click the 'Allele sequences' link in the 'Downloads' section. Depending on the database, you may see either a hierarchical scheme tree or a table of loci. You can choose to display links either by scheme using the scheme tree, as an alphabetical list or a page of all schemes, by selecting the approrpiate link at the top of the page.

8.1.1 Scheme tree

You can drill down through the tree by clicking branch nodes. Clicking the labels of internal nodes will display tables of all schemes belonging to that scheme group. Clicking the labels of terminal nodes will display that single scheme table.

Click the green download link for the required locus



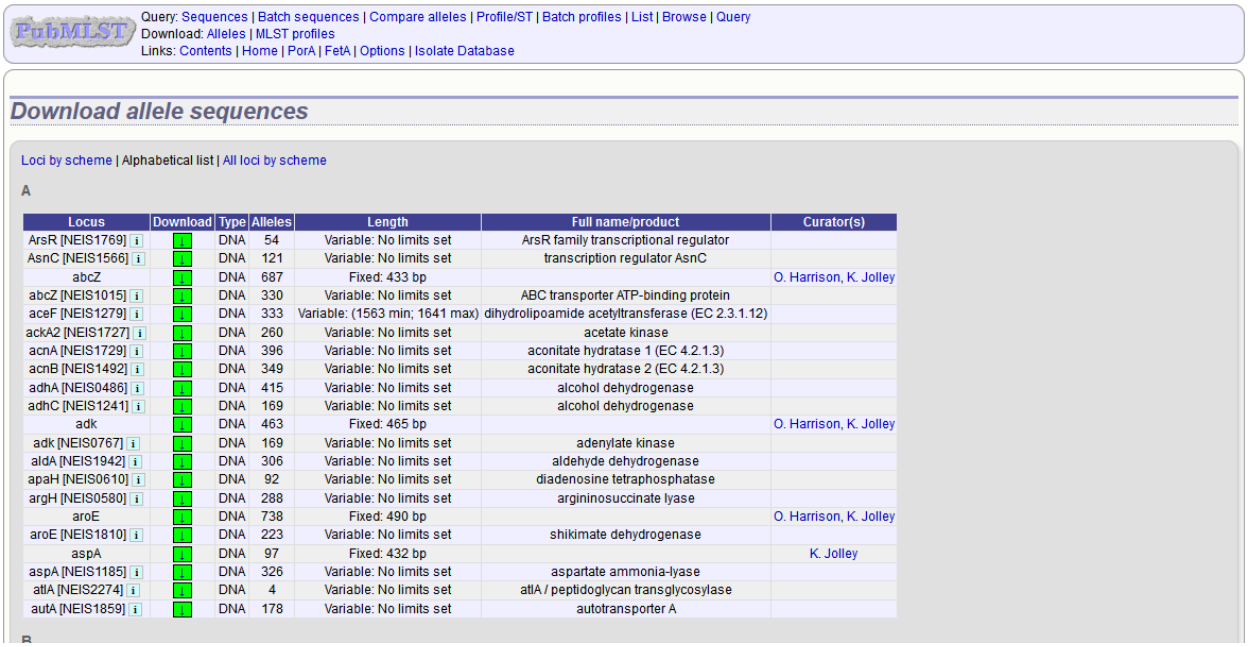
Alleles will be downloaded in FASTA format, e.g.

```
>fumC_1
GAAGCCTTGGGCGGACGCGATGCCGCCGTTGCCGCTTCGGGCGCATTGAAAACGCTGGCG
GCAAGCCTGAATAAAATCGCCAACGACATCCGCTGGCTGGCAAGCGGCCCGCGCTGCGGT
TTGGGCGAAATCAAAATCCCCGAAAACGAGCCGGGTTCGTCCATCATGCCGGGCAAAGTC
AACCCGACCCAATGCGAAGCGATGACCATGGTGTGCTGCCAAGTGTTCGGCAACGACGTT
ACCATCGGTATGGCGGGCGCGTCGGGCAATTTCGAGCTGAACGTCTATATGCCCGTCATC
GCCTACAACCTCTTGCAATCCATCCGCCTGTTGGGCGACGCGTGCAACAGCTTCAACGAA
CACTGCGCCGTCGGCATTGAACCCGTACCGGAAAAAATCGACTATTTCCTGCACCATTCC
CTGATGCTCGTTACCGCGTTAAACCGCAAAATCGGTTACGAAAAC
>fumC_2
GAAGCCTTGGGCGGACGCGATGCCGCCGTTGCCGCTTCGGGCGCATTGAAAACGCTGGCG
GCAAGCCTGAATAAAATCGCCAACGACATCCGCTGGCTGGCAAGCGGCCCGCGCTGCGGT
TTGGGCGAAATCAAAATCCCCGAAAACGAGCCGGGTTCGTCCATCATGCCGGGCAAAGTC
AACCCGACCCAATGCGAAGCGATGACCATGGTGTGCTGCCAAGTGTTCGGCAACGACGTT
ACCATCGGCATGGCGGGCGCGTCGGGCAATTTCGAGCTGAACGTCTATATGCCCGTTATC
GCCTACAACCTCTTGCAATCCATCCGCCTCTTGGGCGACGCGTGCAACAGCTTCAACGAA
CACTGCGCCATCGGCATCGAACCCGTACCGGAAAAAATCGACTATTTCCTGCACCATTCC
```

```
CTGATGCTCGTTACCGCGTTAAACCGCAAAATCGGTTACGAAAAC
>fumC_3
GAAGCCTTGGGCGGACGCGATGCCGCCGTTGCCGCTTCGGGCGCATTGAAAACGCTGGCG
GCAAGCCTGAATAAAATCGCCAACGACATCCGCTGGCTGGCAAGCGGCCCGCGCTGCGGT
TTGGGCGAAATCAAAATCCCCGAAAACGAGCCGGGTTCGTCCATCATGCCGGGCAAAGTC
AACCCGACCCAATGCGAAGCGATGACCATGGTGTGCTGCCAAGTGTTCGGCAACGACGTT
ACCATCGGCATGGCGGGCGCGTCGGGCAATTTCGAGCTGAACGTCTATATGCCCGTTATC
GCCTACAACCTCTTGCAATCCATCCGCCTGTTGGGCGACGCGTGCAACAGCTTCAACGAA
CACTGCGCCGTCGGCATCGAACCCGTACCGGAAAAAATCGACTATTTCCTGCACCATTCC
CTGATGCTGGTTACTGCGTTAAACCGTAAAATCGGCTACGAAAAC
```

8.1.2 Alphabetical list

Loci can be displayed in an alphabetical list. Loci will be grouped in to tables by initial letter. If common names are set for loci, they will be listed by both primary and common names.

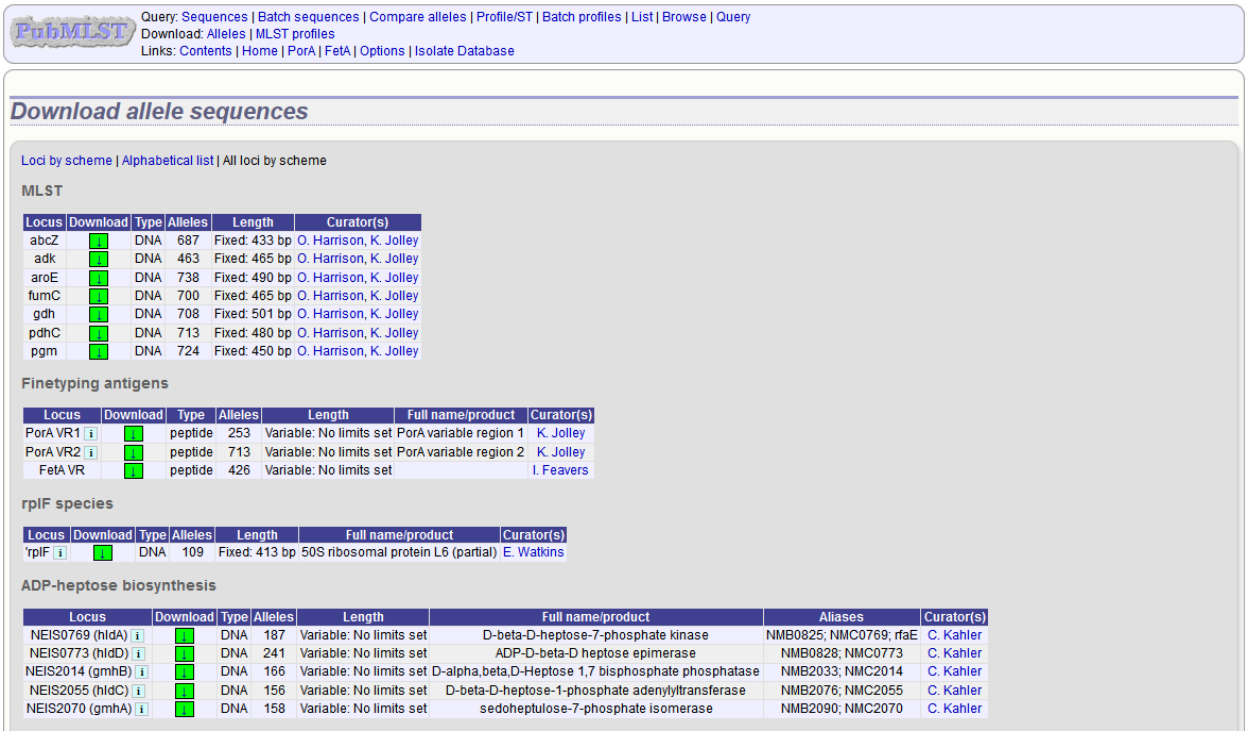


Locus	Download	Type	Alleles	Length	Full name/product	Curator(s)
ArsR [NEIS1769]		DNA	54	Variable: No limits set	ArsR family transcriptional regulator	
AsnC [NEIS1566]		DNA	121	Variable: No limits set	transcription regulator AsnC	
abcZ		DNA	687	Fixed: 433 bp		O. Harrison, K. Jolley
abcZ [NEIS1015]		DNA	330	Variable: No limits set	ABC transporter ATP-binding protein	
aceF [NEIS1279]		DNA	333	Variable: (1563 min; 1641 max)	dihydrolipoamide acetyltransferase (EC 2.3.1.12)	
ackA2 [NEIS1727]		DNA	260	Variable: No limits set	acetate kinase	
acnA [NEIS1729]		DNA	396	Variable: No limits set	aconitate hydratase 1 (EC 4.2.1.3)	
acnB [NEIS1492]		DNA	349	Variable: No limits set	aconitate hydratase 2 (EC 4.2.1.3)	
adhA [NEIS0486]		DNA	415	Variable: No limits set	alcohol dehydrogenase	
adhC [NEIS1241]		DNA	169	Variable: No limits set	alcohol dehydrogenase	
adk		DNA	463	Fixed: 465 bp		O. Harrison, K. Jolley
adk [NEIS0767]		DNA	169	Variable: No limits set	adenylate kinase	
aldA [NEIS1942]		DNA	306	Variable: No limits set	aldehyde dehydrogenase	
apaH [NEIS0610]		DNA	92	Variable: No limits set	diadenosine tetraphosphatase	
argH [NEIS0580]		DNA	288	Variable: No limits set	argininosuccinate lyase	
aroE		DNA	738	Fixed: 490 bp		O. Harrison, K. Jolley
aroE [NEIS1810]		DNA	223	Variable: No limits set	shikimate dehydrogenase	
aspA		DNA	97	Fixed: 432 bp		K. Jolley
aspA [NEIS1185]		DNA	326	Variable: No limits set	aspartate ammonia-lyase	
atlA [NEIS2274]		DNA	4	Variable: No limits set	atlA / peptidoglycan transglycosylase	
autA [NEIS1859]		DNA	178	Variable: No limits set	autotransporter A	

Click the green download links for the required locus.

8.1.3 All loci by scheme

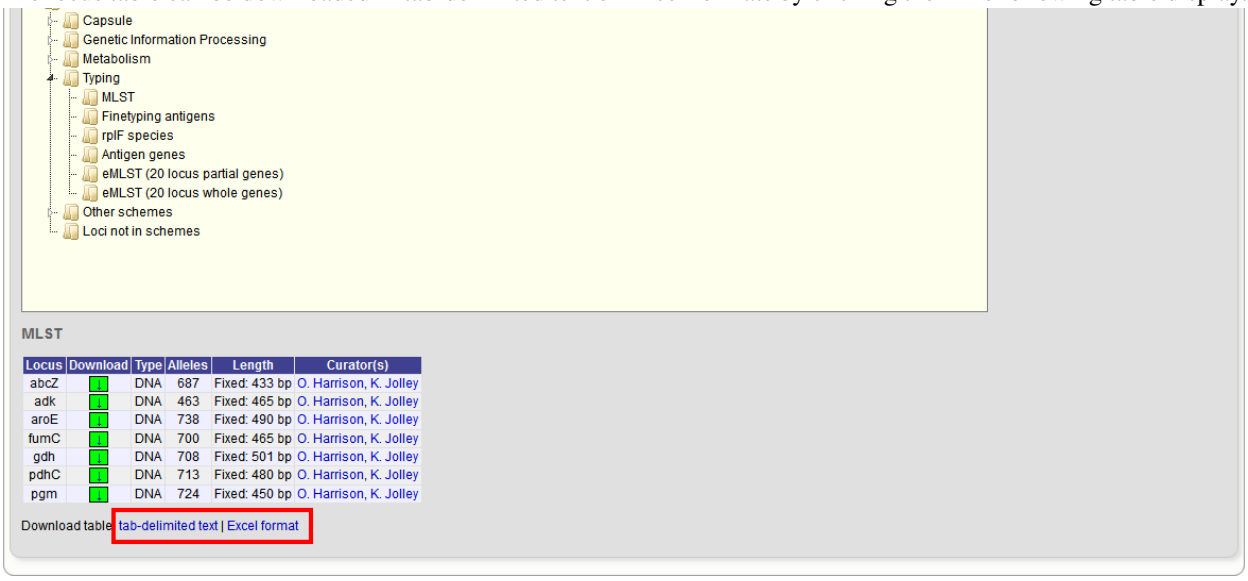
Loci can also be displayed by scheme with all schemes displayed.



Click the green download links for the required locus.

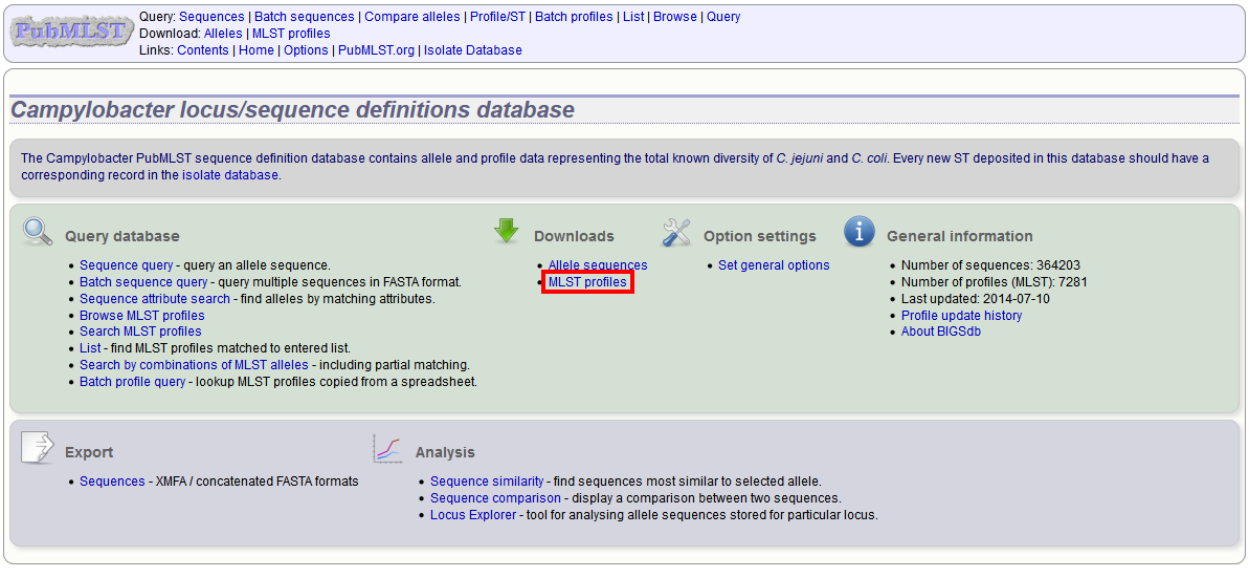
8.1.4 Download locus table

The locus table can be downloaded in tab-delimited text or Excel formats by clicking the links following table display.

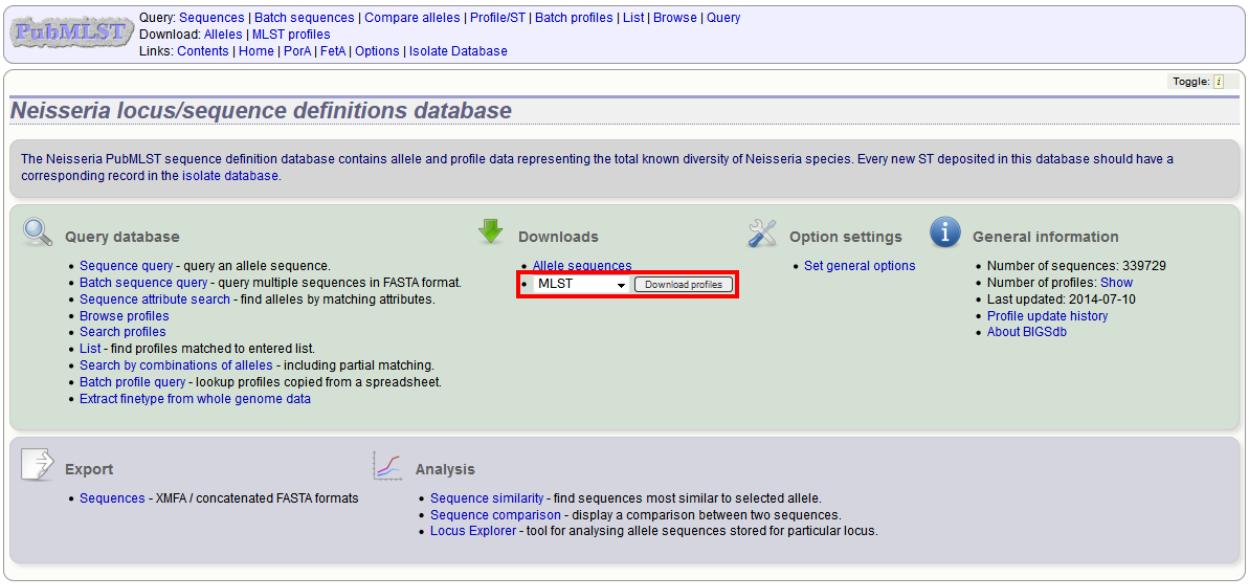


8.2 Scheme profile definitions

Scheme profiles, e.g. those for MLST, can be downloaded by clicking the appropriate link on the contents page.



If multiple schemes are available, you will need to select the scheme in the dropdown box and click 'Download profiles'



Profiles will be downloaded in tab-delimited format, e.g.

ST	abcZ	adk	aroE	fumC	gdh	pdhC	pgm	clonal_complex
1	1	3	1	1	1	1	3	ST-1 complex/subgroup I/II
2	1	3	4	7	1	1	3	ST-1 complex/subgroup I/II
3	1	3	1	1	1	23	13	ST-1 complex/subgroup I/II
4	1	3	3	1	4	2	3	ST-4 complex/subgroup IV
5	1	1	2	1	3	2	3	ST-5 complex/subgroup III
6	1	1	2	1	3	2	11	ST-5 complex/subgroup III
7	1	1	2	1	3	2	19	ST-5 complex/subgroup III
8	2	3	7	2	8	5	2	ST-8 complex/Cluster A4
9	2	3	8	10	8	5	2	ST-8 complex/Cluster A4
10	2	3	4	2	8	15	2	ST-8 complex/Cluster A4
11	2	3	4	3	8	4	6	ST-11 complex/ET-37 complex

```
12    4       3       2       16      8       11      20
13    4       10      15      7       8       11      1       ST-269 complex
14    4       1       15      7       8       11      1       ST-269 complex
```

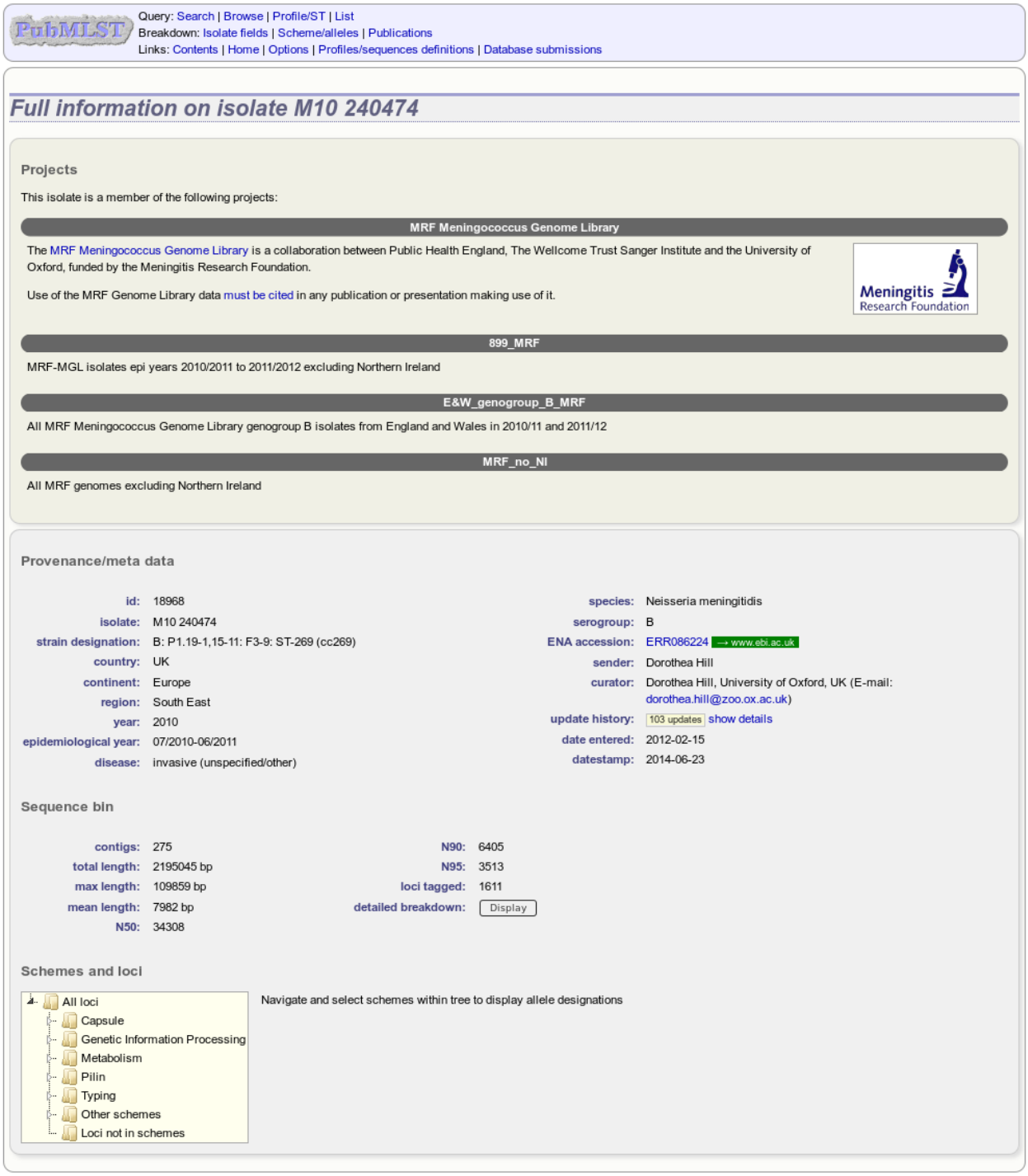
CHAPTER 9

Data records

Record pages for different types of data can be accessed following a query by clicking appropriate hyperlinks.

9.1 Isolate records

An Isolate record page displays everything known about an isolate.



Each record will have some or all of the following sections:

9.1.1 Projects

Projects

This isolate is a member of the following projects:

MRF Meningococcus Genome Library

The MRF Meningococcus Genome Library is a collaboration between Public Health England, The Wellcome Trust Sanger Institute and the University of Oxford, funded by the Meningitis Research Foundation.

Use of the MRF Genome Library data must be cited in any publication or presentation making use of it.

Meningitis Research Foundation

This displays a list of projects that the isolate is a member of. Only projects that have a full description will be displayed.

9.1.2 Provenance metadata

Provenance/meta data

id:	18968	species:	Neisseria meningitidis
isolate:	M10 240474	serogroup:	B
strain designation:	B: P1.19-1,15-11: F3-9: ST-269 (cc269)	ENA accession:	ERR086224 → www.ebi.ac.uk
country:	UK	sender:	Dorothea Hill
continent:	Europe	curator:	Dorothea Hill, University of Oxford, UK (E-mail: dorothea.hill@zoo.ox.ac.uk)
region:	South East	update history:	103 updates show details
year:	2010	date entered:	2012-02-15
epidemiological year:	07/2010-06/2011	datestamp:	2014-06-23
disease:	invasive (unspecified/other)		

This section includes:

- provenance fields
- housekeeping data
  - who sent the isolate
  - who last curated
  - record creation times
  - last update times
  - links to update history

The update link displays page with exact times of who and when updated the record.

PubMLST
Query: Search | Browse | Profile/ST | List
Breakdown: Isolate fields | Scheme/alleles | Publications
Links: Contents | Home | Options | Profiles/sequences definitions | Database submissions

Full information on isolate M10 240474

Update history

Back to isolate information

Timestamp	Curator	Action
2014-06-23 09:44	Dorothea Hill	NEIS2363: new designation '28' (sequence bin scan) NEIS2363: sequence tagged. Seqbin id: 4836; 3070-5108 (sequence bin scan)
2014-06-17 10:55	Carina Brehony	gyrA: designation '1000' deleted
2014-06-16 16:17	Carina Brehony	gyrA: sequence tagged. Seqbin id: 4885; 23385-23909 (sequence bin scan)
2014-06-16 14:48	Carina Brehony	gyrA: new designation '12' (sequence bin scan)
2014-06-05 15:55	Carina Brehony	gyrA: new designation '1000'
2014-06-05 15:55	Carina Brehony	gyrA: designations '12,30' deleted
2014-05-30 13:26	Eloise Orton	gyrA: new designation '30' (sequence bin scan) gyrA: sequence tagged. Seqbin id: 4989; 25611-26135 (sequence bin scan)
2014-05-17 09:26	Auto Tagger	NEIS2155: new designation '244' (sequence bin scan) NEIS2155: sequence tagged. Seqbin id: 5030; 977-1984 (sequence bin scan) pip: new designation '127' (sequence bin scan) pip: sequence tagged. Seqbin id: 4818; 35321-35736 (sequence bin scan) serC: new designation '123' (sequence bin scan) serC: sequence tagged. Seqbin id: 4765; 3629-4078 (sequence bin scan)
2014-03-16 11:15	Auto Tagger	NEIS0020: new designation '3' (sequence bin scan) NEIS0020: sequence tagged. Seqbin id: 4845; 4412-5980 (sequence bin scan) NEIS0036: new designation '8' (sequence bin scan) NEIS0036: sequence tagged. Seqbin id: 4977; 2774-3817 (sequence bin scan) NEIS0408: new designation '70' (sequence bin scan) NEIS0408: sequence tagged. Seqbin id: 4850; 28381-30666 (sequence bin scan) NEIS0409: new designation '25' (sequence bin scan) NEIS0409: sequence tagged. Seqbin id: 4850; 30685-31230 (sequence bin scan) NEIS0410: new designation '7' (sequence bin scan) NEIS0410: sequence tagged. Seqbin id: 4850; 31248-31895 (sequence bin scan) NEIS0411: new designation '2' (sequence bin scan) NEIS0411: sequence tagged. Seqbin id: 4850; 31896-32495 (sequence bin scan) NEIS0412: new designation '3' (sequence bin scan) NEIS0412: sequence tagged. Seqbin id: 4850; 32498-33613 (sequence bin scan) NEIS0721: new designation '14' (sequence bin scan) NEIS0721: sequence tagged. Seqbin id: 4950; 33102-34214 (sequence bin scan) NEIS1838: new designation '12' (sequence bin scan)

9.1.3 Publications

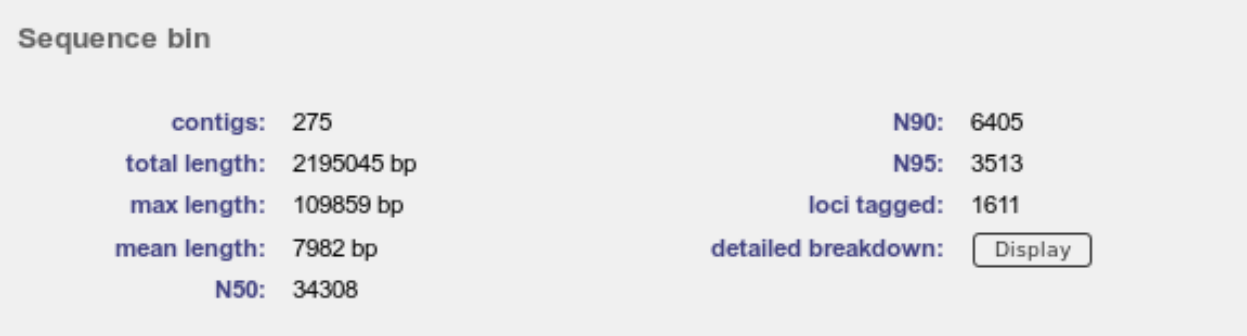
Publications (8) show/hide

- Bennett JS, Jolley KA, Sparling PF, Saunders NJ, Hart CA, Feavers IM, Maiden MC (2007). Species status of Neisseria gonorrhoeae: evolutionary and epidemiological inferences from multilocus sequence typing. *BMC Biol* **5**:35 576 isolates
- Didelot X, Urwin R, Maiden MC, Falush D (2009). Genealogical typing of Neisseria meningitidis. *Microbiology* **155**:3176-86 93 isolates
- Jolley KA, Sun L, Moxon ER, Maiden MC (2004). Dam inactivation in Neisseria meningitidis: prevalence among diverse hyperinvasive lineages. *BMC Microbiol* **4**:34 84 isolates
- Jolley KA, Wilson DJ, Kriz P, McVean G, Maiden MC (2005). The influence of mutation, recombination, population history, and selection on patterns of genetic diversity in Neisseria meningitidis. *Mol Biol Evol* **22**:562-9 378 isolates
- Maiden MC, Bygraves JA, Feil E, Morelli G, Russell JE, Urwin R, Zhang Q, Zhou J, Zurth K, Caugant DA, Feavers IM, Achtman M, Spratt BG (1998). Multilocus sequence typing: a portable approach to the identification of clones within populations of pathogenic microorganisms. *Proc Natl Acad Sci U S A* **95**:3140-5 107 isolates
- Thompson EA, Feavers IM, Maiden MC (2003). Antigenic diversity of meningococcal enterobactin receptor FetA, a vaccine component. *Microbiology* **149**:1849-58 107 isolates
- Urwin R, Russell JE, Thompson EA, Holmes EC, Feavers IM, Maiden MC (2004). Distribution of surface protein variants among hyperinvasive meningococci: implications for vaccine design. *Infect Immun* **72**:5955-62 78 isolates
- Wang JF, Caugant DA, Li X, Hu X, Poolman JT, Crowe BA, Achtman M (1992). Clonal and antigenic analysis of serogroup A Neisseria meningitidis with particular reference to epidemiological features of epidemic meningitis in the People's Republic of China. *Infect Immun* **60**:5267-82 47 isolates

This section includes full citation for papers linked to the isolate record. Each citation has a button that will return a dataset of all isolates linked to the paper.

If there are five or more references they will be hidden by default to avoid cluttering the page too much. Click the 'Show/hide' button to display them in this case.

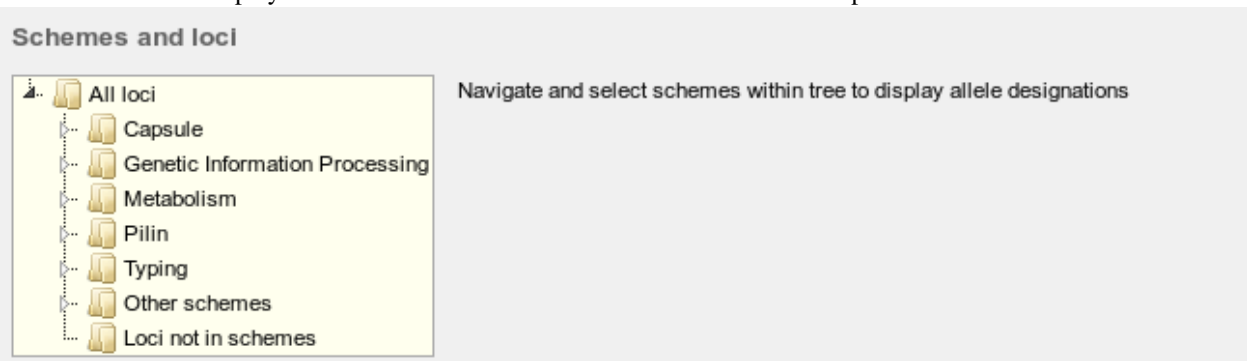
9.1.4 Sequence bin summary



This section contains basic statistics describing the sequence bin. Clicking the 'Display' button navigates to the *sequence bin record*.

9.1.5 Scheme and locus data

A hierarchical tree displays available schemes. Click within internal nodes to expand them.

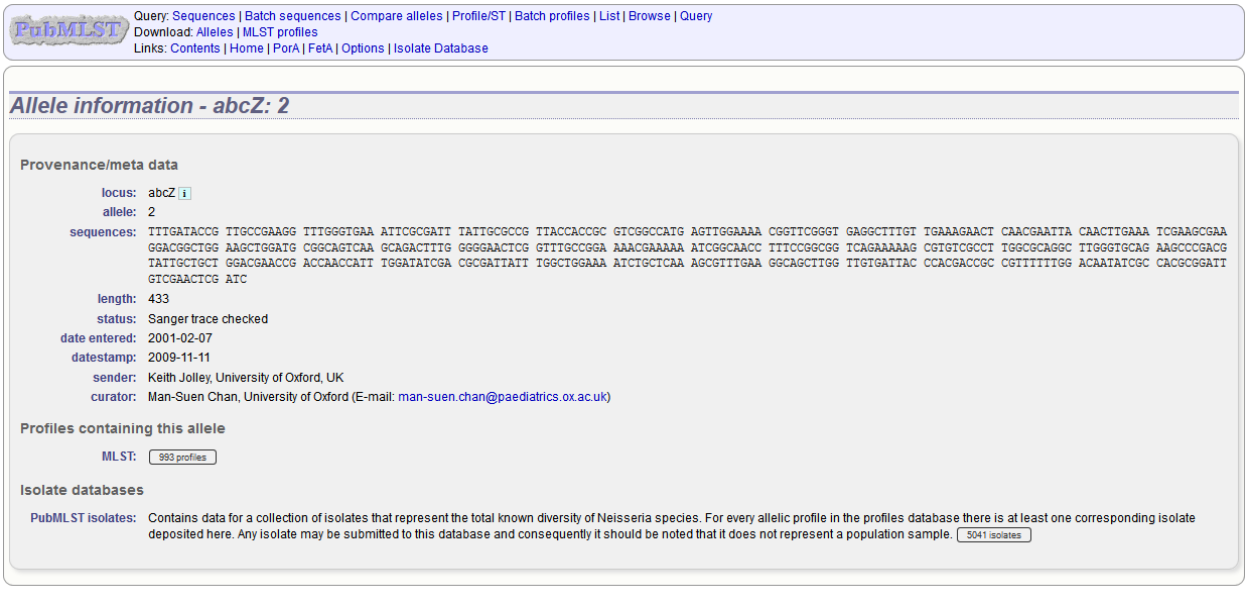


Clicking any terminal node will display data available for a scheme or group of schemes.

Click an allele number within the scheme profile, will display the appropriate *allele definition record*. Clicking the green 'S' link will display the appropriate *sequence tag record*.

9.2 Allele definition records

An allele definition record displays information about a defined allele in a sequence definition database.



Query: Sequences | Batch sequences | Compare alleles | Profile/ST | Batch profiles | List | Browse | Query
Download: Alleles | MLST profiles
Links: Contents | Home | PorA | FetA | Options | Isolate Database

Allele information - abcZ: 2

Provenance/meta data

locus: abcZ
allele: 2
sequences: TTTGATACCG TTGCCGAAGG TTTGGGTGAA ATTCGCGATT TATTGCGCCG TTACCACCGC GTCGGCCATG AGTTGGAAAA CGGTTCGGGT GAGGCTTTGT TGAAAGAACT CAACGAATTA CAACTTGAAA TCGAAGCGAA GGACGGCTGG AAGCTGGATG CGGCAGTCAA GCAGACTTTG GGGGAACTCG GTTTGCCGGA AAACGAAAAA ATCGGCAACC TTTCCGGCGG TCAGAAAAAG CGTGTCGCCT TGGCGCAGGC TTGGGTGCAG AAGCCCGACG TATTGCTGCT GGACGAACCG ACCAACCATT TGGATATCGA CGCGATTATT TGGCTGGAAA ATCTGCTCAA AGCGTTTGAA GGCAGCTTGG TTGTGATTAC CCACGACCGC CGTTTTTTGG ACAATATCGC CACGCGGATT GTCGAACTCG ATC
length: 433
status: Sanger trace checked
date entered: 2001-02-07
datestamp: 2009-11-11
sender: Keith Jolley, University of Oxford, UK
curator: Man-Suen Chan, University of Oxford (E-mail: man-suen.chan@paediatrics.ox.ac.uk)

Profiles containing this allele

MLST: 993 profiles

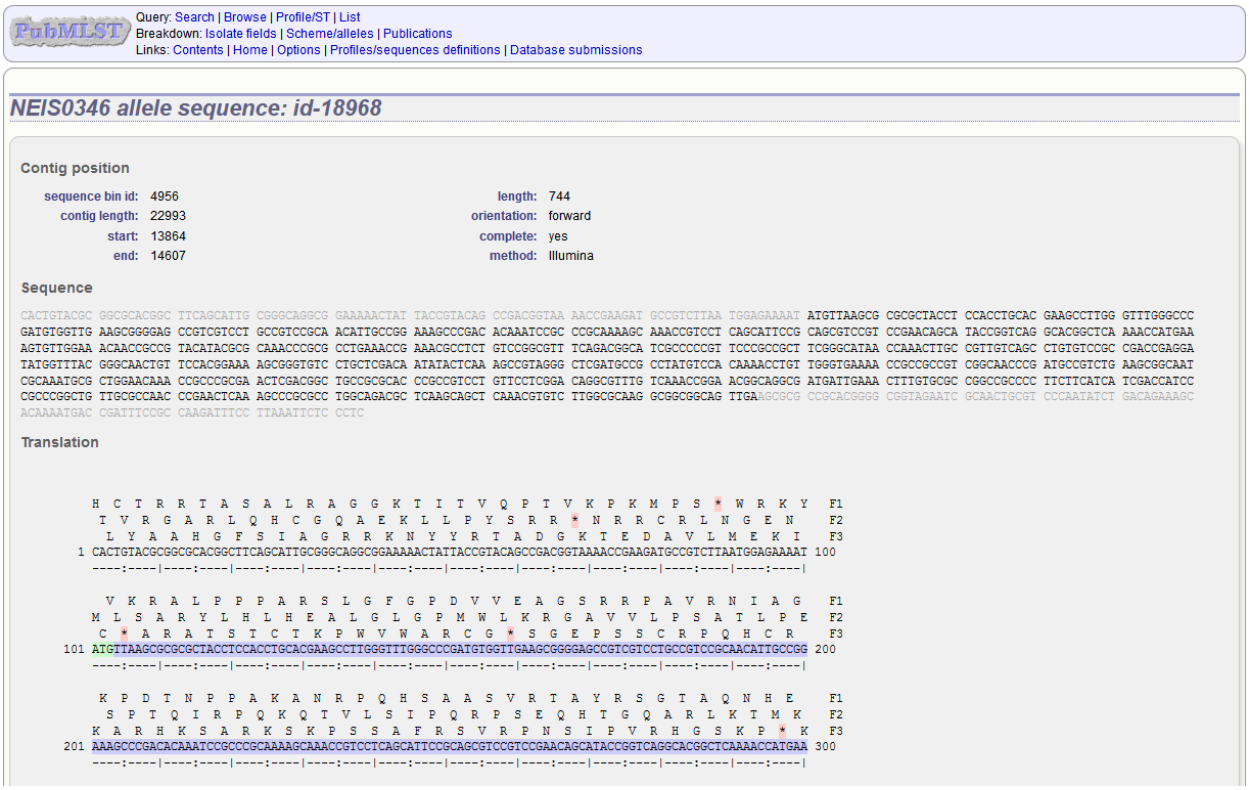
Isolate databases

PubMLST isolates: Contains data for a collection of isolates that represent the total known diversity of Neisseria species. For every allelic profile in the profiles database there is at least one corresponding isolate deposited here. Any isolate may be submitted to this database and consequently it should be noted that it does not represent a population sample. 5041 isolates

If the allele is a member of a scheme profile, e.g. MLST, this will be listed. In this case, there will be a button to display all profiles of that scheme that contain the allele.

Similarly, if a *client database* has been setup for the database and the allele has been identified in an isolate, there will be a button to display all isolates that have that allele.

9.3 Sequence tag records



Query: Search | Browse | Profile/ST | List
Breakdown: Isolate fields | Scheme/alleles | Publications
Links: Contents | Home | Options | Profiles/sequences definitions | Database submissions

NEIS0346 allele sequence: id-18968

Contig position

sequence bin id: 4956
contig length: 22993
start: 13864
end: 14607
length: 744
orientation: forward
complete: yes
method: Illumina

Sequence

CACTGTACGC GGCGCACGGC TTCAGCATTG CGGGCAGGCG GAAAAACTAT TACCGTACAG CCGACGGTAA AACCGAAGAT GCCGTCTTAA TGGAGAAAAT ATGTTAAGCG CGCGCTACCT CCACCTGCAC GAAGCCTTGG GTTTGGGCCC
GATGTGGTTG AAGCGGGGAG CCGTCGTCCT GCCGTCCGCA ACATTGCCGG AAAGCCCGAC ACAAATCCGC CCGCAAAAGC AAACCGTCCT CAGCATTCCG CAGCGTCCGT CCGAACAGCA TACCGGTCAG GCACGGCTCA AAACCATGAA
AGTGTTGGAA ACAACCGCCG TACATACGCG CAAACCCGCG CCTGAAACCG AAACGCCTCT GTCCGGCGTT TCAGACGGCA TCGCCCCCGT TCCCGCCGCT TCGGGCATAA CCAAACTTGC CGTTGTCAGC CTGTGTCCGC CGACCGAGGA
TATGGTTTAC GGGCAACTGT TCCACGGAAA AGCGGGTGTC CTGCTCGACA ATATACTCAA AGCCGTAGGG CTCGATGCCG CCTATGTCCA CAAAACCTGT TGGGTGAAAA CCGCCGCCGT CGGCAACCCG ATGCCGTCTG AAGCGGCAAT
CGCAAATGCG CTGGAACAAA CCGCCCGCGA ACTCGACGGC TGCCGCGCAC CCGCCGTCCT GTTCCTCGGA CAGGCGTTTG TCAAACCGGA ACGGCAGGCG ATGATTGAAA CTTTGTGCGC CGGCCGCCCC TTCTTCATCA TCGACCATCC
CGCCCGGCTG TTGCGCCAAC CCGAACTCAA AGCCCGCGCC TGGCAGACGC TCAAGCAGCT CAAACGTGTC TTGGCGCAAG GCGGCGGCAG TTGAAGCGCG CCGCACGGGG CGGTAGAATC GCAACTGCGT CCCAATATCT GACAGAAAGC
ACAAAATGAC CGATTTCCGC CAAGATTTCC TTAAATTCTC CCTC

Translation

```
     H  C  T  R  R  T  A  S  A  L  R  A  G  G  K  T  I  T  V  Q  P  T  V  K  P  K  M  P  S  *  W  R  K  Y   F1
      T  V  R  G  A  R  L  Q  H  C  G  Q  A  E  K  L  L  P  Y  S  R  R  *  N  R  R  C  R  L  N  G  E  N    F2
       L  Y  A  A  H  G  F  S  I  A  G  R  R  K  N  Y  Y  R  T  A  D  G  K  T  E  D  A  V  L  M  E  K  I   F3
   1 CACTGTACGCGGCGCACGGCTTCAGCATTGCGGGCAGGCGGAAAAACTATTACCGTACAGCCGACGGTAAAACCGAAGATGCCGTCTTAATGGAGAAAAT 100
     ----:----|----:----|----:----|----:----|----:----|----:----|----:----|----:----|----:----|----:----|

      V  K  R  A  L  P  P  P  A  R  S  L  G  F  G  P  D  V  V  E  A  G  S  R  R  P  A  V  R  N  I  A  G   F1
     M  L  S  A  R  Y  L  H  L  H  E  A  L  G  L  G  P  M  W  L  K  R  G  A  V  V  L  P  S  A  T  L  P  E   F2
      C  *  A  R  A  T  S  T  C  T  K  P  W  V  W  A  R  C  G  *  S  G  E  P  S  S  C  R  P  Q  H  C  R    F3
 101 ATGTTAAGCGCGCGCTACCTCCACCTGCACGAAGCCTTGGGTTTGGGCCCGATGTGGTTGAAGCGGGGAGCCGTCGTCCTGCCGTCCGCAACATTGCCGG 200
     ----:----|----:----|----:----|----:----|----:----|----:----|----:----|----:----|----:----|----:----|

      K  P  D  T  N  P  P  A  K  A  N  R  P  Q  H  S  A  A  S  V  R  T  A  Y  R  S  G  T  A  Q  N  H  E    F1
       S  P  T  Q  I  R  P  Q  K  Q  T  V  L  S  I  P  Q  R  P  S  E  Q  H  T  G  Q  A  R  L  K  T  M  K   F2
     K  A  R  H  K  S  A  R  K  S  K  P  S  S  A  F  R  S  V  R  P  N  S  I  P  V  R  H  G  S  K  P  *  K   F3
 201 AAAGCCCGACACAAATCCGCCCGCAAAAGCAAACCGTCCTCAGCATTCCGCAGCGTCCGTCCGAACAGCATACCGGTCAGGCACGGCTCAAAACCATGAA 300
     ----:----|----:----|----:----|----:----|----:----|----:----|----:----|----:----|----:----|----:----|
```

A sequence tag record displays information about the location within a contig of a region associated with a locus. The nucleotide sequence will be displayed along with upstream and downstream flanking sequence. The length of these flanking sequences can be modified within the *general options*.

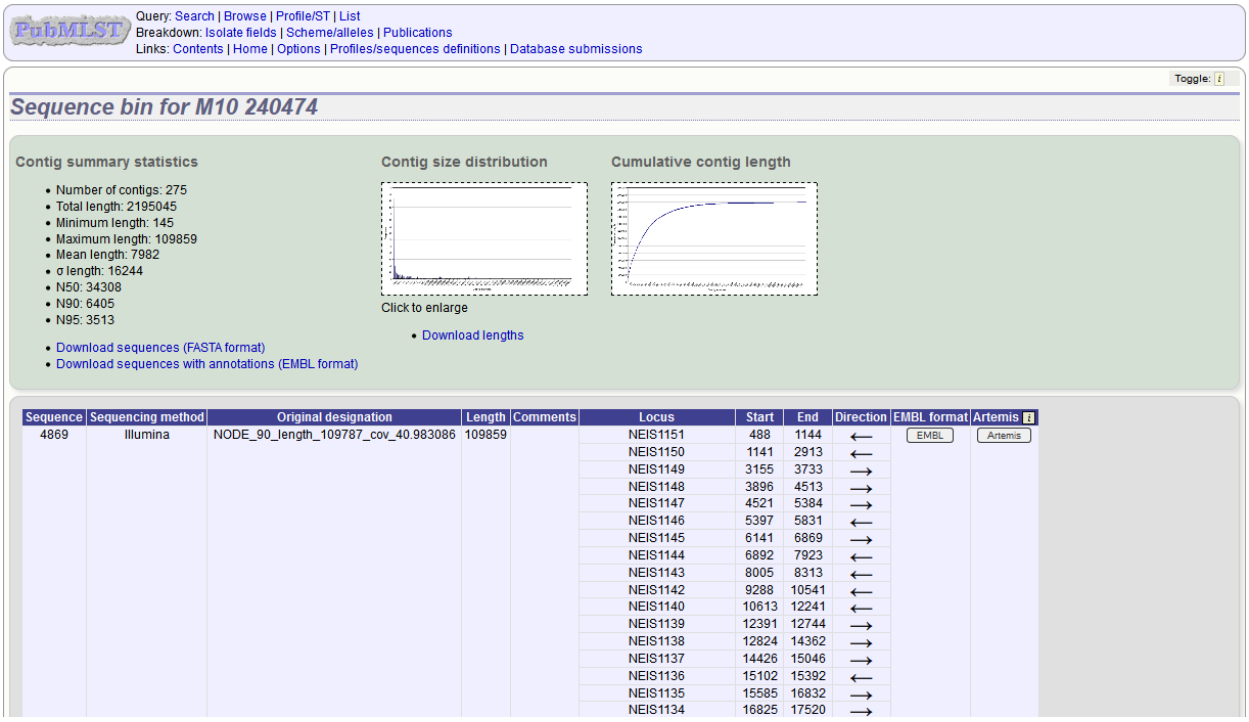
If the tag is for a DNA locus and it is marked as a coding sequence, the three-frame translation will also be displayed.

9.4 Profile records

A profile record displays information about a scheme, e.g. MLST, profile. Each allele number within the profile will be hyperlinked. Clicking these will take you to the appropriate *allele definition record*.

If a *client database* has been setup for the database and an isolate has the profile, there will be a button to display all isolates that have the profile.

9.5 Sequence bin records



A sequence bin record contains information about that contigs associated with an isolate record. This includes:

- Number of contigs
- Total length
- Minimum length
- Maximum length
- N50, N90 and N95 values
- Size distribution charts

There are also links to download the contigs in FASTA or EMBL format.

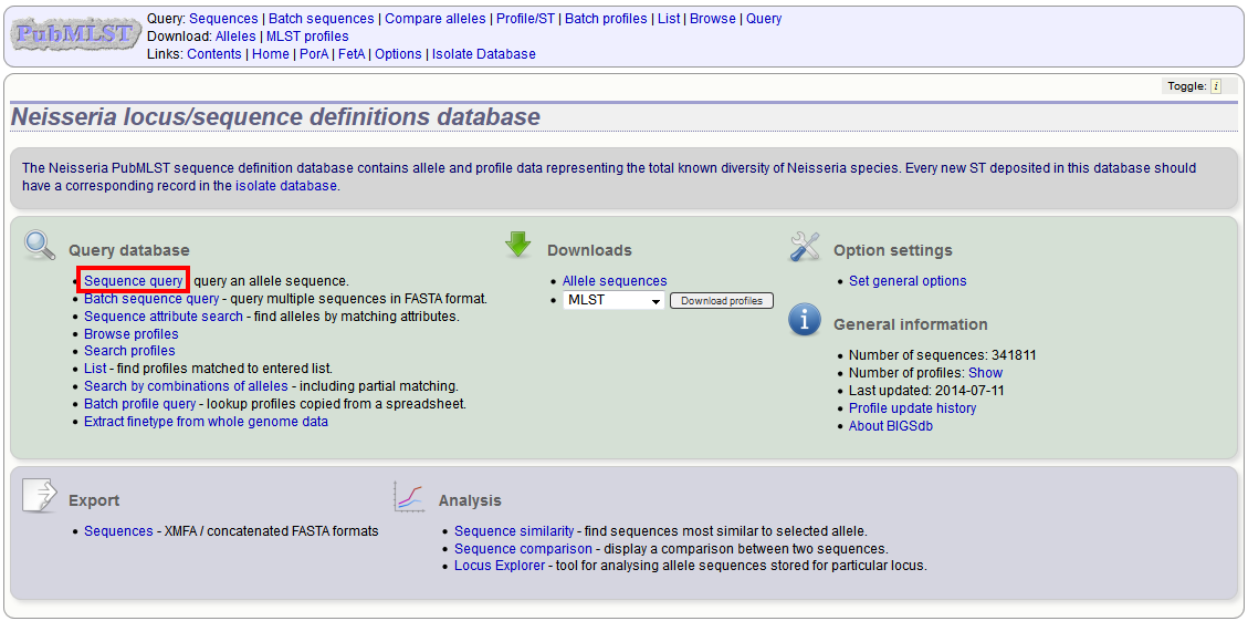
Finally there is a table that shows the loci that are tagged on each contig. Individual contigs can also be downloaded in EMBL format.

CHAPTER 10

Querying data

10.1 Querying sequences to determine allele identity

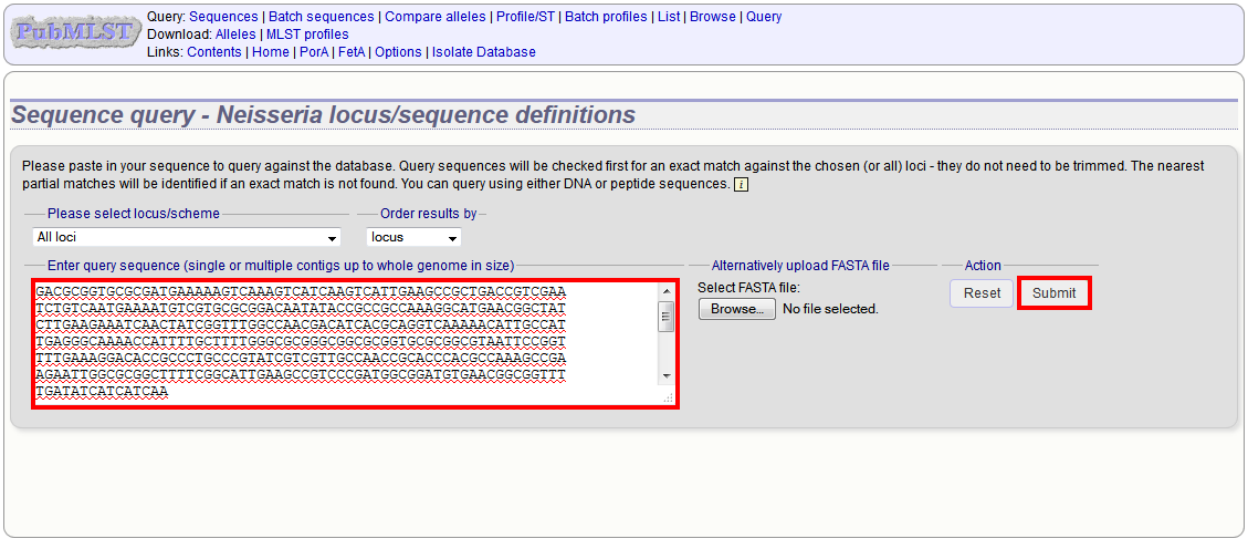
Sequence queries are performed in the sequence definition database. Click 'Sequence query' from the contents page.



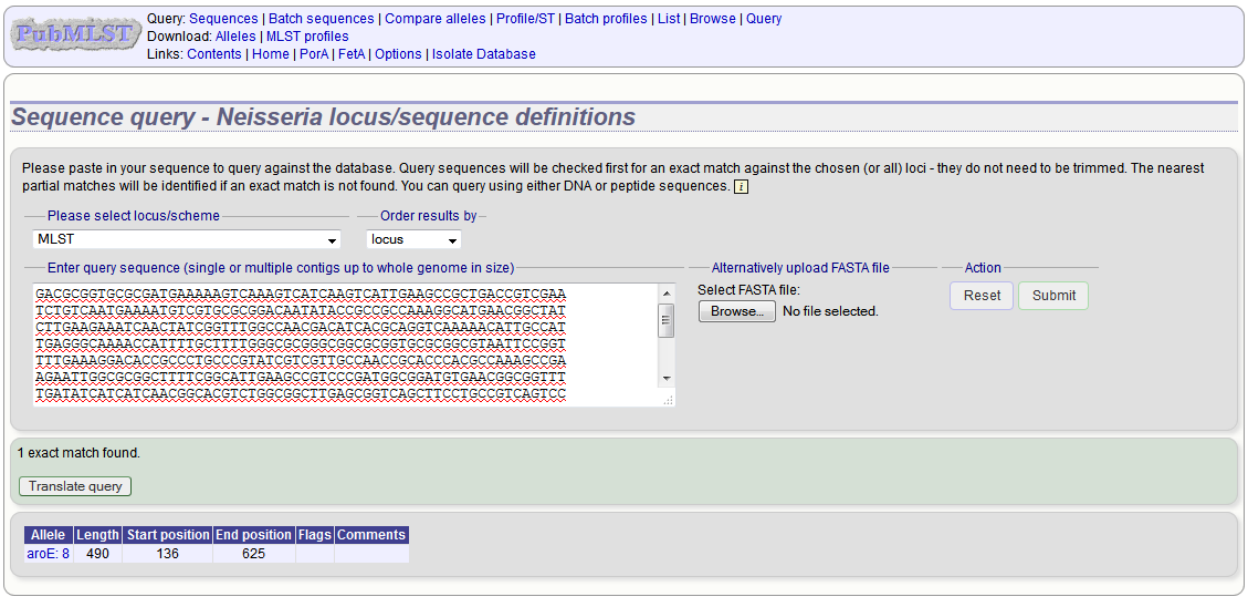
Paste your sequence in to the box - there is no need to trim. Normally, you can leave the locus setting on 'All loci' - the software should identify the correct locus based on your sequence. Sometimes, it may be quicker, however, to select the specific locus or scheme (e.g. MLST) that a locus belongs to.

Note: If the locus you are querying is a shorter version of another, e.g. an MLST fragment of a gene where the full length gene is also defined, you will need to select the specific locus or the scheme from the dropdown box. Leaving the selection on 'All loci' will return a match to the longer sequence in preference to the shorter one.

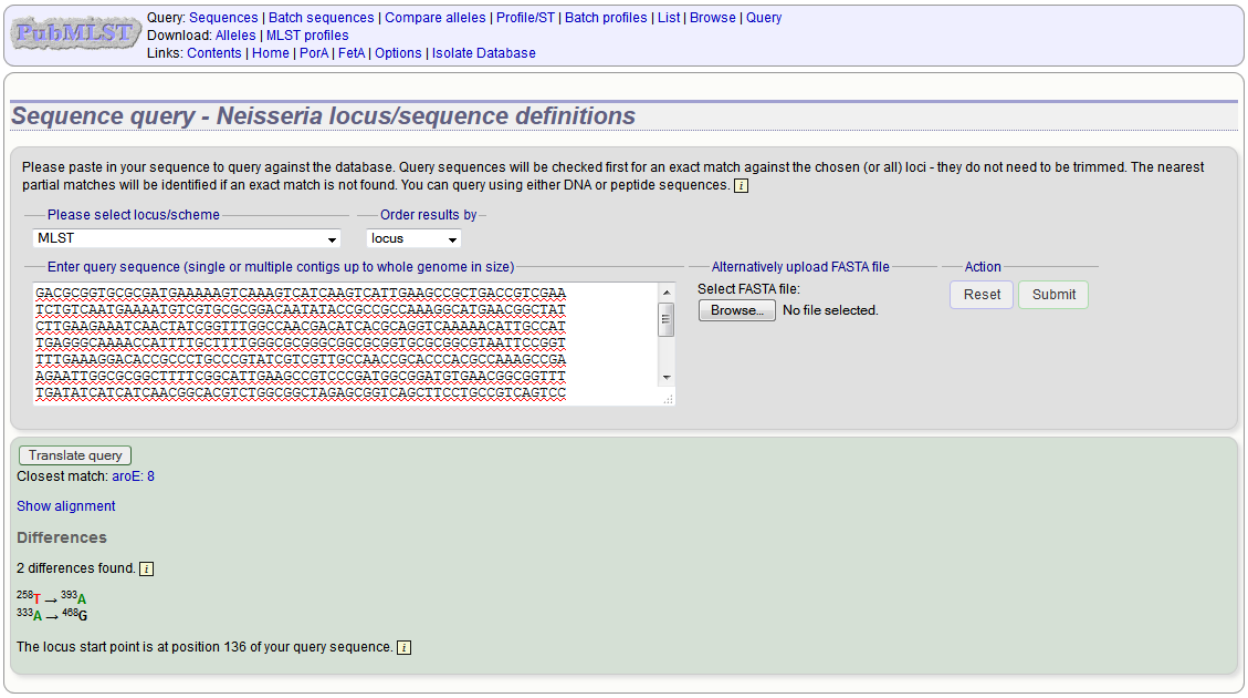
Click 'Submit'.



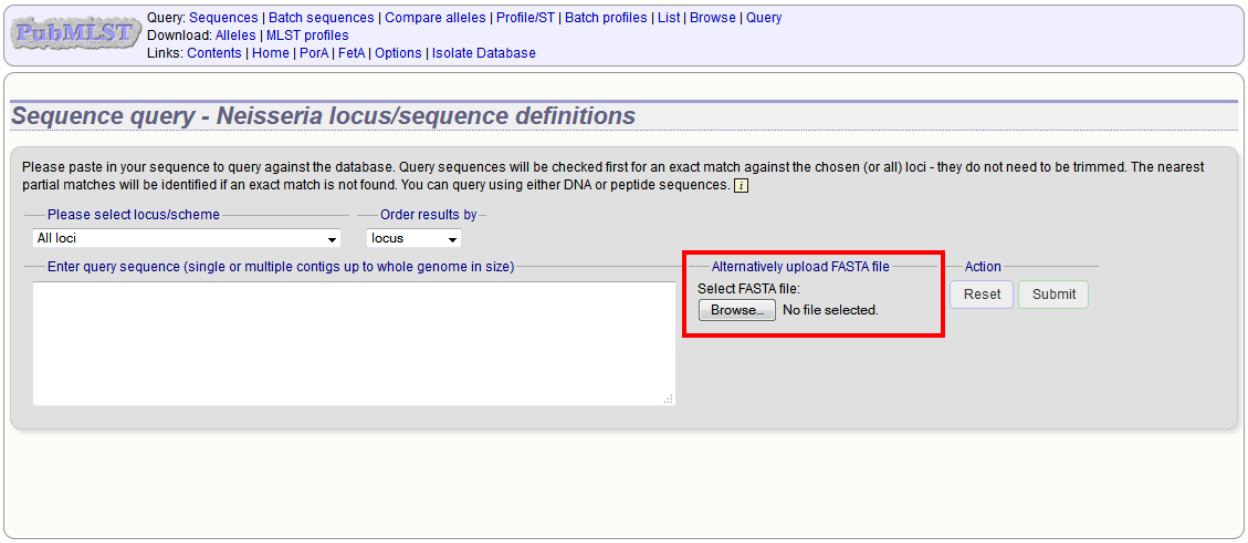
If an exact match is found, this will be indicated along with the start position of the locus within your sequence.



If only a partial match is found, the most similar allele is identified along with any nucleotide differences. The varying nucleotide positions are numbered both relative to the pasted in sequence and to the reference sequence. The start position of the locus within your sequence is also indicated.

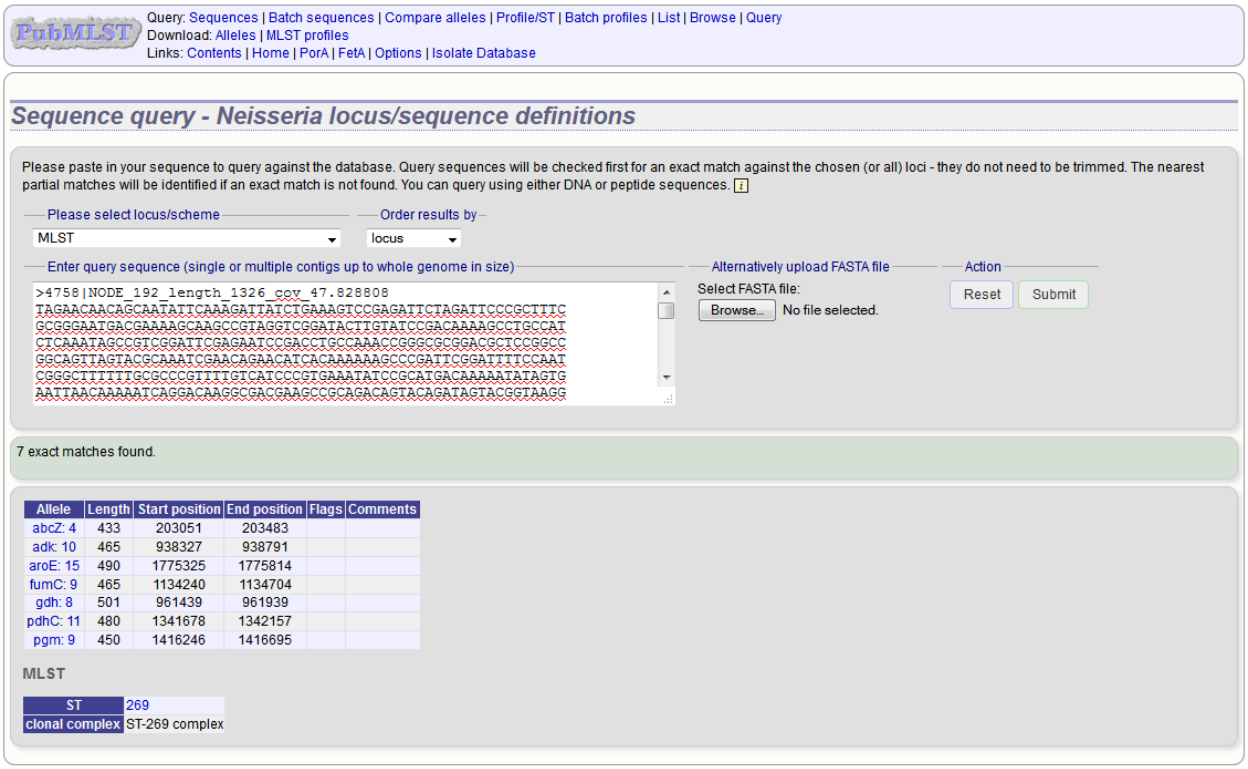


As an alternative to pasting a sequence in to the box, you can also choose to upload sequences in FASTA format by clicking the file browse button.



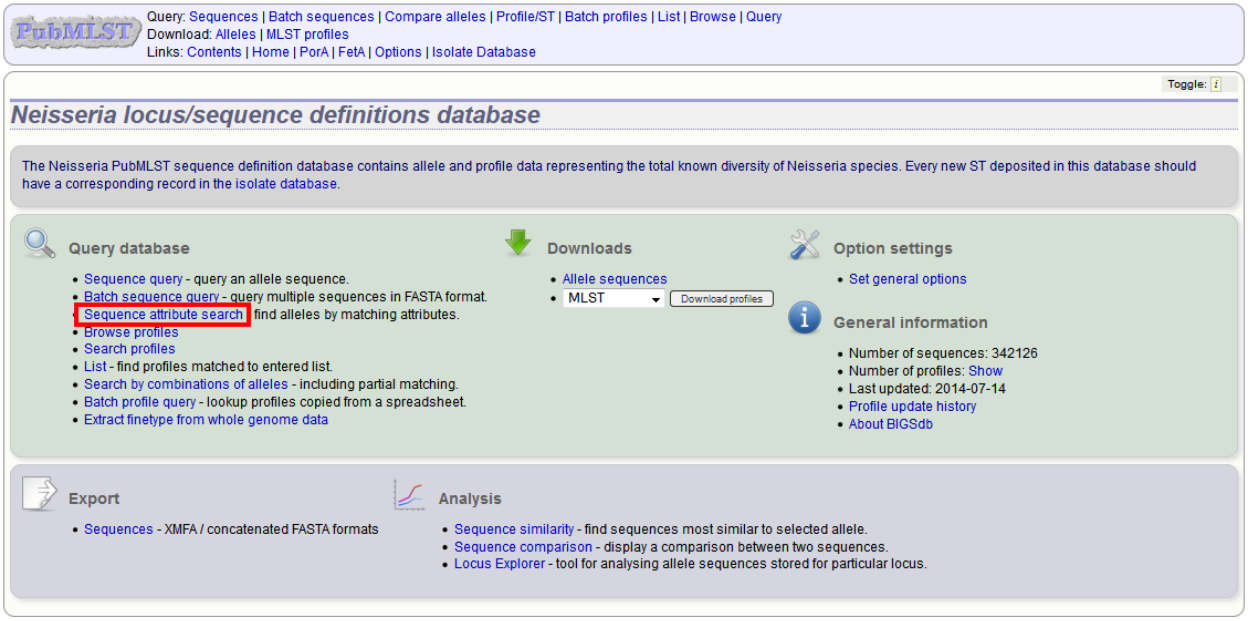
10.1.1 Querying whole genome data

The sequence query is not limited to single genes. You can also paste or upload whole genomes - these can be in multiple contigs. If you select a specific scheme from the dropdown box, all loci belonging to that scheme will be checked (although only exact matches are reported for a locus if one of the other loci has an exact match). If all loci are matched, scheme fields will also be returned if these are defined. This, for example, enables you to identify the MLST sequence type of a genome in one step.



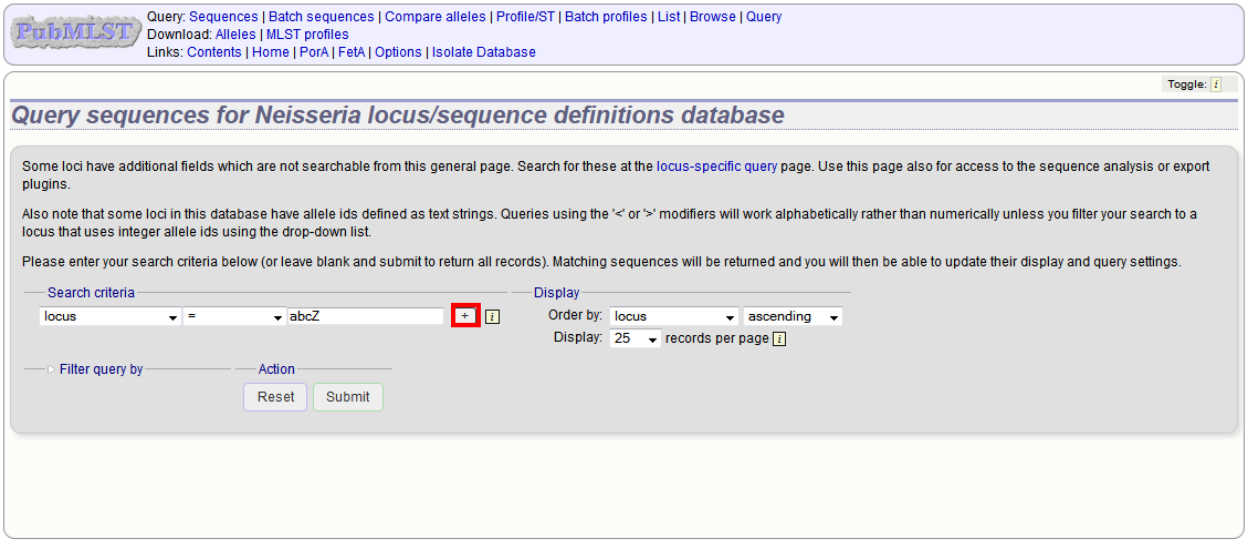
10.2 Searching for specific allele definitions

To retrieve specific allele designations, click 'Sequence attribute search' on a sequence definition database contents page.

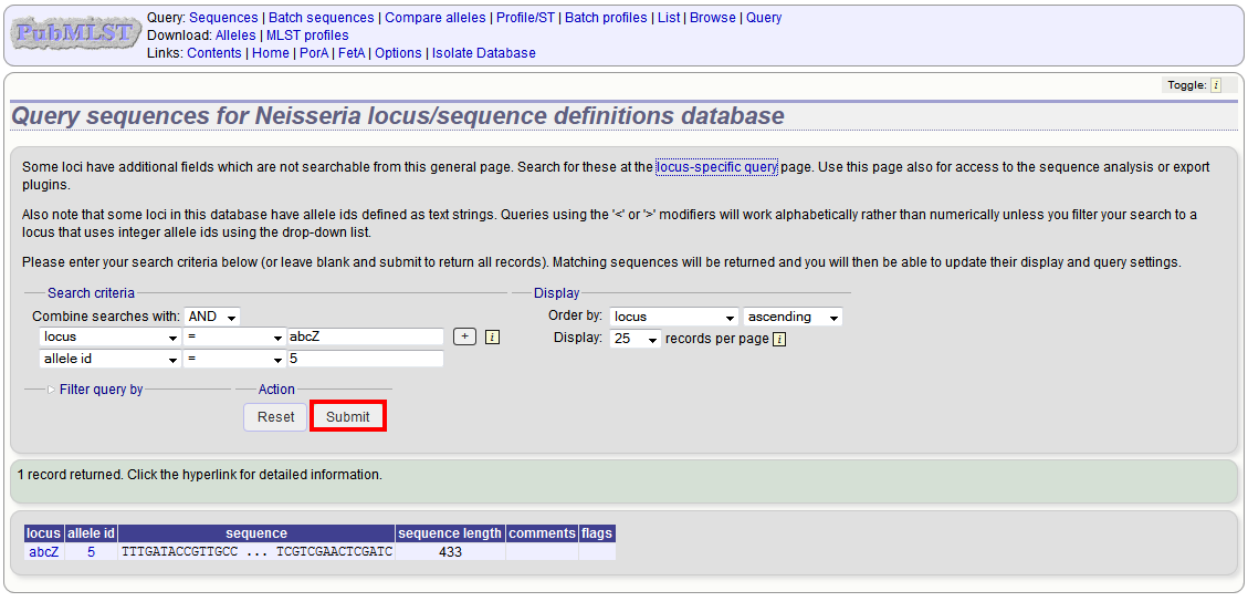


Enter your query using the dropdown search box - additional terms can be added by clicking the '+' button.

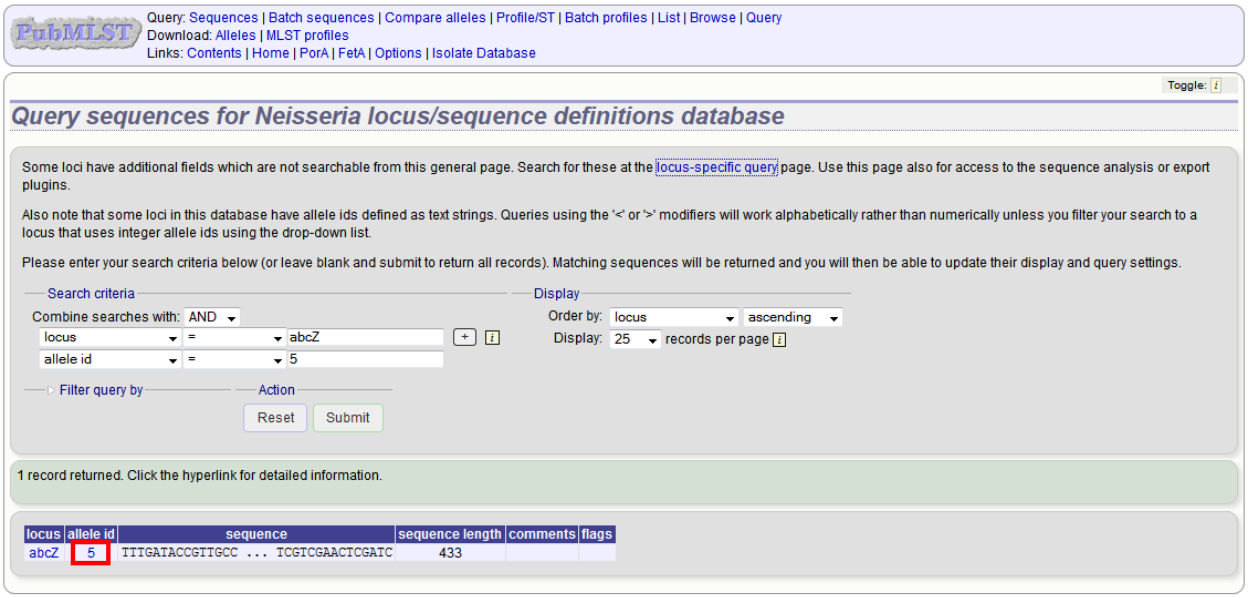
Designations can be queried using *standard operators*.



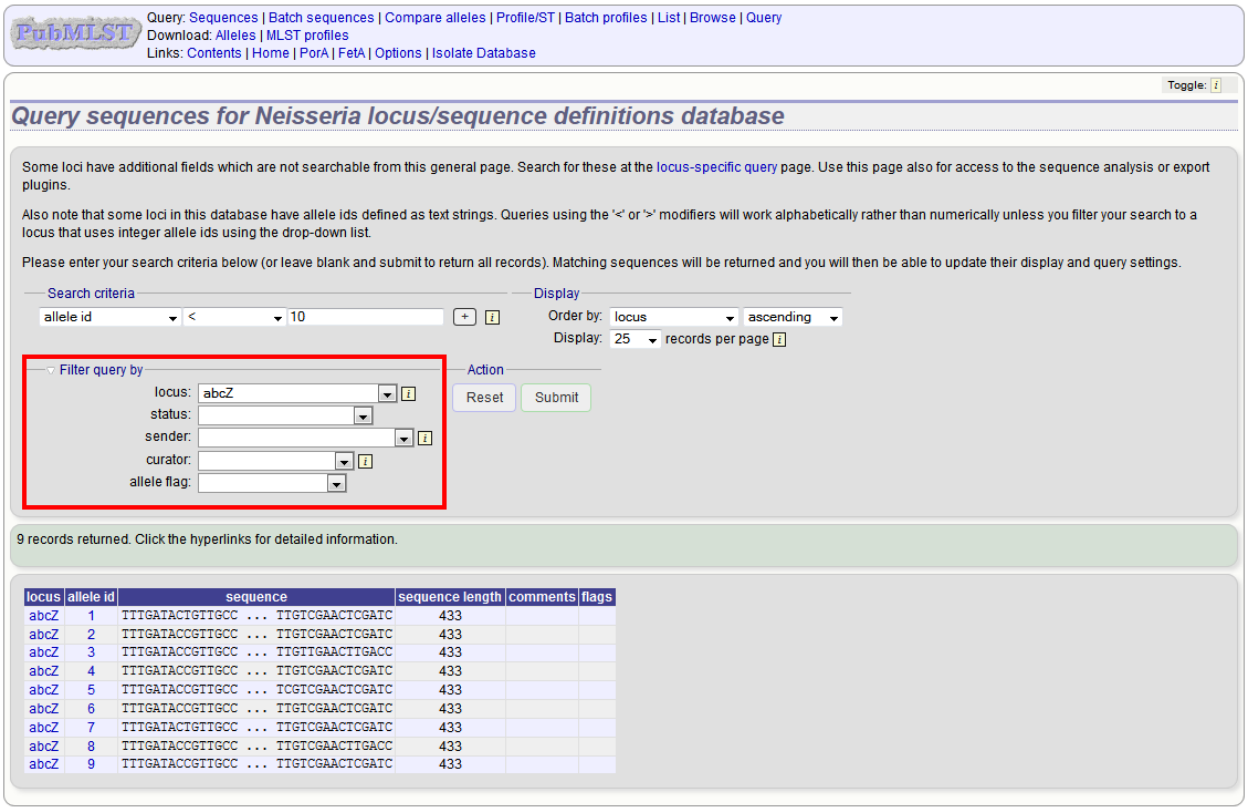
Click submit.



Click the hyperlinked results to display allele records.

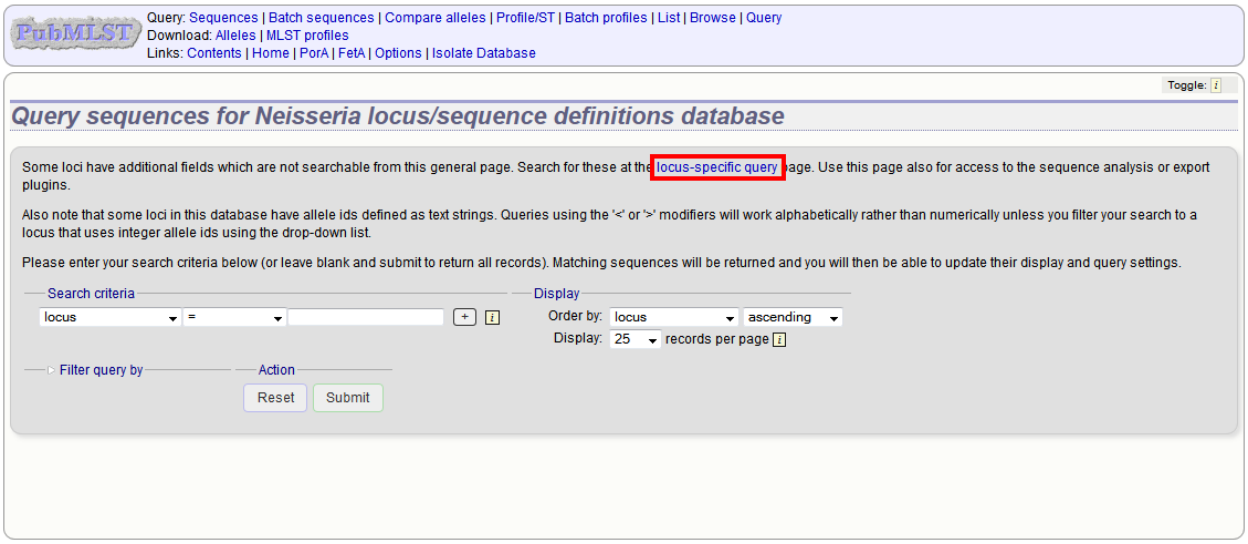


Various search criteria can also be selected by combining with filters. Click the filter heading to display these.

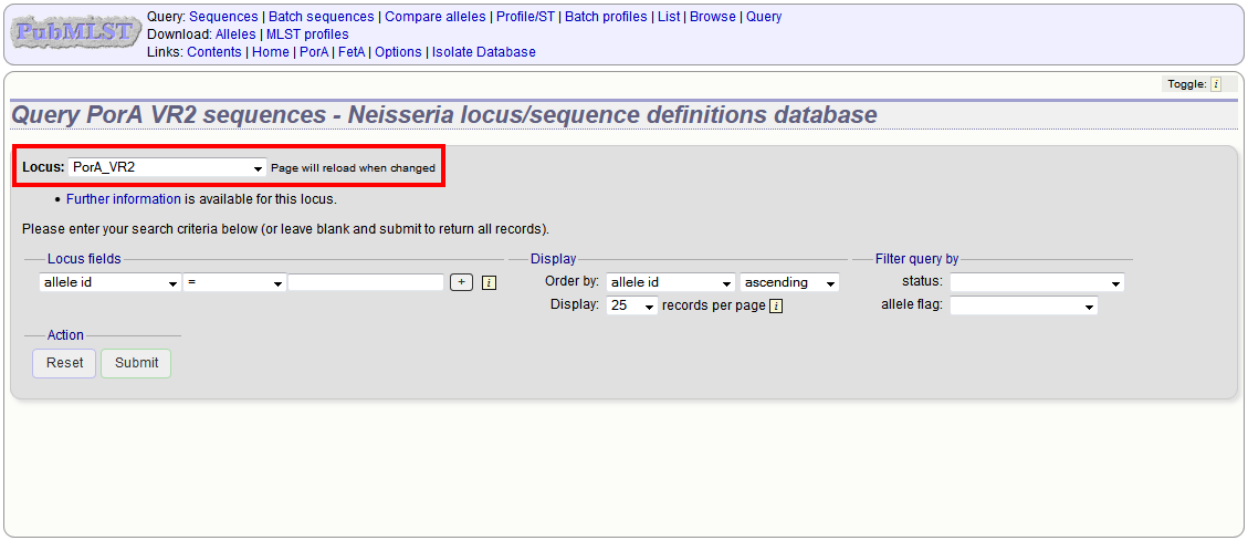


10.2.1 Locus-specific attributes

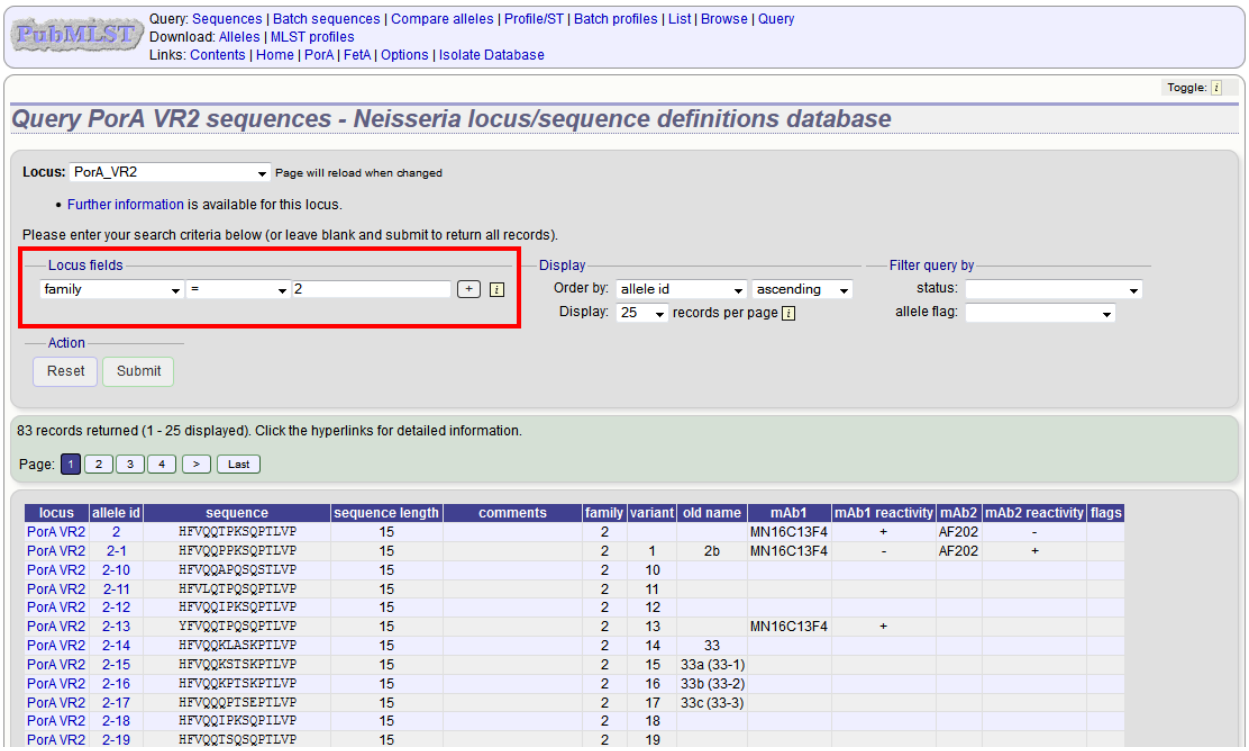
Some loci have *extended attribute fields*. To query these, you need to navigate to a locus-specific query page, by clicking the 'locus-specific query' link on the sequence attribute search page.



Pick the required locus from the dropdown box.



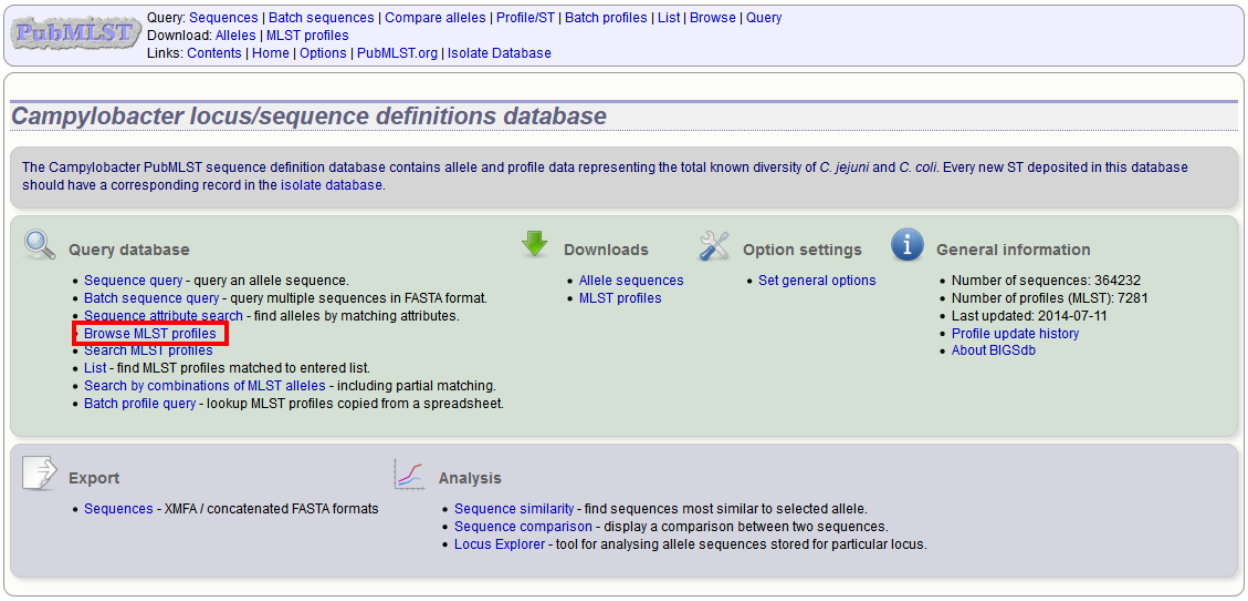
The fields specific for that locus will be added to the dropdown query boxes.



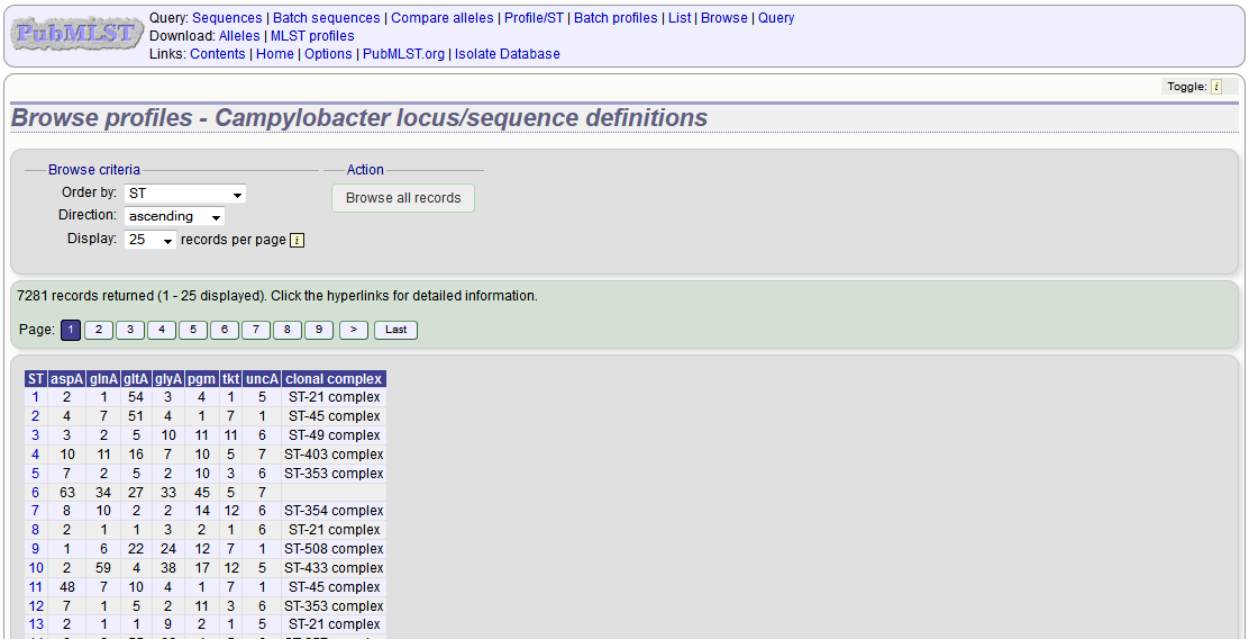
locus	allele id	sequence	sequence length	comments	family	variant	old name	mAb1	mAb1 reactivity	mAb2	mAb2 reactivity	flags
PorA VR2	2	HFVQQTPKSQPTLVP	15		2			MN16C13F4	+	AF202	-	
PorA VR2	2-1	HFVQQPPKSQPTLVP	15		2	1	2b	MN16C13F4	-	AF202	+	
PorA VR2	2-10	HFVQQAPQSQSTLVP	15		2	10						
PorA VR2	2-11	HFVLQTPQSQPTLVP	15		2	11						
PorA VR2	2-12	HFVQQIPKSQPTLVP	15		2	12						
PorA VR2	2-13	YFVQQTPQSQPTLVP	15		2	13		MN16C13F4	+			
PorA VR2	2-14	HFVQQKLASKPTLVP	15		2	14	33					
PorA VR2	2-15	HFVQQKSTSKPTLVP	15		2	15	33a (33-1)					
PorA VR2	2-16	HFVQQKPTSKPTLVP	15		2	16	33b (33-2)					
PorA VR2	2-17	HFVQQQPTSEPTLVP	15		2	17	33c (33-3)					
PorA VR2	2-18	HFVQQIPKSQPTLVP	15		2	18						
PorA VR2	2-19	HFVQQTSQSQPTLVP	15		2	19						

10.3 Browsing scheme profile definitions

If a sequence definition database has schemes defined that include a primary key field, i.e. collections of loci that together create profiles, e.g. for MLST, click the link to 'Browse profiles'.



Choose the field to order the results by, the number of results per page to display, and click 'Browse all records'.

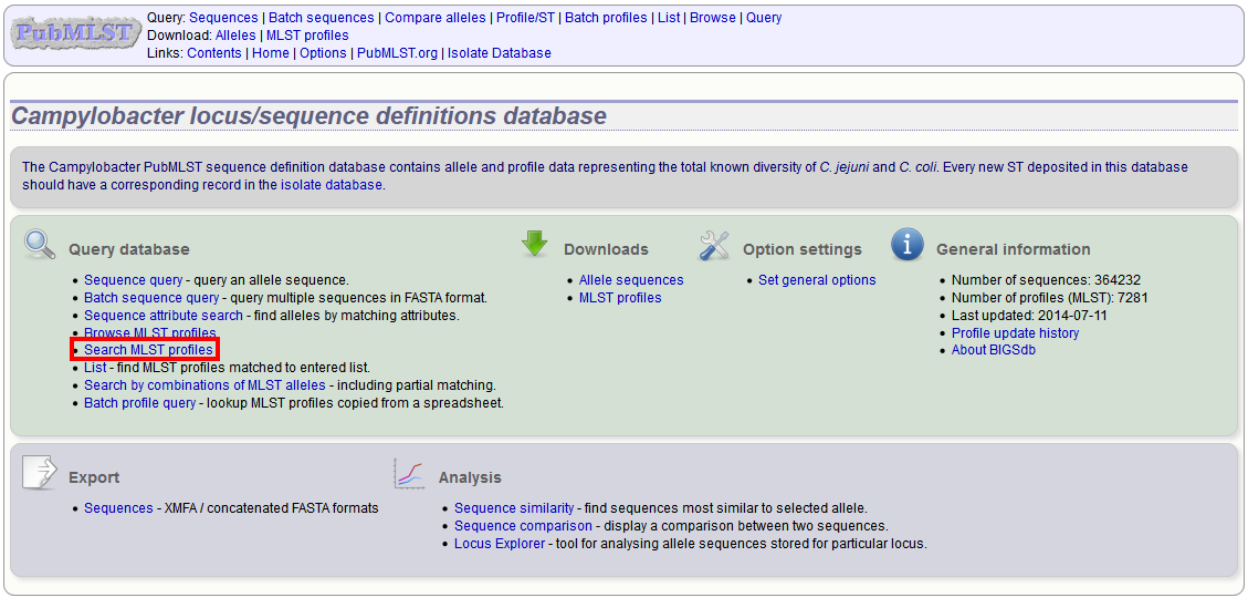


ST	aspA	glnA	gltA	glyA	pgm	tkt	uncA	clonal complex
1	2	1	54	3	4	1	5	ST-21 complex
2	4	7	51	4	1	7	1	ST-45 complex
3	3	2	5	10	11	11	6	ST-49 complex
4	10	11	16	7	10	5	7	ST-403 complex
5	7	2	5	2	10	3	6	ST-353 complex
6	63	34	27	33	45	5	7	
7	8	10	2	2	14	12	6	ST-354 complex
8	2	1	1	3	2	1	6	ST-21 complex
9	1	6	22	24	12	7	1	ST-508 complex
10	2	59	4	38	17	12	5	ST-433 complex
11	48	7	10	4	1	7	1	ST-45 complex
12	7	1	5	2	11	3	6	ST-353 complex
13	2	1	1	9	2	1	5	ST-21 complex

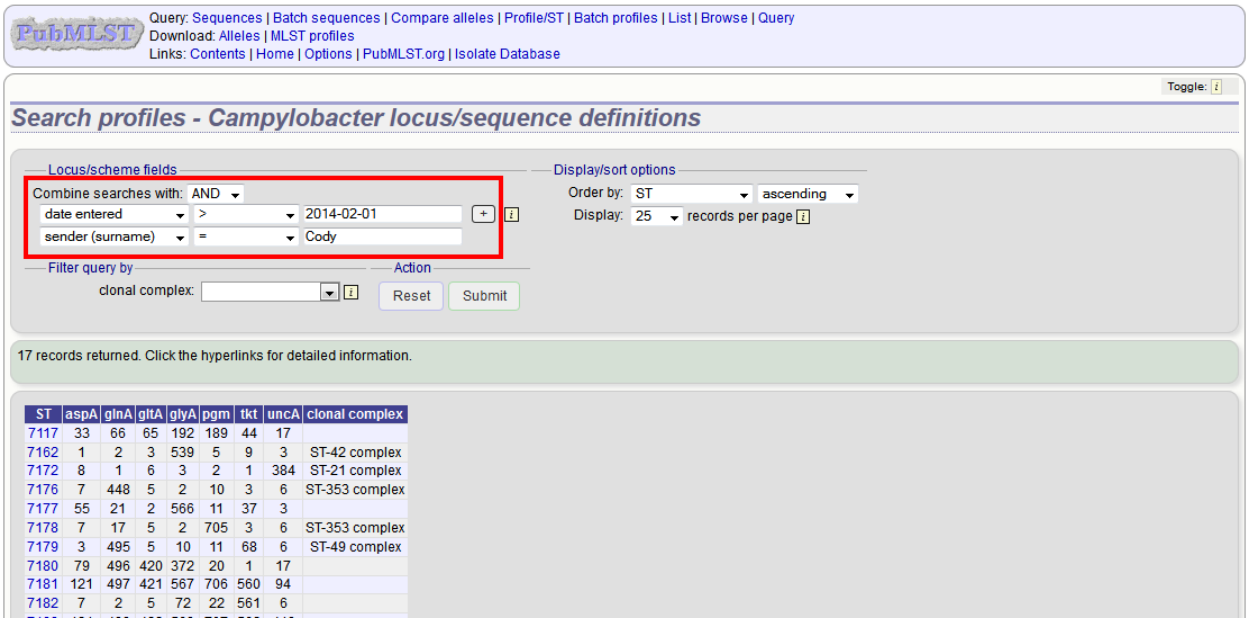
Clicking the hyperlink for any profile will display full information about the profile.

10.4 Querying scheme profile definitions

click the link to 'Search profiles' for the appropriate scheme on the main contents page.

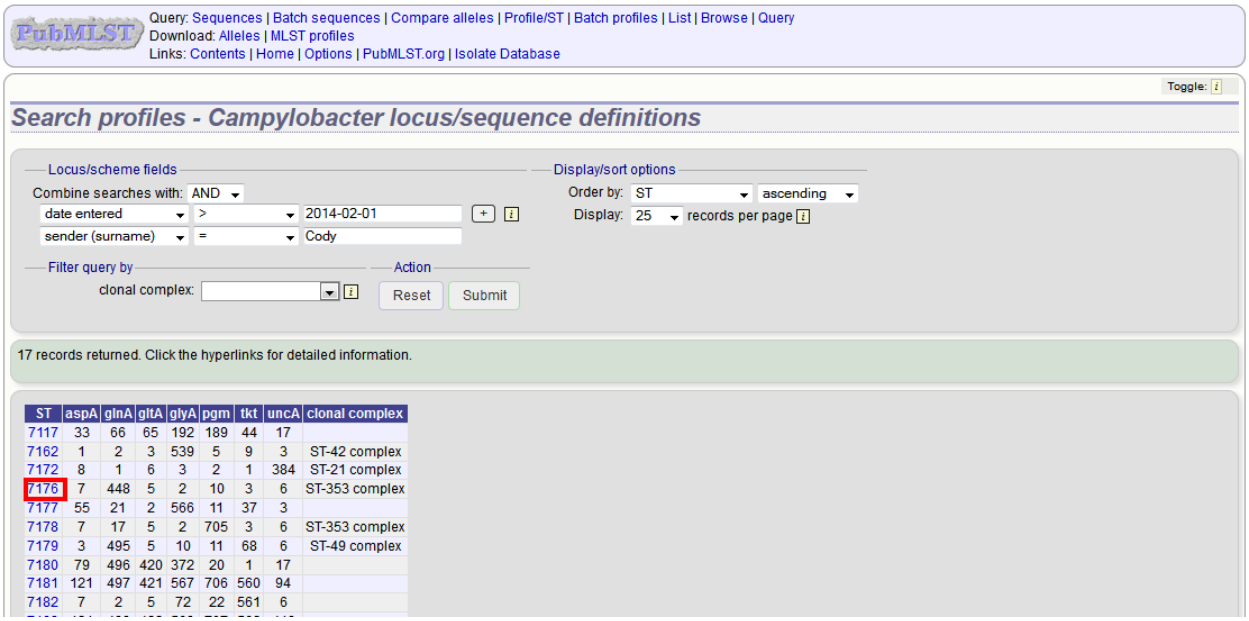


Enter the search criteria you wish to search on. You may also see some drop-down list boxes that allow further filtering of results. You can add search criteria by clicking the '+' button in the 'Locus/scheme fields' section. These can be combined using 'AND' or 'OR'.



Each field can be queried using *standard operators*.

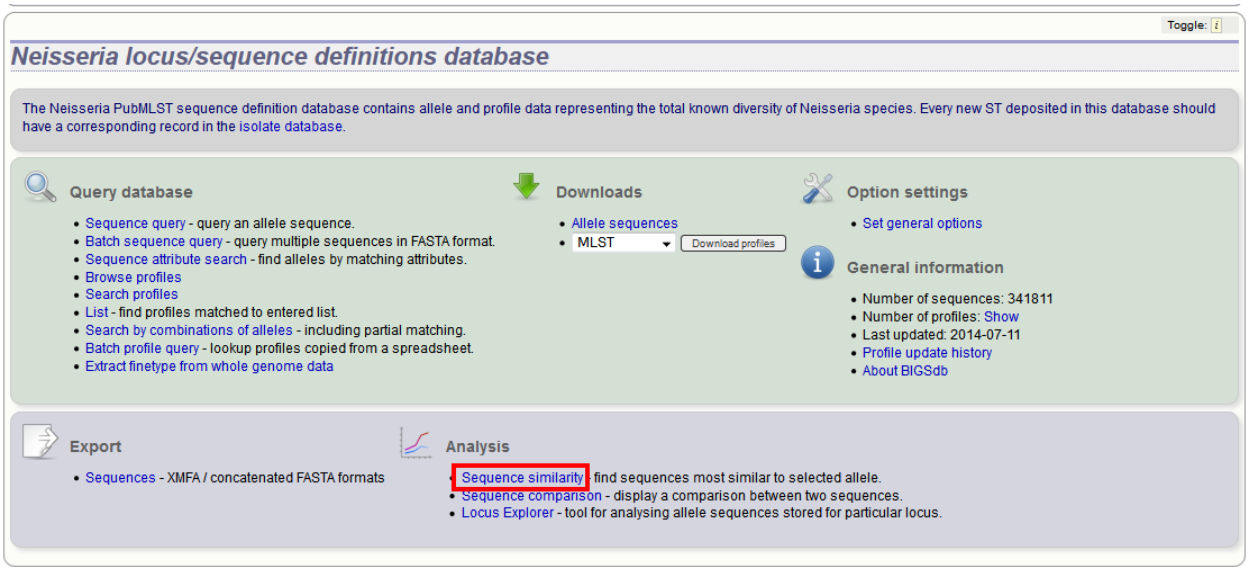
Clicking the hyperlink for any profile will display full information about the profile.



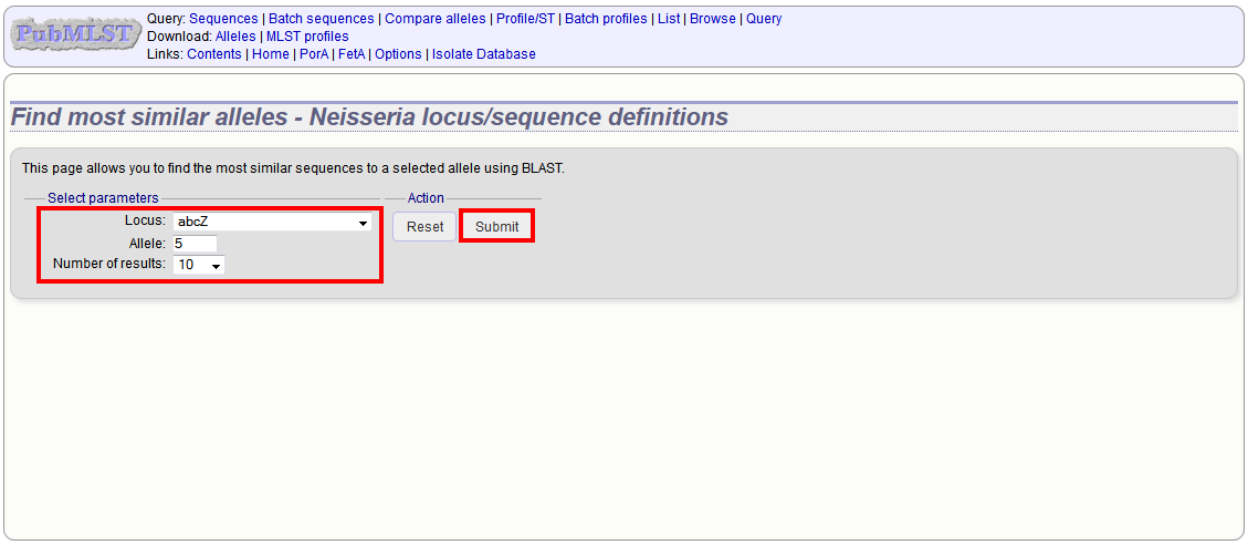
10.5 Investigating allele differences

10.5.1 Sequence similarity

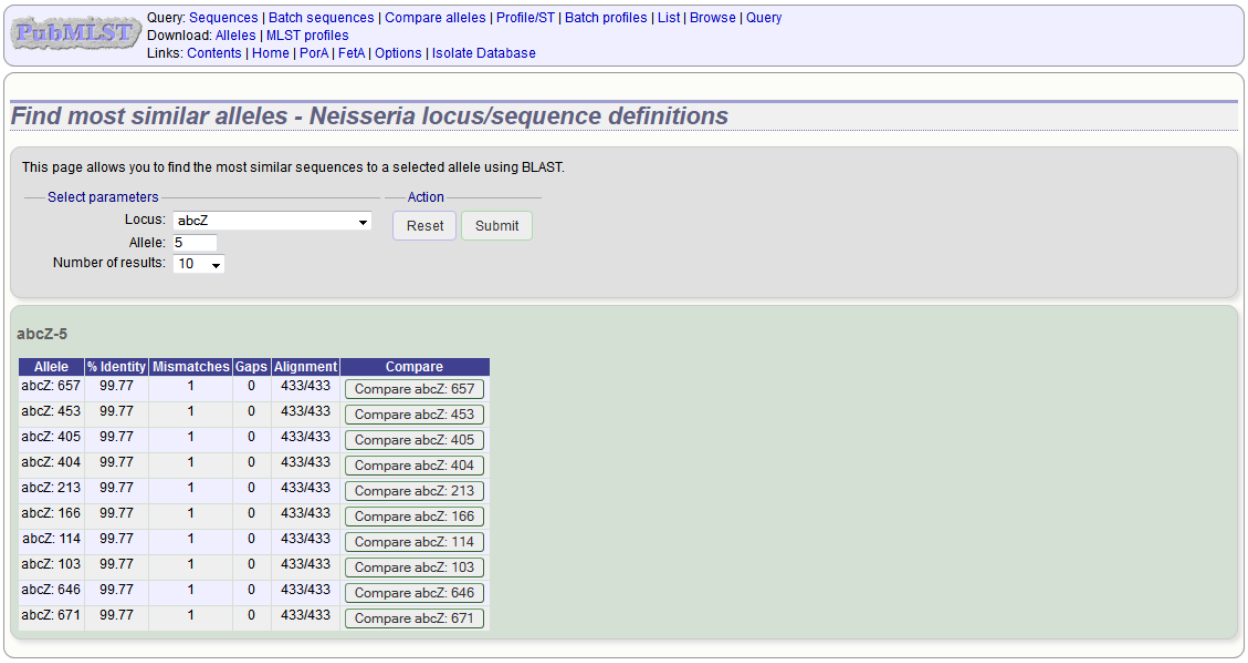
To find sequences most similar to a selected allele within a sequence definition database, click 'Sequence similarity' on the contents page.



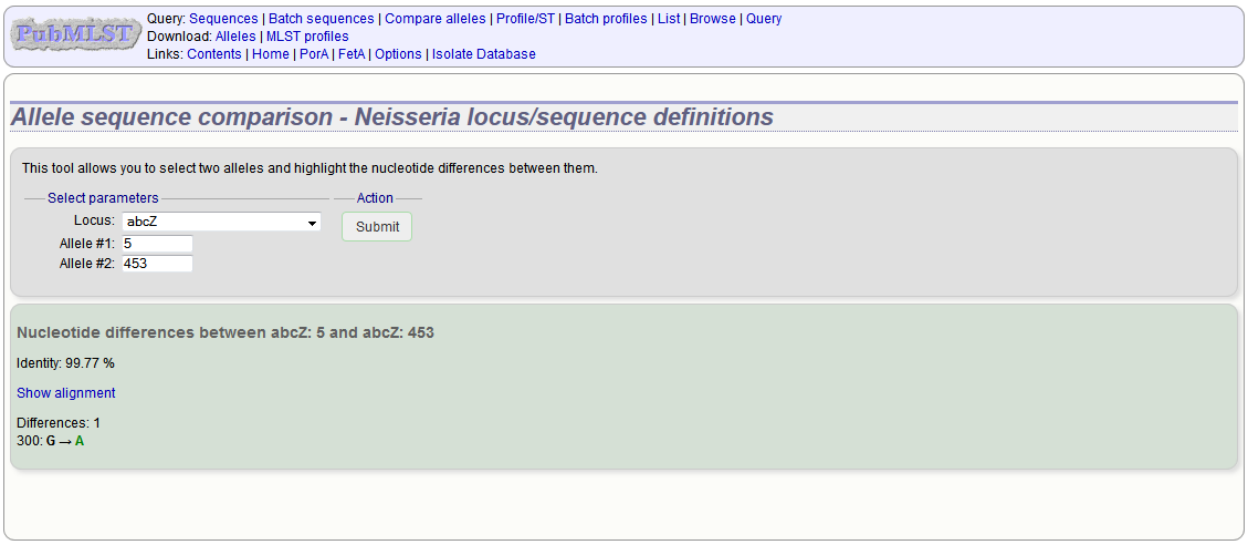
Enter the locus and allele identifer of the sequence to investigate and the number of nearest matches you'd like to see, then press submit.



A list of nearest alleles will be displayed, along with the percentage identity and number of gaps between the sequences.

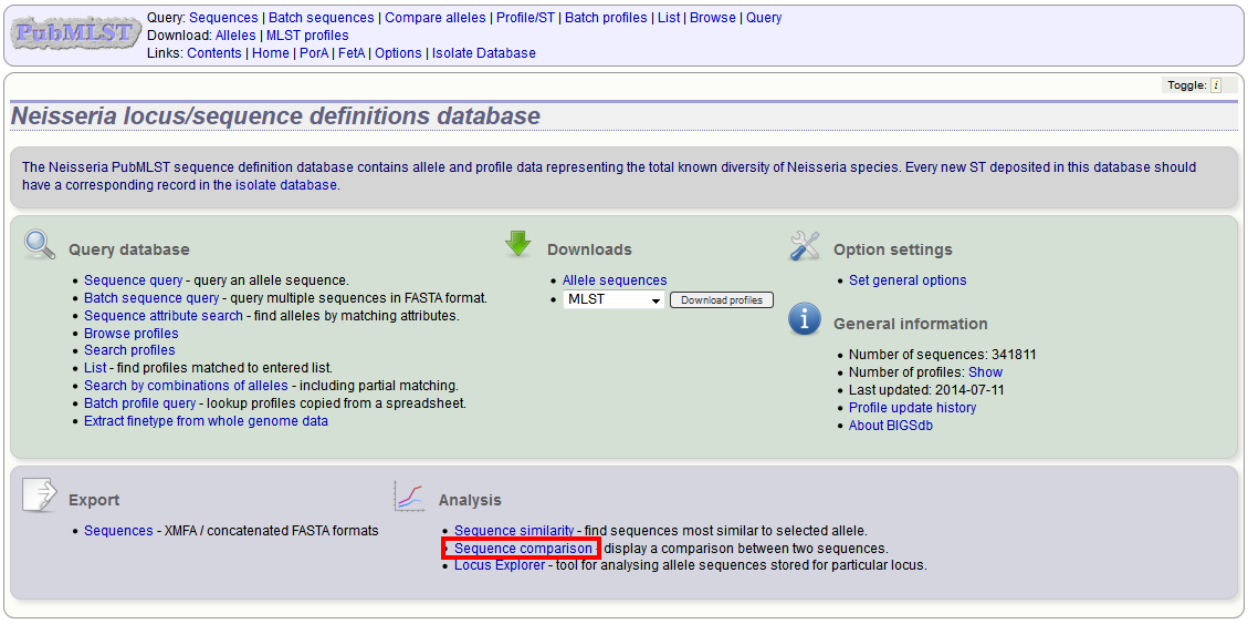


Click the appropriate 'Compare' button to display a list of nucleotide differences and/or a sequence alignment.

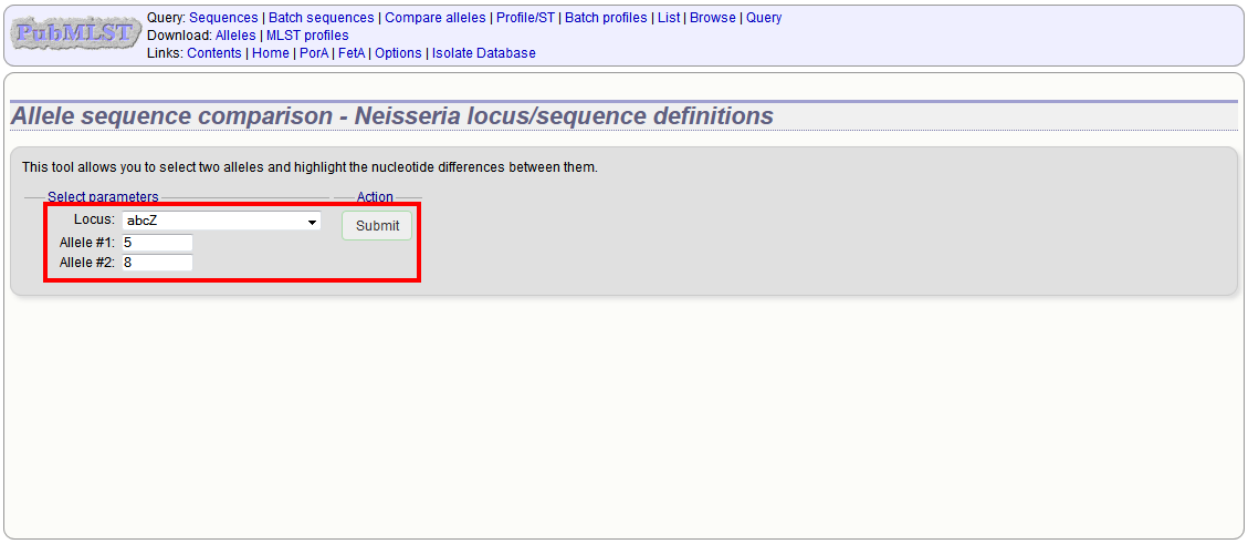


10.5.2 Sequence comparison

To directly compare two sequences click 'Sequence comparison' from the contents page of a sequence definition database.



Enter the locus and two allele identifiers to compare. Press submit.



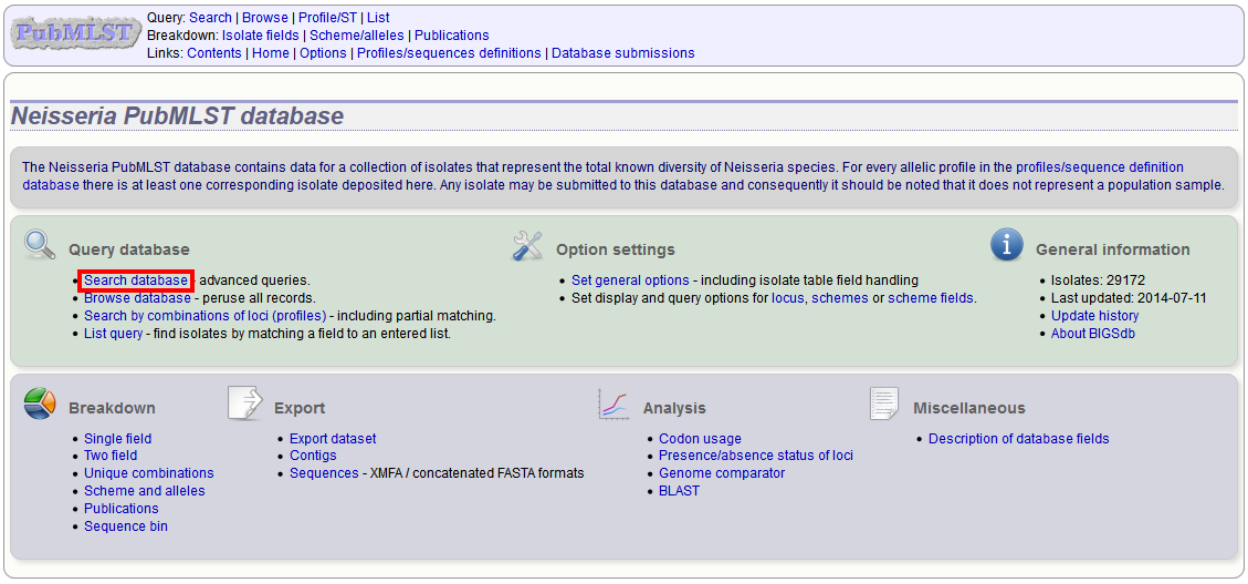
A list of nucleotide differences and/or an alignment will be displayed.

See also:

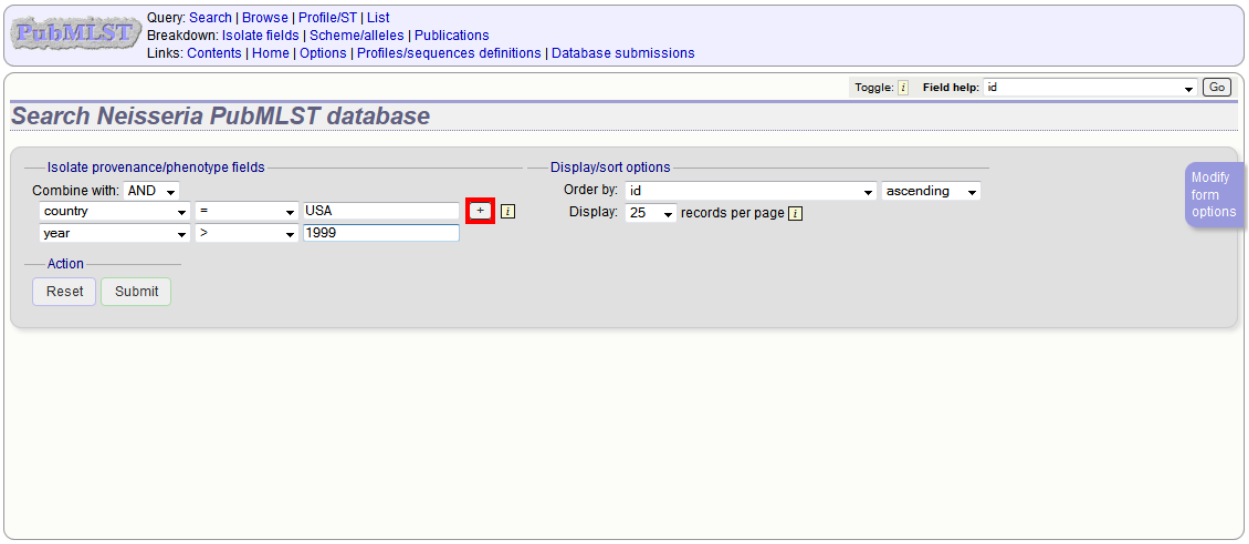
Locus explorer plugin.

10.6 Querying isolate data

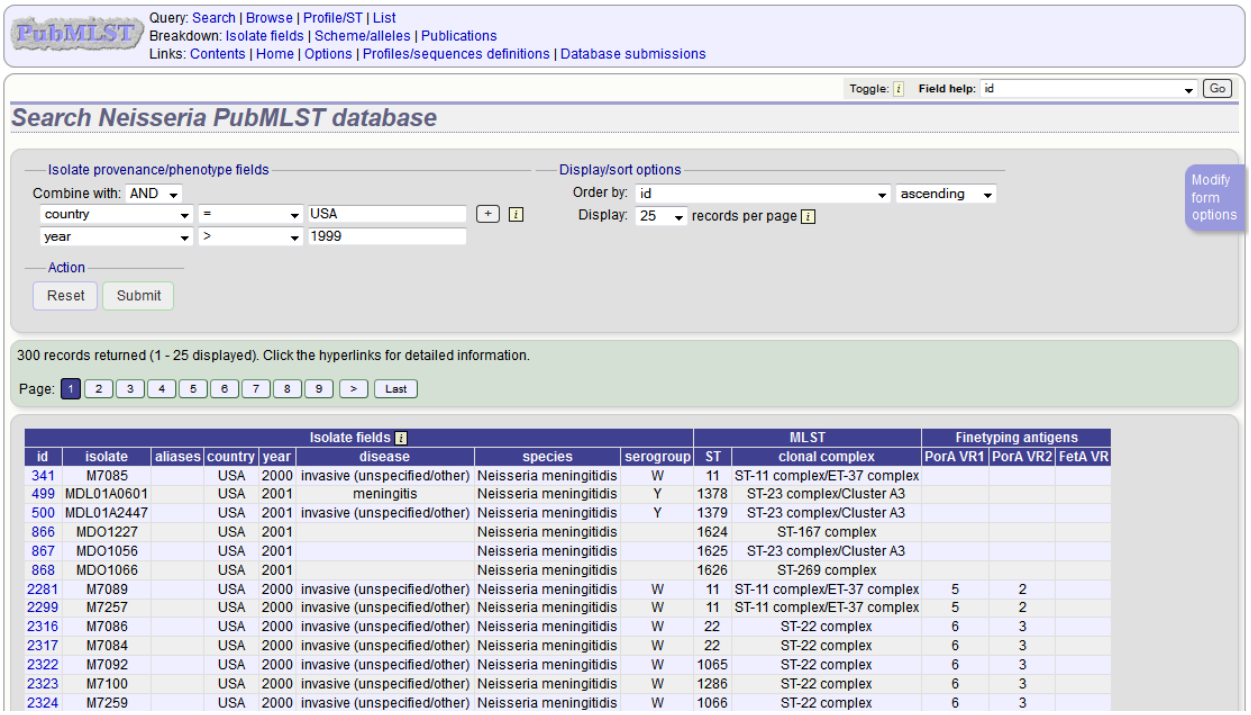
The 'Search database' page of an isolate database allows you to search by combinations of provenance criteria, scheme and locus data, and more.



To start with, only one provenance field search box is displayed but more can be added by clicking the '+' button (highlighted). These can be linked together by 'and' or 'or'.



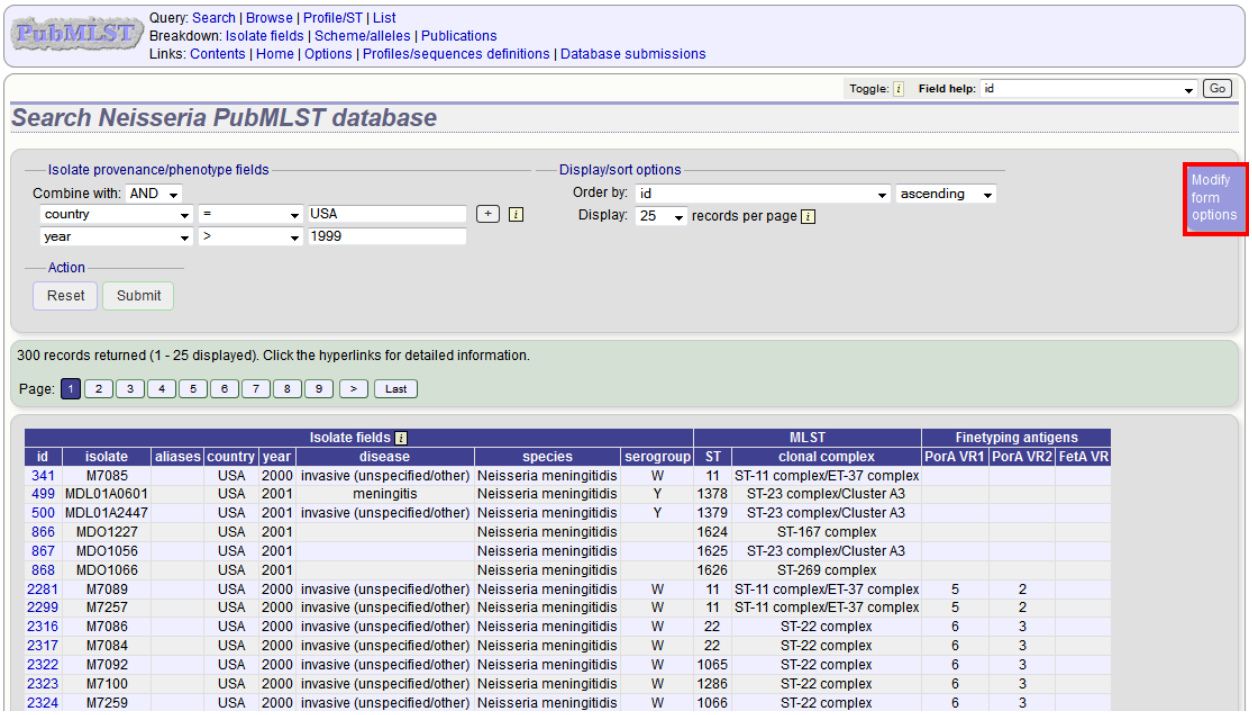
After the search has been submitted, the results will be displayed in a table.



Isolate fields								MLST		Finetyping antigens		
id	isolate	aliases	country	year	disease	species	serogroup	ST	clonal complex	PorA VR1	PorA VR2	FetA VR
341	M7085		USA	2000	invasive (unspecified/other)	Neisseria meningitidis	W	11	ST-11 complex/ET-37 complex			
499	MDL01A0601		USA	2001	meningitis	Neisseria meningitidis	Y	1378	ST-23 complex/Cluster A3			
500	MDL01A2447		USA	2001	invasive (unspecified/other)	Neisseria meningitidis	Y	1379	ST-23 complex/Cluster A3			
866	MDO1227		USA	2001		Neisseria meningitidis		1624	ST-167 complex			
867	MDO1056		USA	2001		Neisseria meningitidis		1625	ST-23 complex/Cluster A3			
868	MDO1066		USA	2001		Neisseria meningitidis		1626	ST-269 complex			
2281	M7089		USA	2000	invasive (unspecified/other)	Neisseria meningitidis	W	11	ST-11 complex/ET-37 complex	5	2	
2299	M7257		USA	2000	invasive (unspecified/other)	Neisseria meningitidis	W	11	ST-11 complex/ET-37 complex	5	2	
2316	M7086		USA	2000	invasive (unspecified/other)	Neisseria meningitidis	W	22	ST-22 complex	6	3	
2317	M7084		USA	2000	invasive (unspecified/other)	Neisseria meningitidis	W	22	ST-22 complex	6	3	
2322	M7092		USA	2000	invasive (unspecified/other)	Neisseria meningitidis	W	1065	ST-22 complex	6	3	
2323	M7100		USA	2000	invasive (unspecified/other)	Neisseria meningitidis	W	1286	ST-22 complex	6	3	
2324	M7259		USA	2000	invasive (unspecified/other)	Neisseria meningitidis	W	1066	ST-22 complex	6	3	

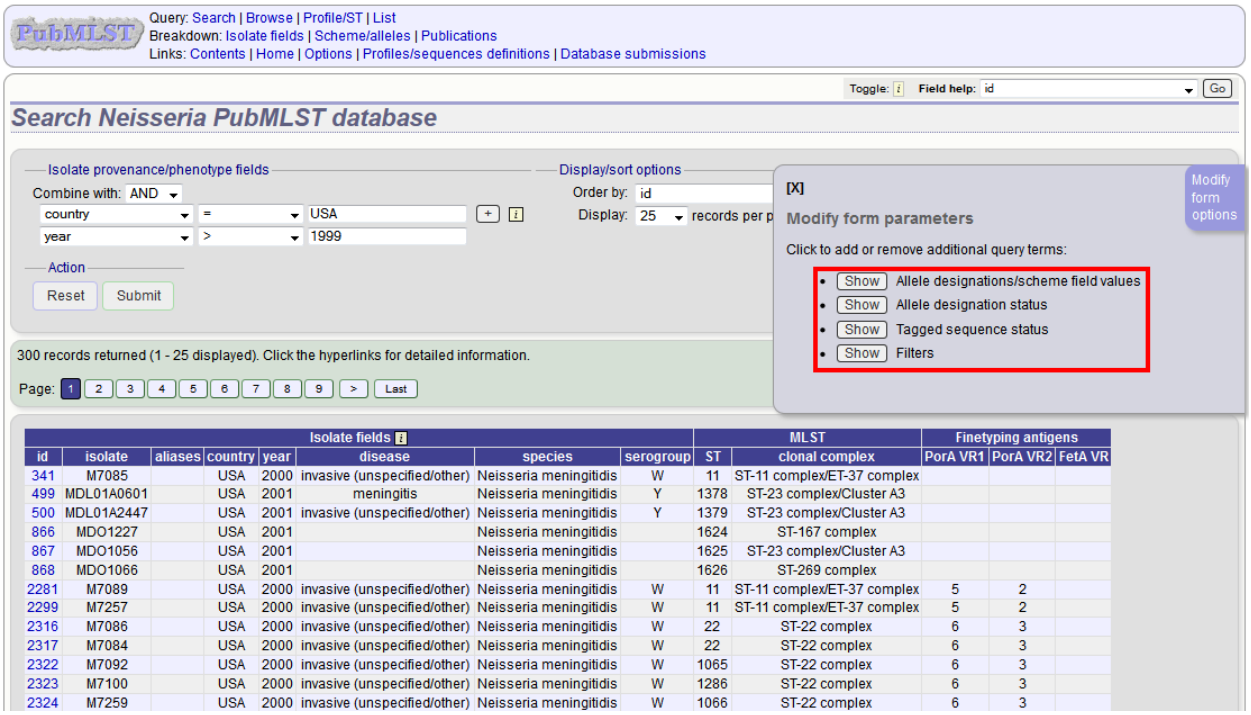
Each field can be queried using *standard operators*.

More search features are available by clicking the 'Modify form options' tab on the right-hand side of the screen.



A tab will be displayed. Different options will be available here depending on the database. Queries will be combined from the values entered in all form sections. Possible options are:

- Allele designations/scheme field values
  - Search by combination of allele designations and/or scheme fields e.g. ST, clonal complex information.
- Allele designation status
  - Search by whether allele designation status is confirmed or provisional.
- Tagged sequence status
  - Search by whether tagged sequence data is available for a locus. You can also search by sequence flags.
- Filters
  - Various filters may be available, including
    - Publications
    - Projects
    - MLST profile completion status
    - Clonal complex
    - Sequence bin size
    - Inclusion/exclusion of *old versions*

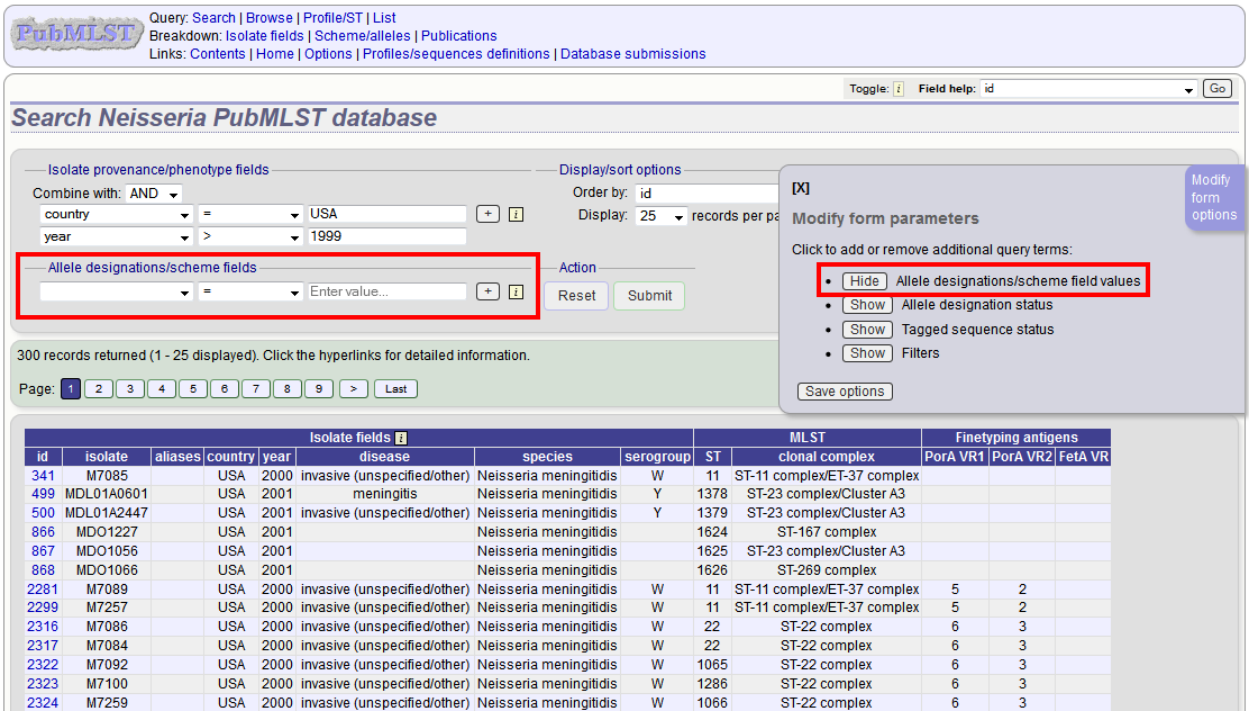


If the interface is modified, a button to 'Save options' becomes available within the tab. If this is clicked, the modified form will be displayed the next time you go to the query page.

10.6.1 Query by allele_designation/scheme field

Queries can be combined with allele designation/scheme field values.

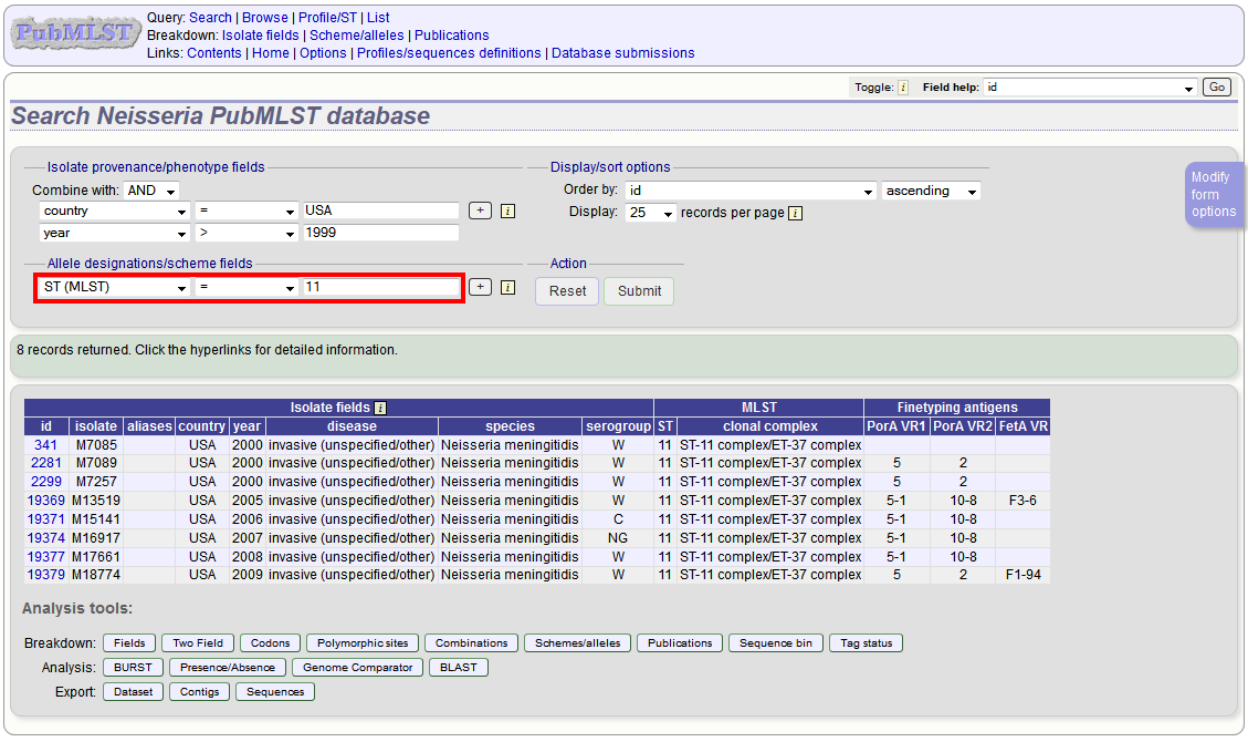
Make sure that the allele designation/scheme field values fieldset is displayed by selecting it in the 'Modify form options' tab.



Designations can be queried using *standard operators*.

Additional search terms can be combined using the '+' button.

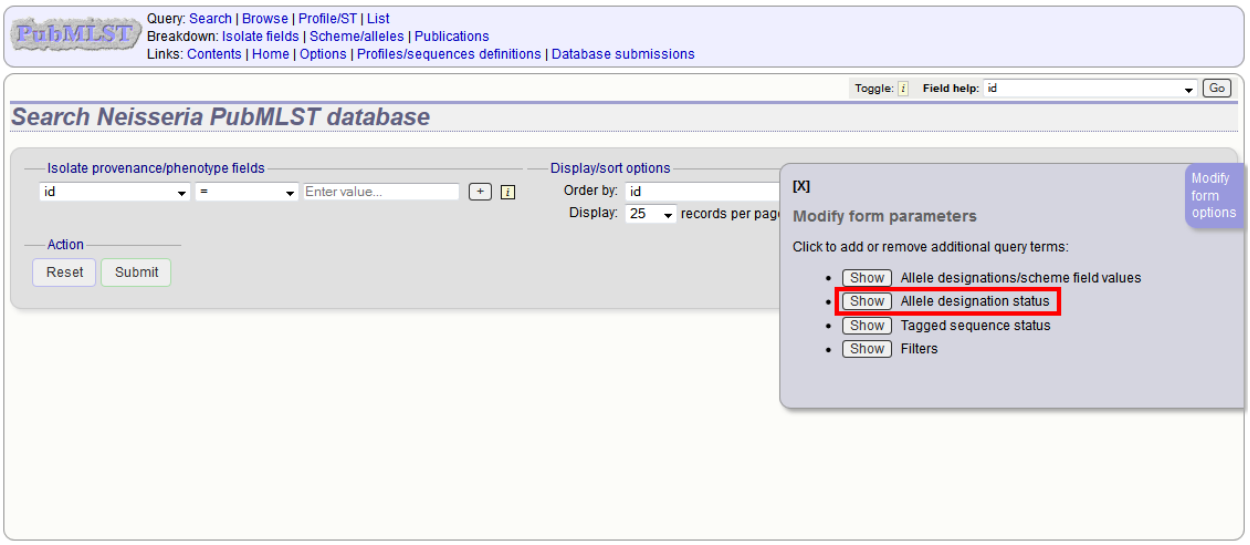
Add your search terms and click 'Submit'. Allele designation/scheme field queries will be combined with terms entered in other sections.



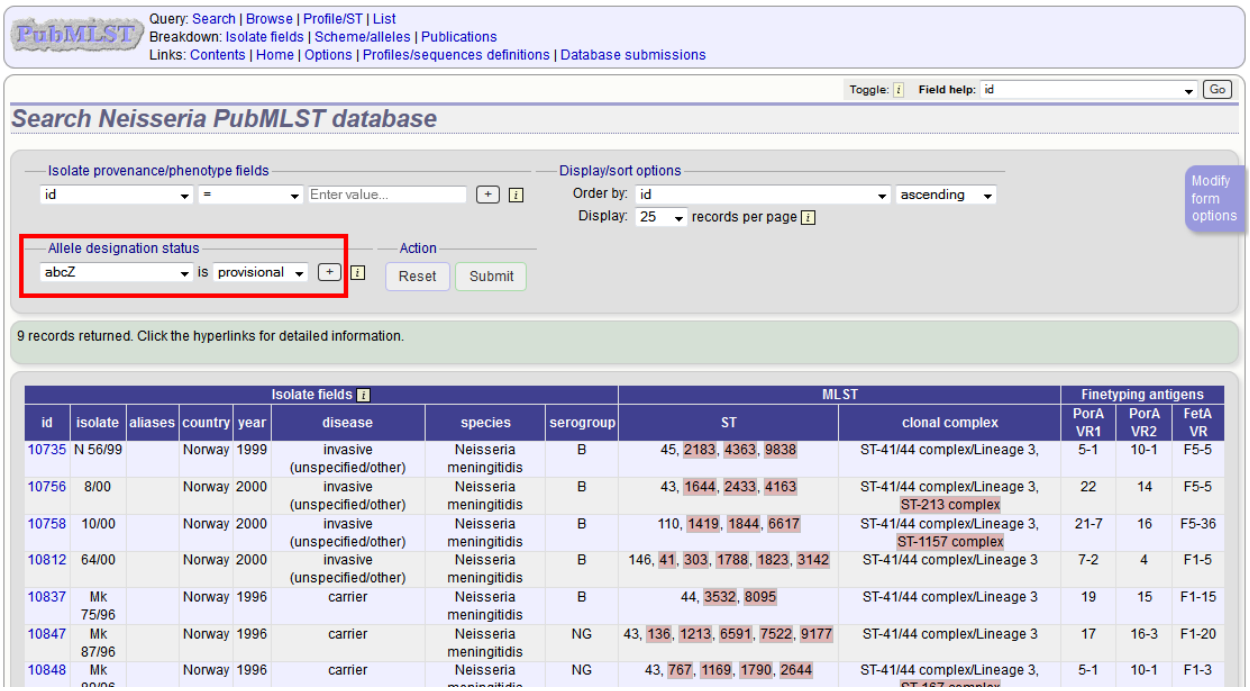
10.6.2 Query by allele designation status

Allele designations can be queried based on their status, i.e. whether they are confirmed or provisional. Queries will be combined from the values entered in all form sections.

Make sure that the allele designation staus fieldset is displayed by selecting it in the 'Modify form options' tab.



Select a locus from the dropdown box and either 'provisional' or 'confirmed'. Additional query fields can be displayed by clicking the '+' button. Click 'Submit'.

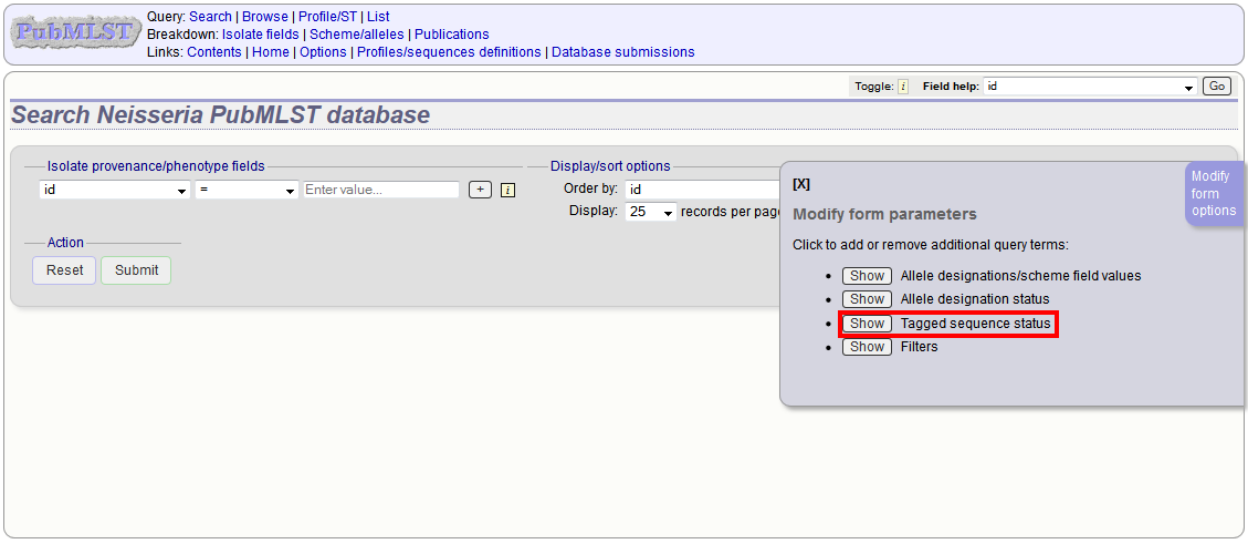


Provisional allele designations are marked within the results tables with a pink background. Any scheme field designations that depend on the allele in question, e.g. a MLST ST, will also be marked as provisional.

10.6.3 Query by tagged sequence status

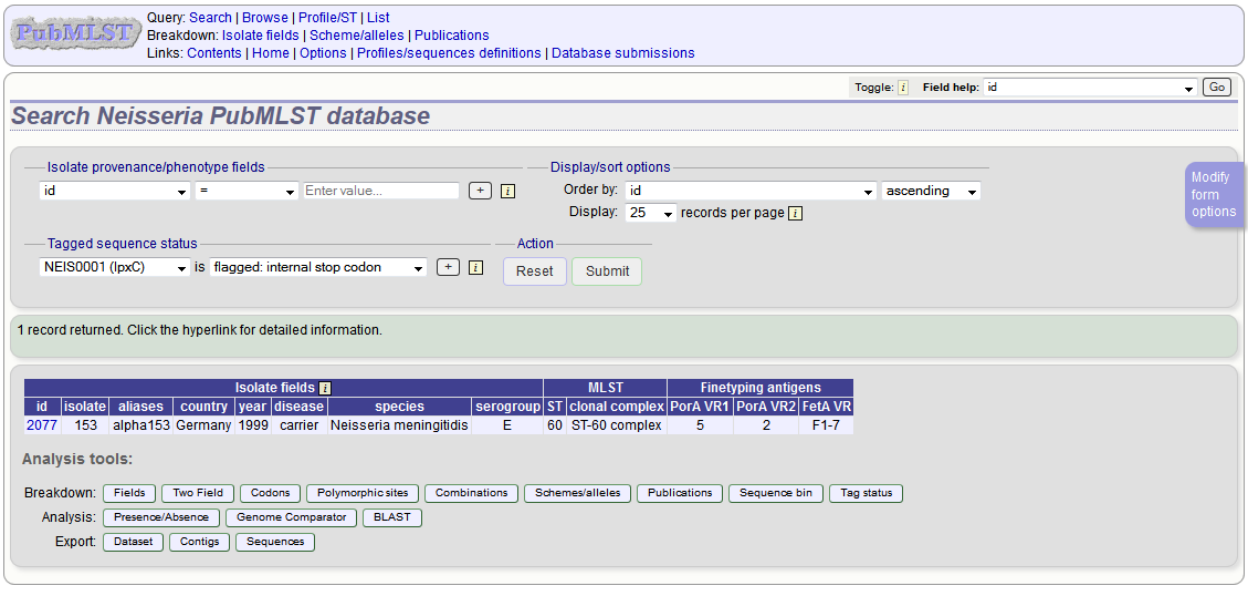
Sequence tags identify the region of a contig within an isolate's sequence bin entries that correspond to a particular locus. The presence or absence of these tags can be queried as can whether or not the sequence has an a flag associated with. These flags designate specific characteristics of the sequences. Queries will be combined from the values entered in all form sections.

Make sure that the tagged sequences status fieldset is displayed by selecting it in the 'Modify form options' tab.



Select a specific locus in the dropdown box (or alternatively 'any locus') and a status. Available status values are:

- untagged
  - The locus has not been tagged within the sequence bin.
- tagged
  - The locus has been tagged within the sequence bin.
- complete
  - The locus sequence is complete.
- incomplete
  - The locus sequence is incomplete - normally because it continues beyond the end of a contig.
- flagged: any
  - The sequence for the locus has a flag set.
- flagged: none
  - The sequence for the locus does not have a flag set.
- flagged: <specific flag>
  - The sequence for the locus has the specific flag chosen.



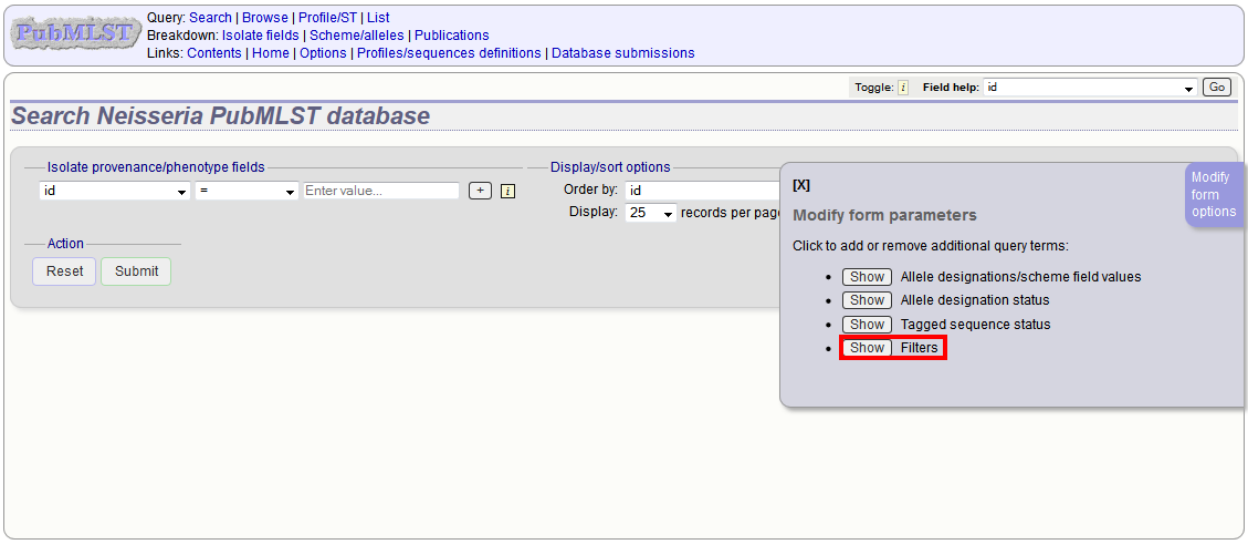
See also:

Sequence tag flags

10.6.4 Query filters

There are various filters that can additionally be applied to queries, or the filters can be applied solely on their own so that they filter the entire database.

Make sure that the filters fieldset is displayed by selecting it in the 'Modify form options' tab.



The filters displayed will depend on the database and what has been defined within it. Common filters are:

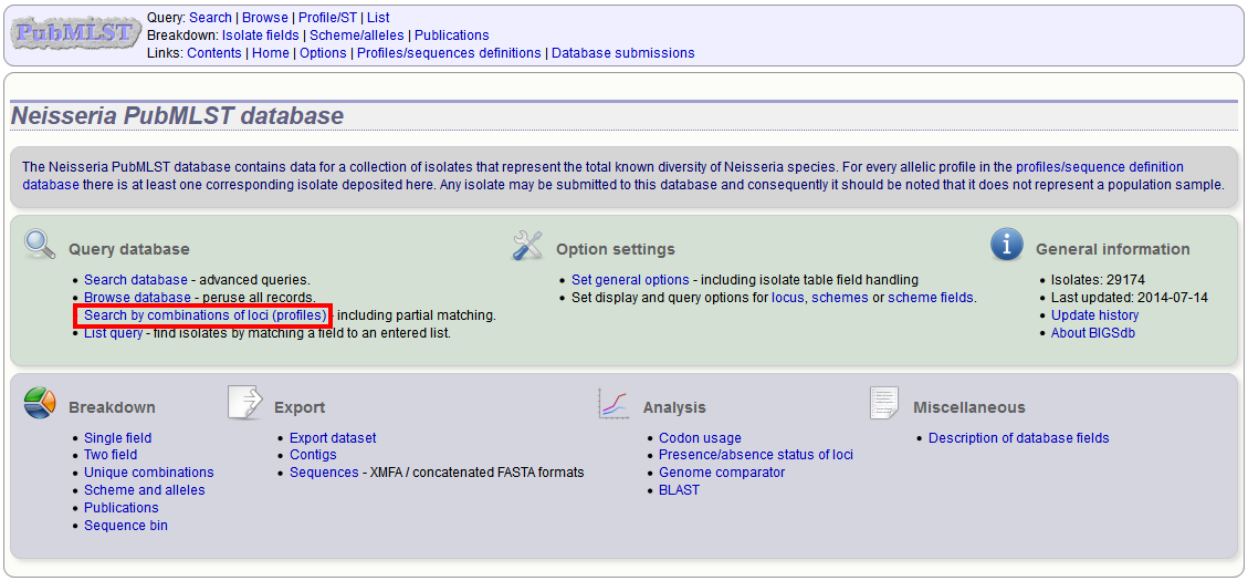
- Publication - Select one or more publication that has been linked to isolate records.
- Project - Select one or more project that isolates belong to.
- Profile completion - This is commonly displayed for MLST schemes. Available options are:

  - complete - All loci of the scheme have alleles designated.
  - incomplete - One or more loci have not yet been designated.
  - partial - The scheme is incomplete, but at least one locus has an allele designated.
  - started - At least one locus has an allele designated. The scheme mat be complete or partial.
  - not started - The scheme has no loci with alleles designated.
- Sequence bin - Specify whether any sequence data has been associated with a record. Specific threshold values may be selected if these have been *set up for the database*.
- Provenance fields - Dropdown list boxes of values for specific provenance fields may be present if set for the database. Users can choose to *add additional filters*.

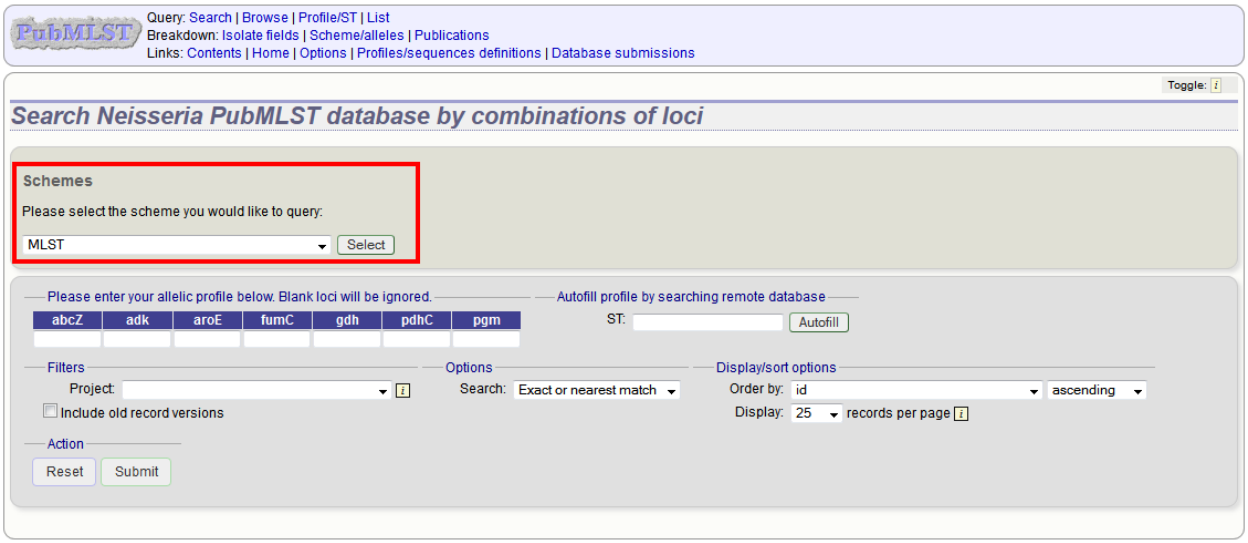
10.7 Querying by allelic profile

If a scheme, such as MLST, has been defined for either an isolate database it is possible to query the database against complete or partial allelic profiles. Even if no scheme is defined, queries can be made against all loci. This can also be done in sequence definition databases if the scheme has a primary key field defined.

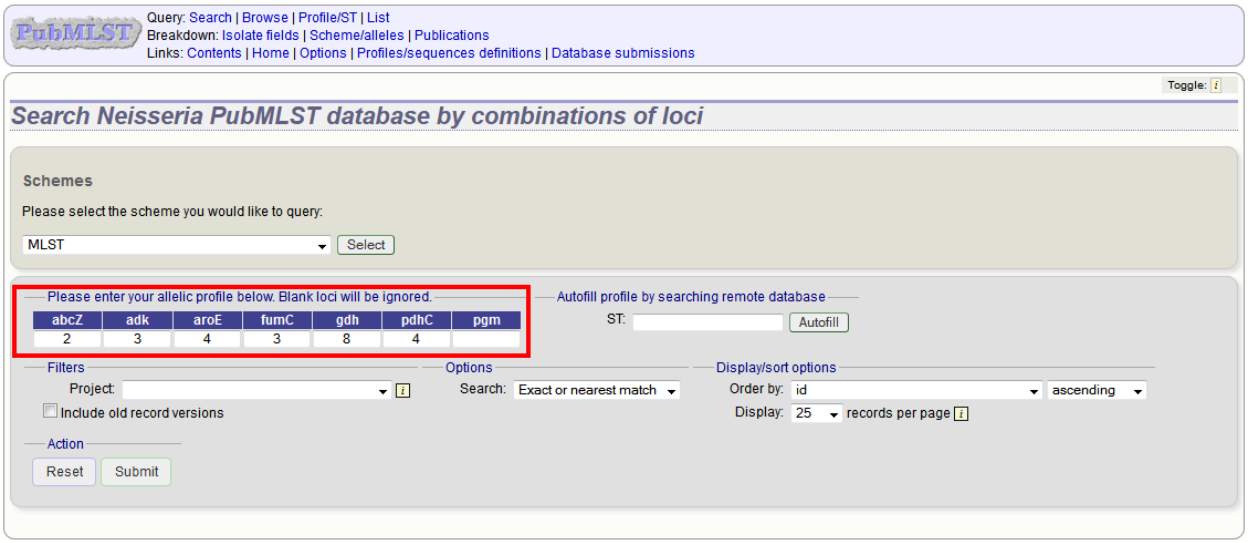
On the index page, click 'Search by combinations of loci (profiles)' for any defined scheme. Enter either a partial (any combination of loci) or complete profile.



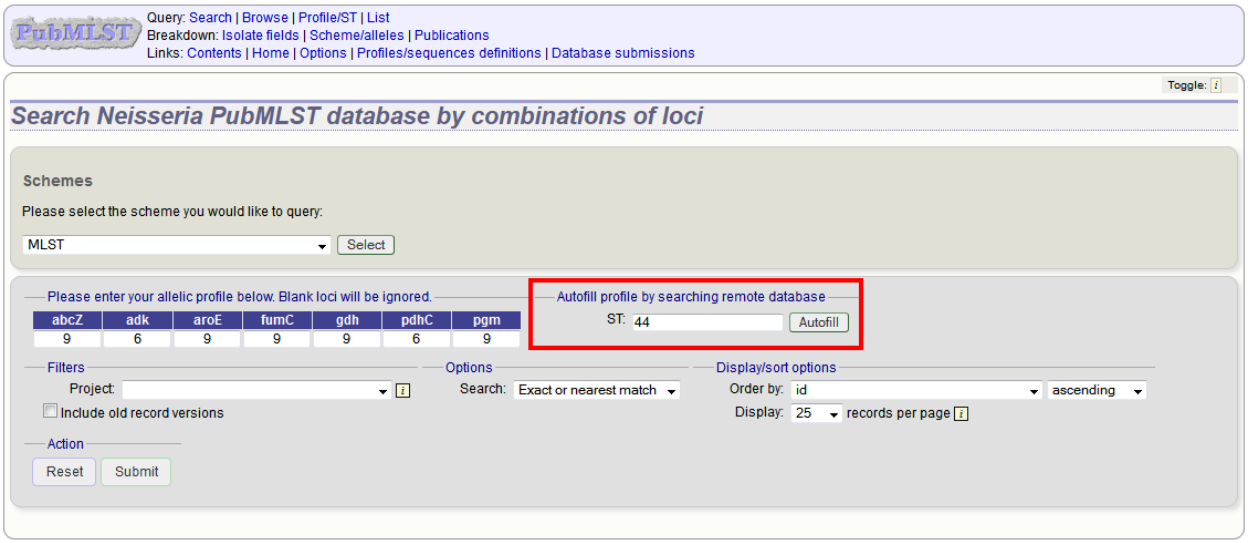
If multiple schemes are defined, you may have to select the scheme you wish to query in the 'Schemes' dropdown box and click 'Select'.



Enter the combination of alleles that you want to query for. Fields can be left blank.



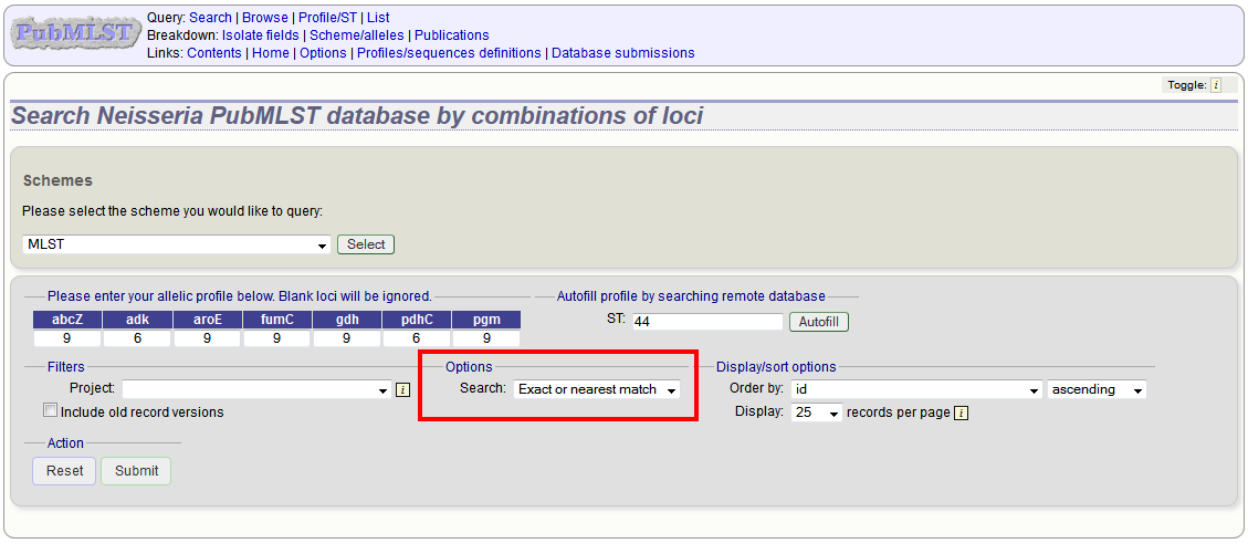
Alternatively, for scheme profiles, you can enter a primary key value (e.g. ST) and select 'Autofill' to automatically fill in the associated profile.



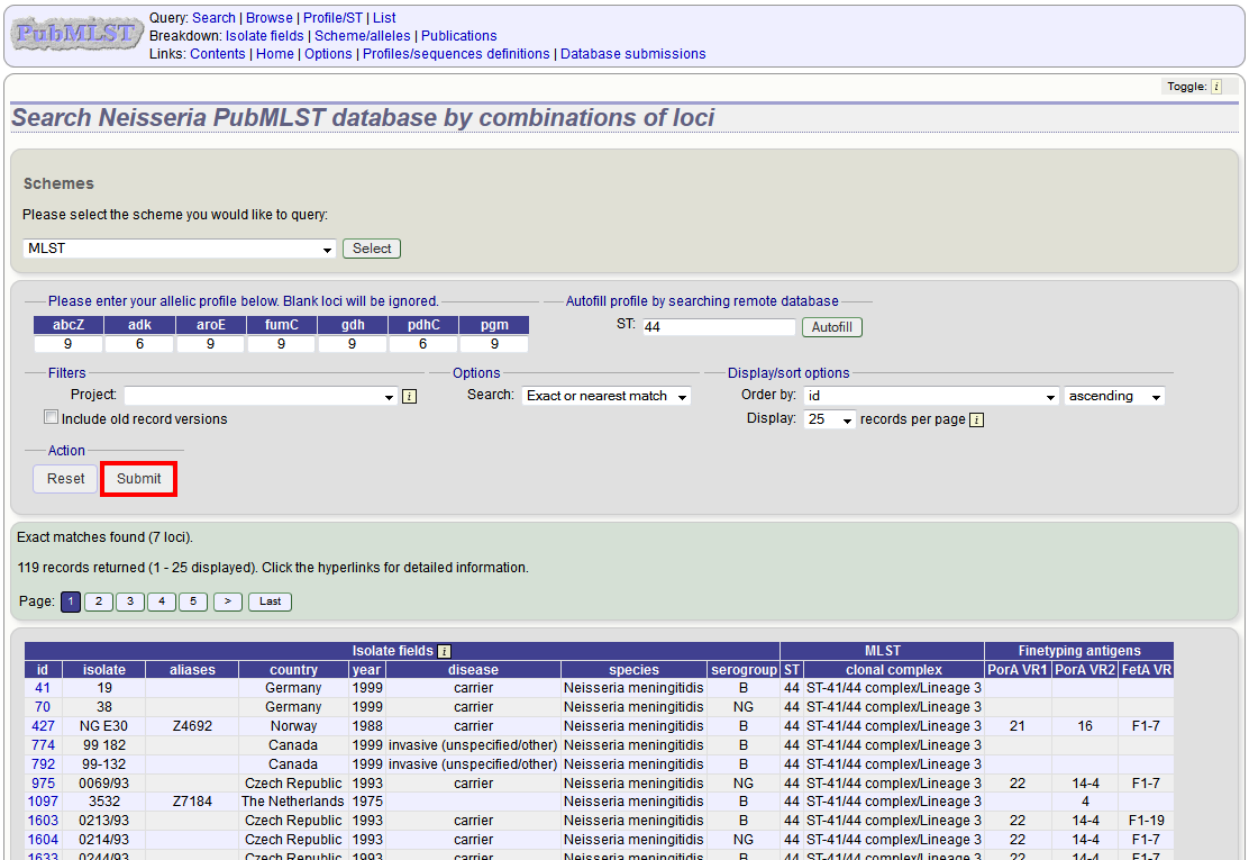
Select the number of loci that you'd like to match in the options dropdown box. Available options are:

- Exact or nearest match
- Exact match only
- x or more matches
- y or more matches
- z or more matches

Where x,y, and z will range from n-1 to 1 where n is the number of loci in the scheme.



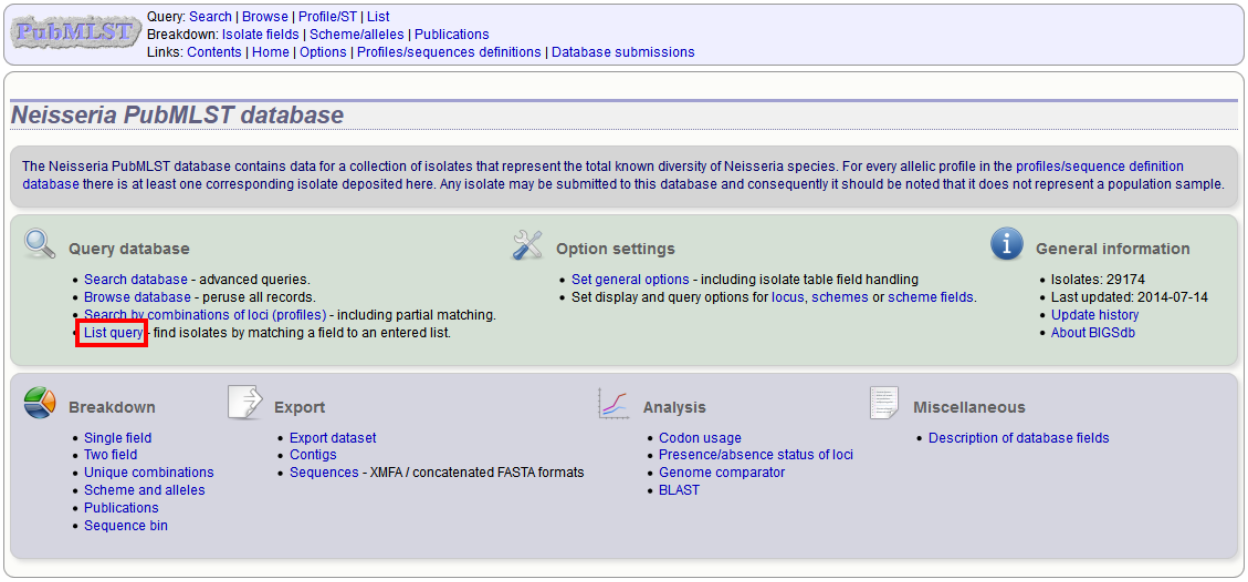
Click 'Submit'.



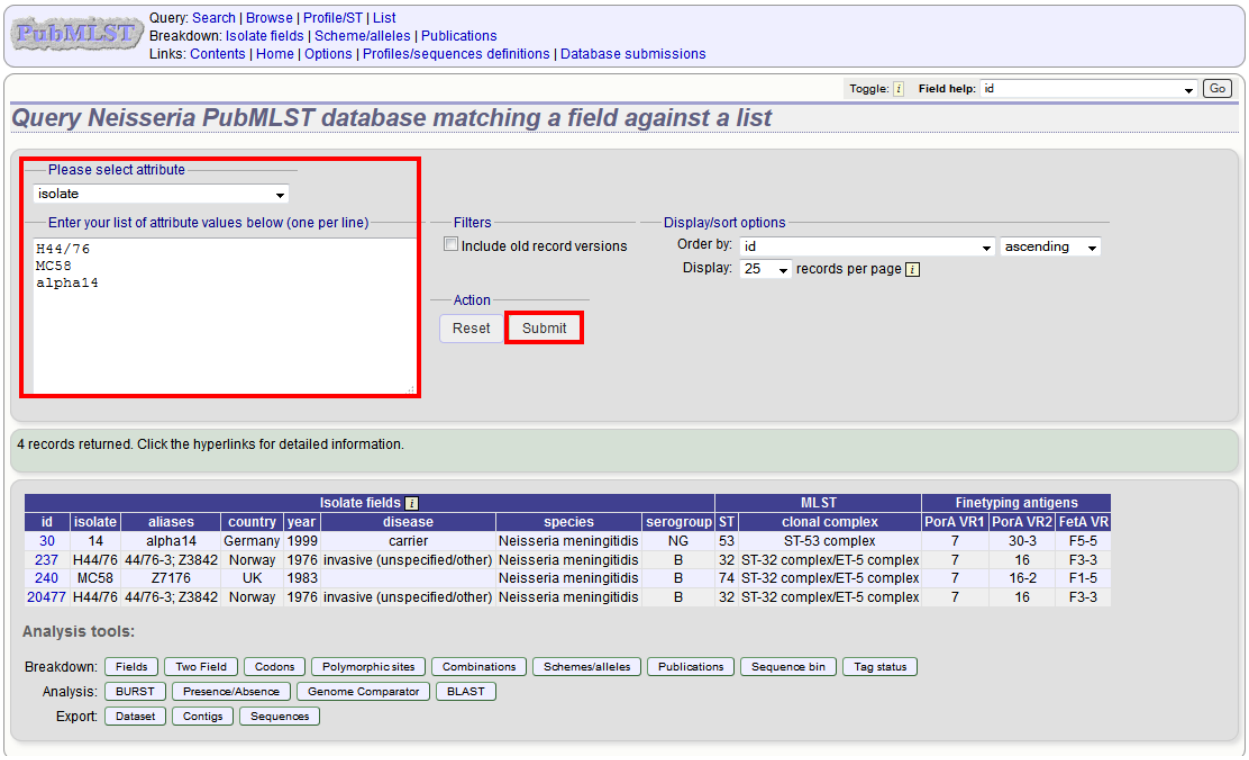
10.8 Retrieving list of isolates or profiles

Both isolate and sequence definition databases can be queried against a list of values matching any criteria (isolate provenace fields, alleles, or scheme fields).

Click 'List query' on the main contents page.

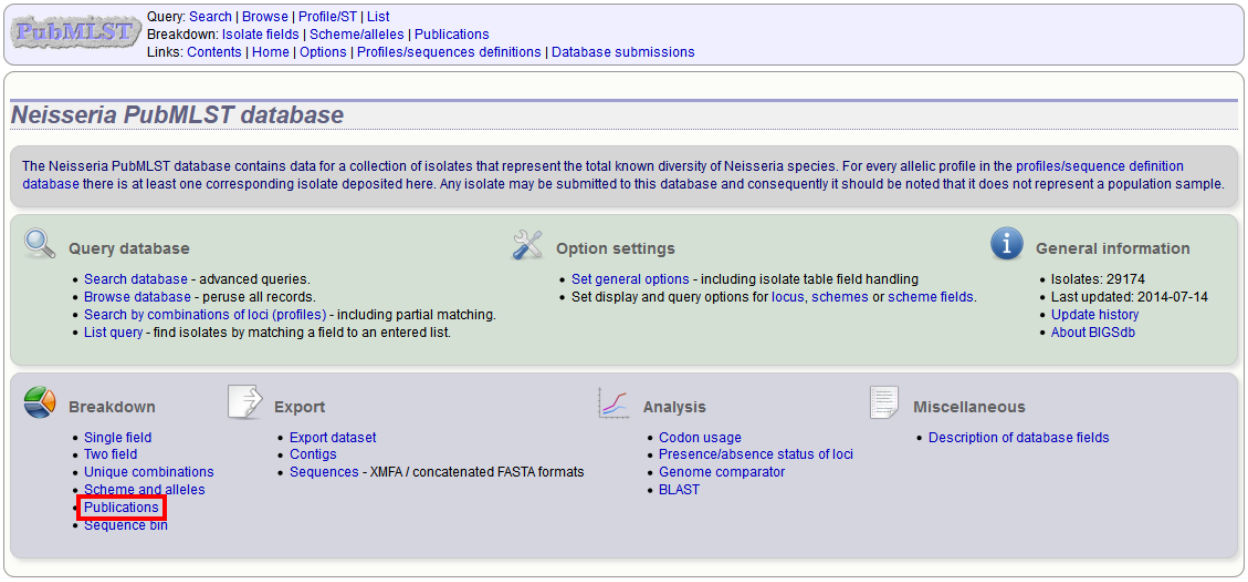


Select the attribute you wish to search against in the drop-down list box and enter the list of attributes in the box (one per line). Click 'Submit'.

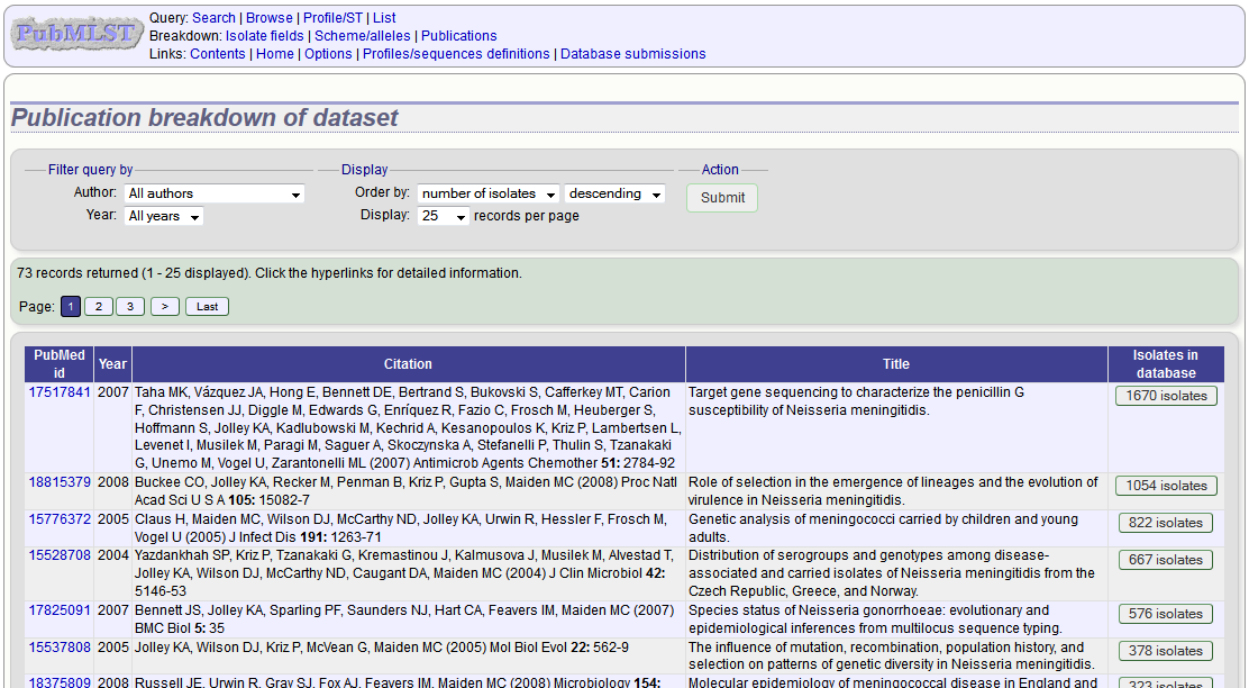


10.9 Retrieving isolates by linked publication

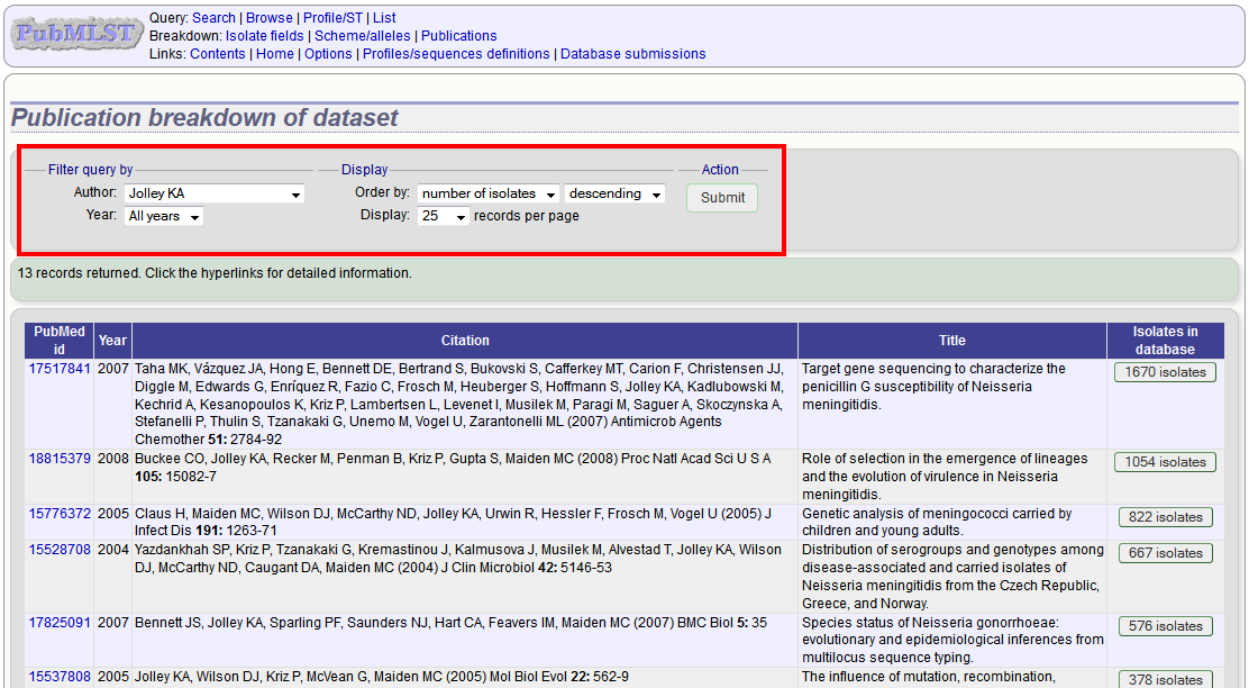
Click 'Publications' in the Breakdown section of the contents page.



A list of publications linked by isolates within the database will be displayed.

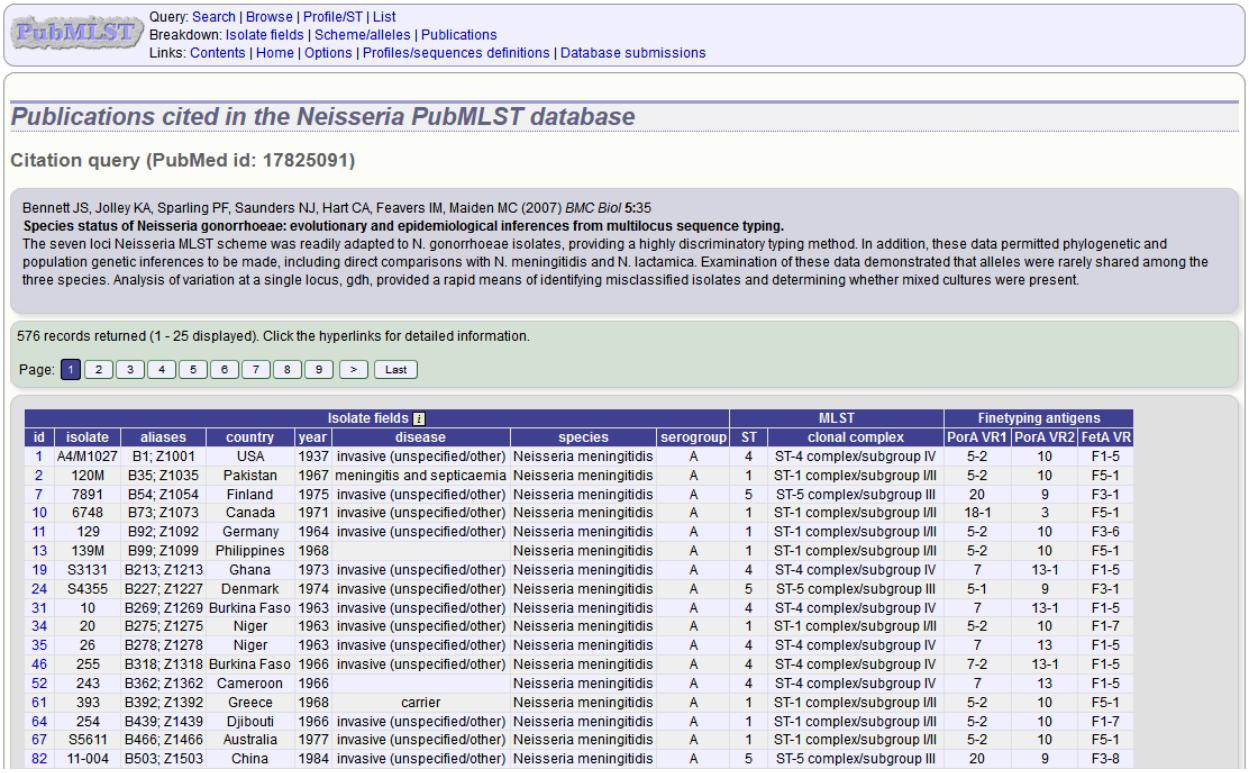


These can be filtered by author and/or year, and the sort order changed.



To display the isolate records for any of the displayed publications, click the button to the right of the citation.

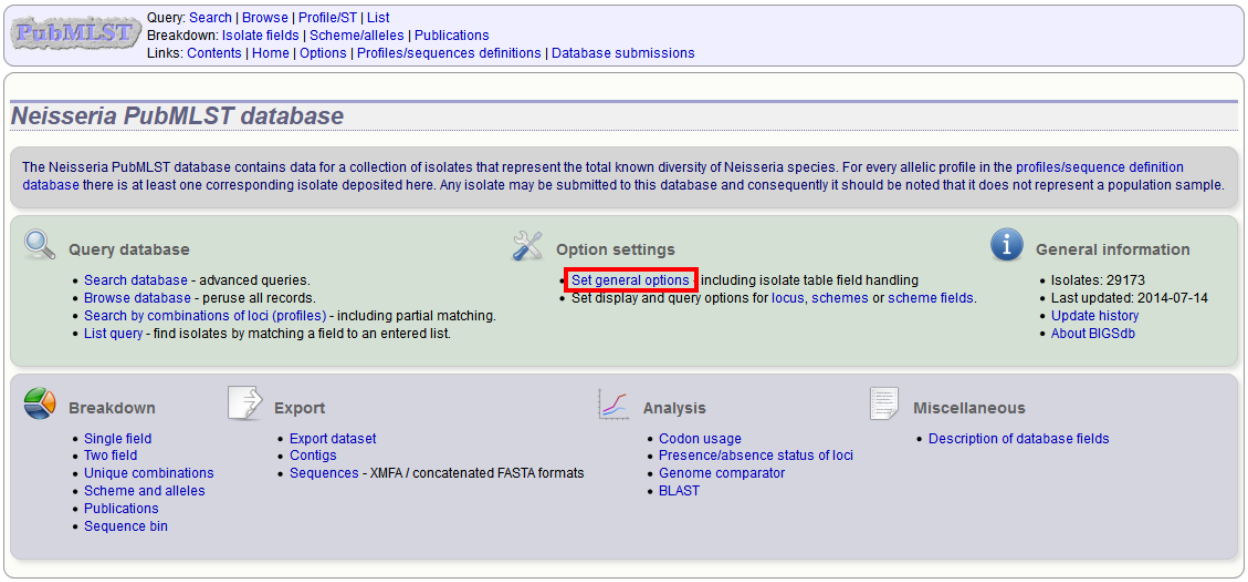
The abstract of the paper will be displayed (if available), along with all isolates linked to it.



10.10 User-configurable options

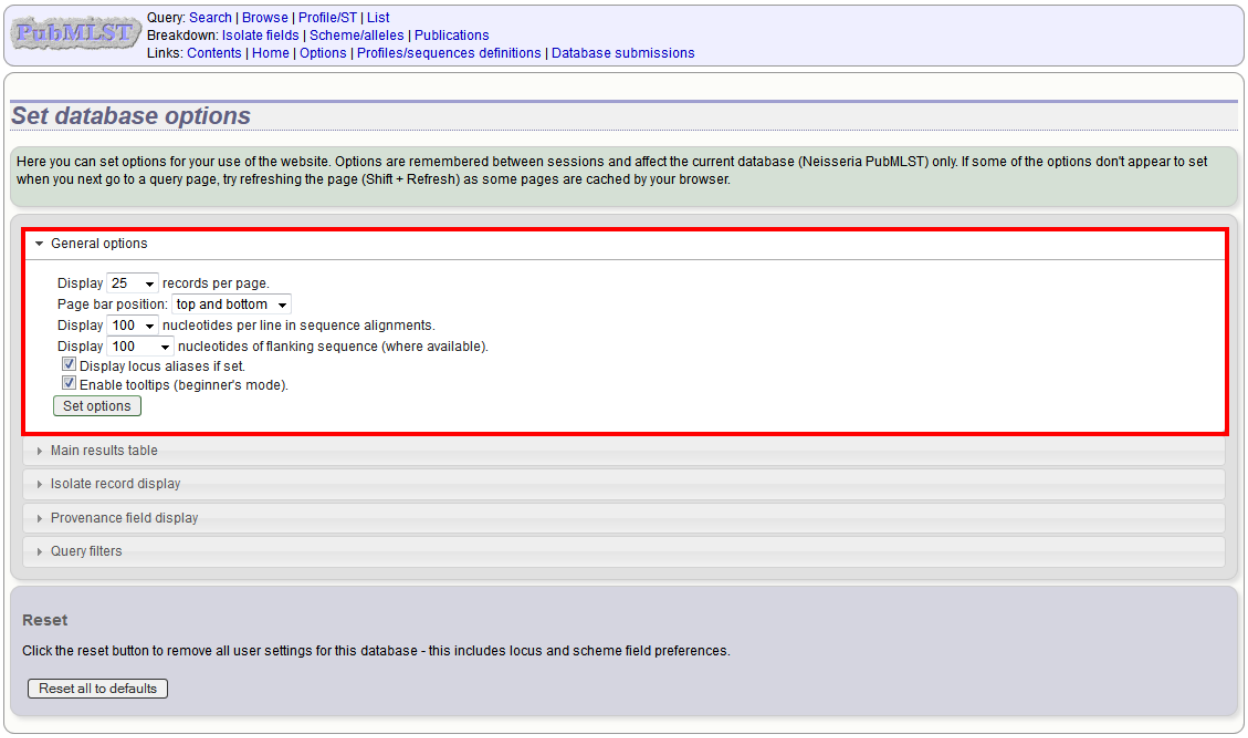
The BIGSdb user interface is configurable in a number of ways. Choices made are remembered between sessions. If the database requires you to log on, the options are associated with your user account, whereas if it is a public database, that you haven't logged in to, the options are associated with a browser cookie so they will be remembered if you connect from the same computer (using the same browser).

Most options are set by clicking the 'Set general options' link on the database contents page. Most of the available options are visible for isolate databases, whereas sequence definition databases have fewer available.



10.10.1 General options

The general options tab is displayed by default. If another tab is being shown, click the 'General options' header.



The general tab allows the following options to be modified:

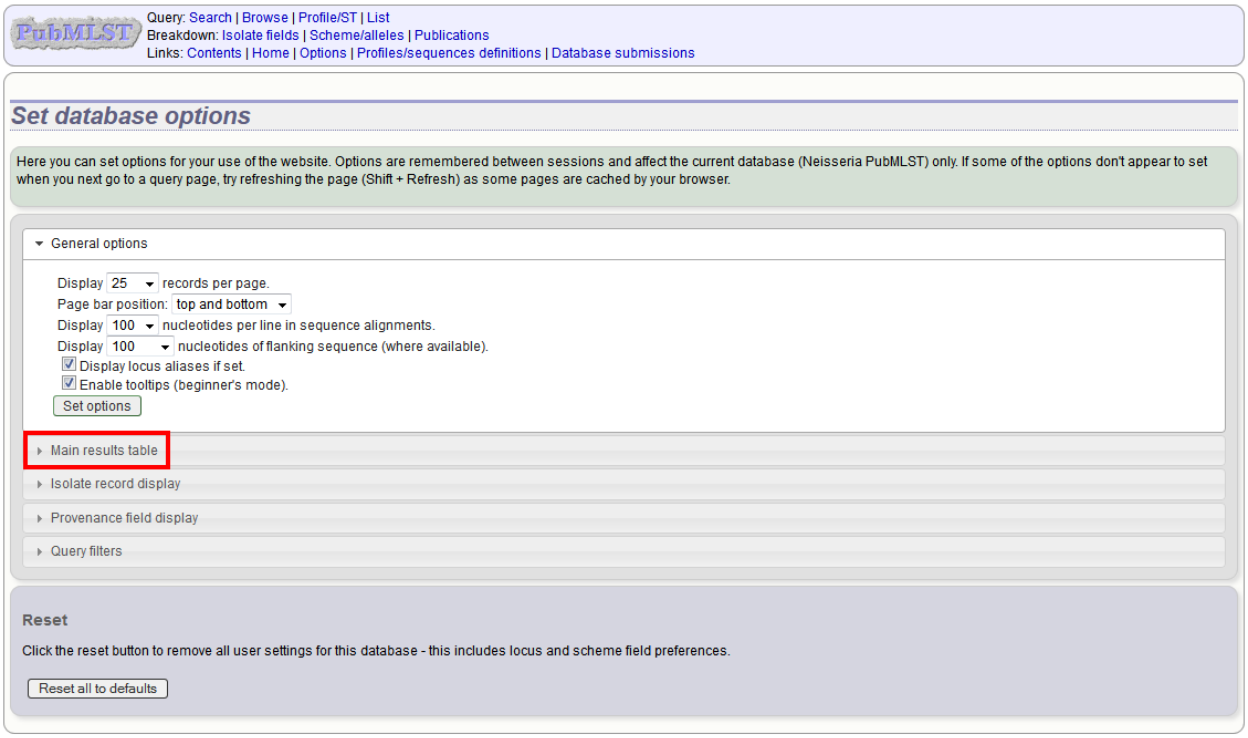
- Records per page
- Page bar position
- Nucleotides per line - Some analyses display sequence alignments. This option allows you to set the width of these alignments so suit your display.
- Flanking sequence length - This sets the length of flanking sequence upstream and downstream of a particular locus that is included whenever a sequence is displayed. Flanking sequences are displayed fainter that the locus sequence.
- Locus aliases - Loci can have multiple names (aliases). Setting this option will display all alternative names in results tables.
- Tooltips (beginner's mode) - Most query forms have help available in the form of information tooltips. These can be switched on/off here. They can also be toggled off by clicking the Toggle: 'i' button at the top-right of the display of some pages.

Click 'Set options' to remember any changes you make.

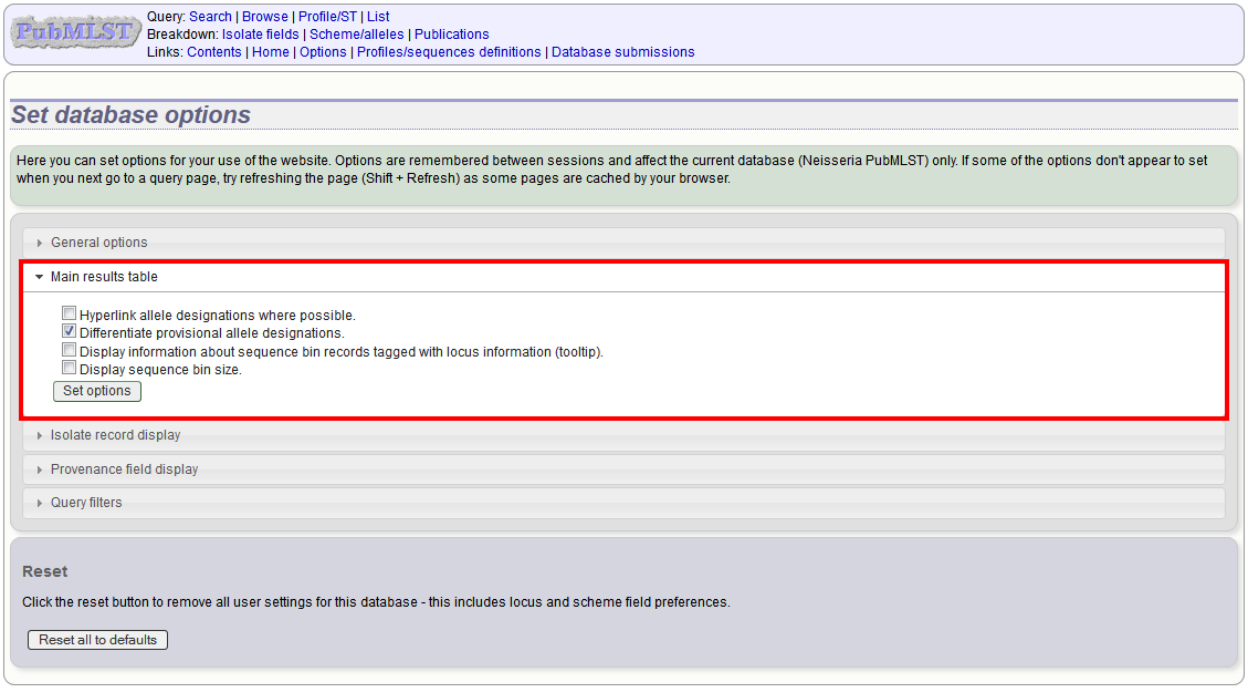
10.10.2 Main results table

The 'main results table' tab contains options for the display of paged results following a query.

Click the 'Main results table' header to display the tab.



The 'main results table' tab will scroll up.



This tab allows the following options to be modified:

- Hyperlink allele designations - Hyperlinks point to an information page about the particular allele definition. Depending on the locus, these may exist on a different website.
- Differentiate provisional allele designations - Allele designations can be set as confirmed or provisional, usually depending on the method of assignment. Selecting this option will display provisional designations in a different

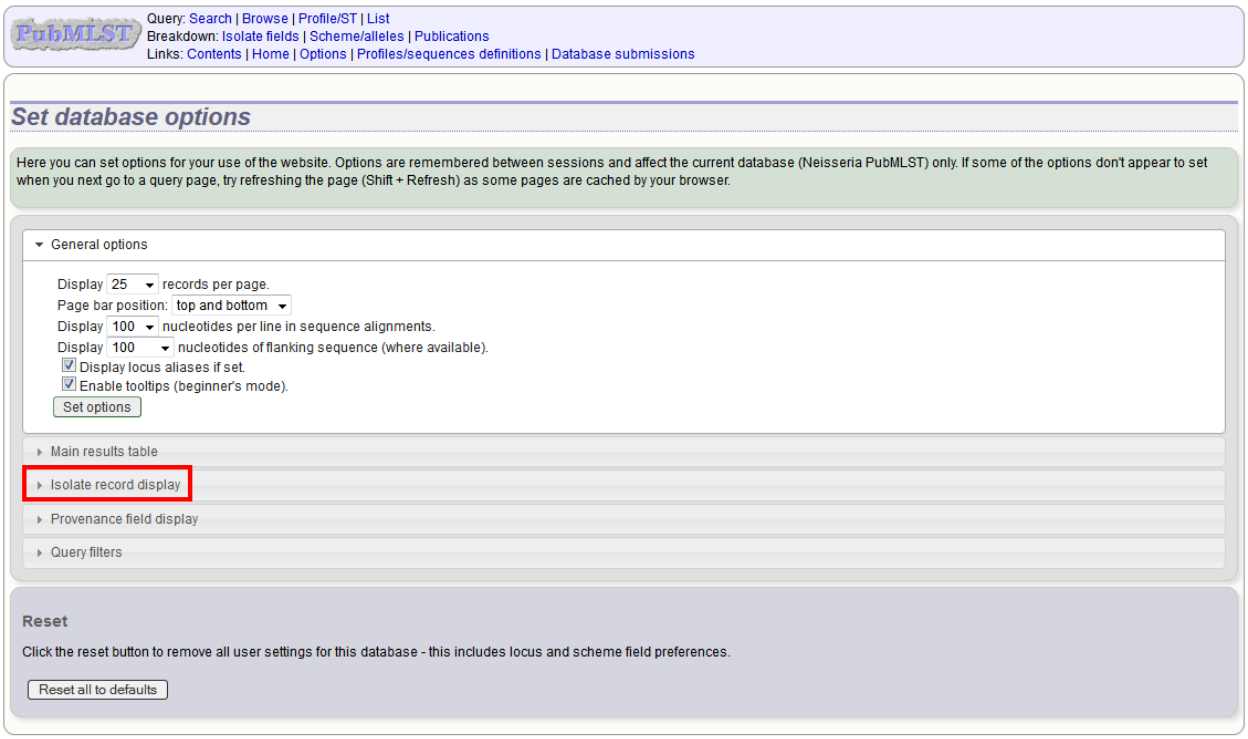
colour to confirmed designations.

- Sequence bin records - Displays a tooltip linking to the sequence tag if available.
- Sequence bin size - Displays the size of the sum of all contigs associated with each isolate record.

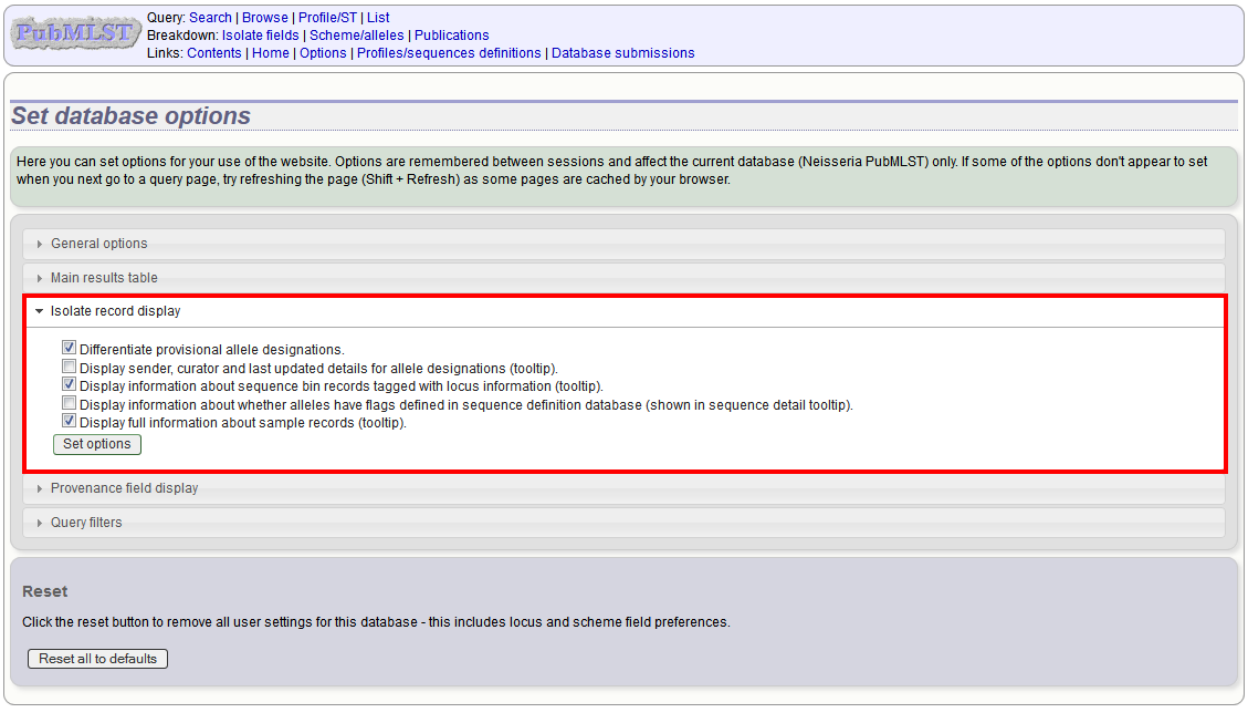
10.10.3 Isolate record display

The 'isolate record display' tab contains options for the display of a full isolate record.

Click the 'Isolate record display' tab to display the tab.



The 'Isolate record display' tab will scroll up.



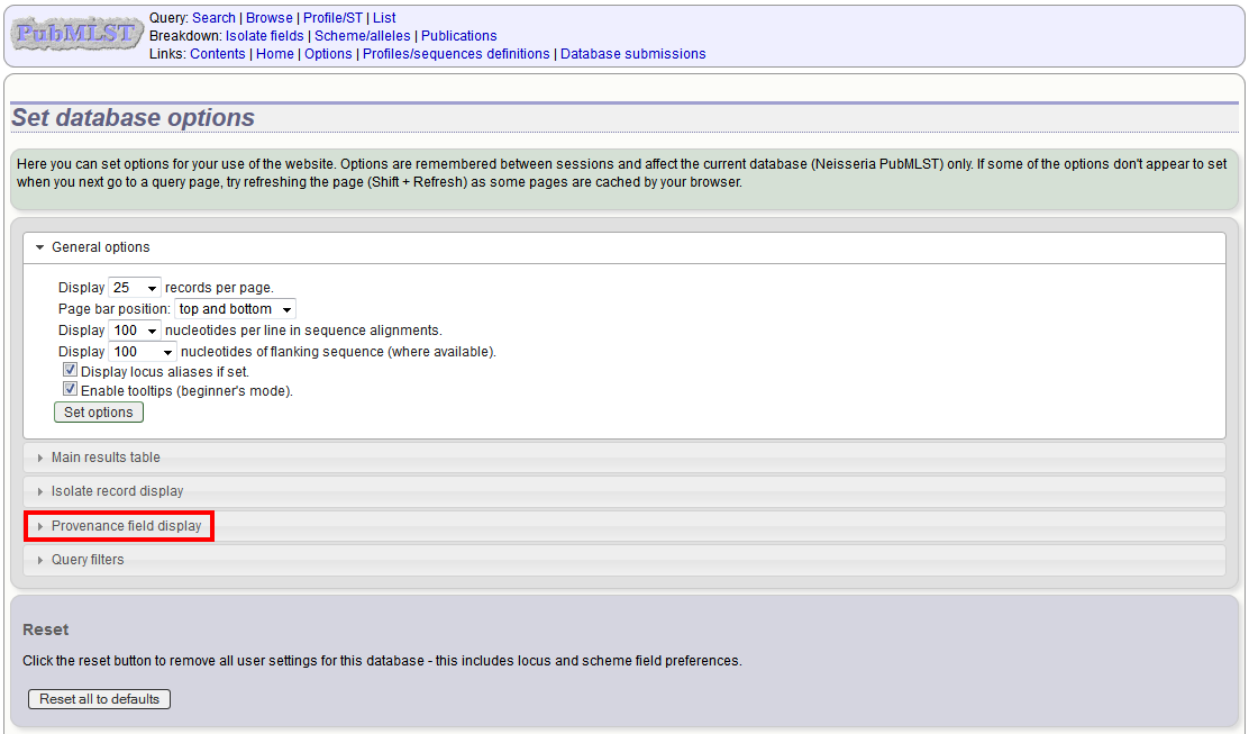
This tab allows the following options to be modified:

- Differentiate provisional allele designations - Allele designations can be set as confirmed or provisional, usually depending on the method of assignment. Selecting this option will display provisional designations in a different colour to confirmed designations.
- Display sender, curator and last updated records - Displays a tooltip containing sender information next to each allele designation.
- Sequence bin information - Displays a tooltip with information about the position of the sequence if tagged within the sequence bin.
- Allele flags - Displays information about whether alleles have flags defined in sequence definition databases.
- Display full information about sample records - Used when the database is used as part of a basic laboratory information management system (LIMS). This option will display records of samples available for the displayed isolate.

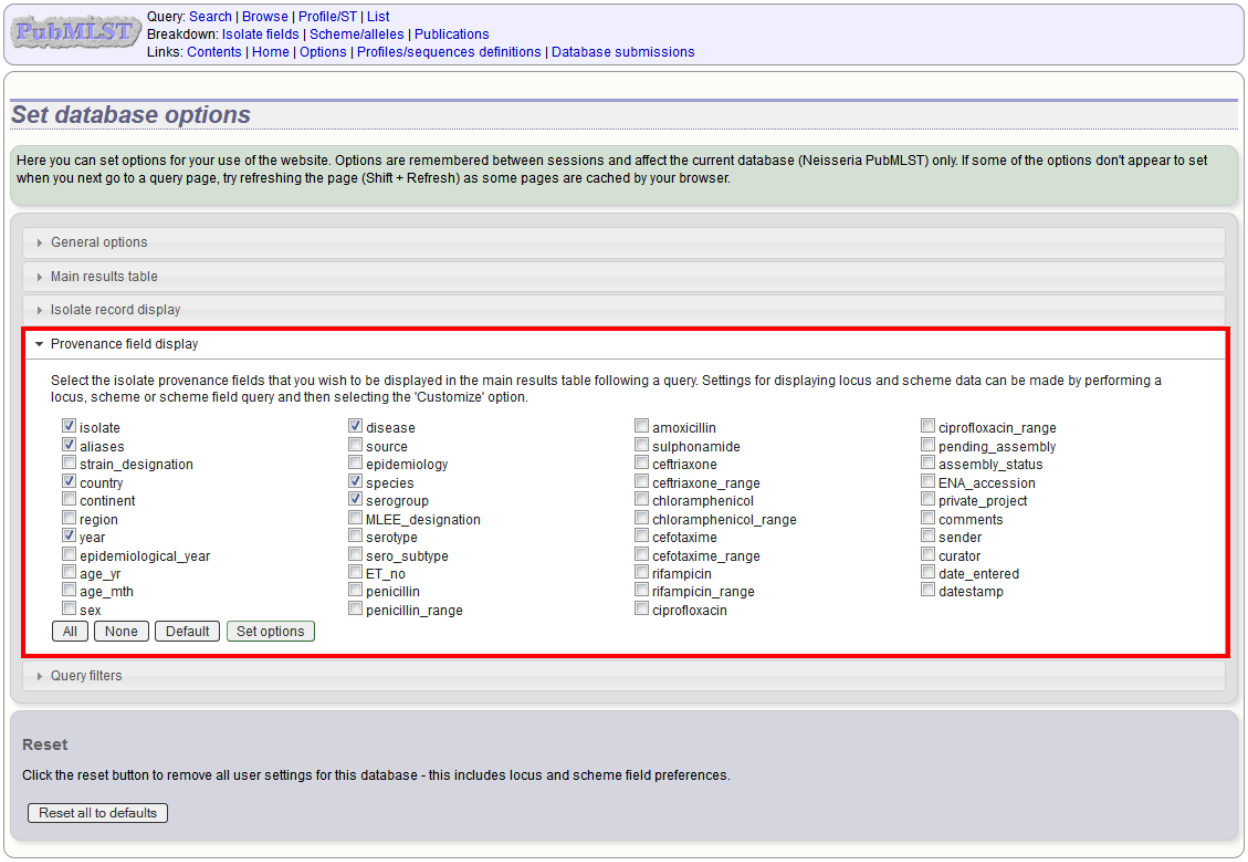
10.10.4 Provenance field display

The 'provenance field display' tab contains checkboxes for fields to display in the main results table.

Click the 'Provenance field display' tab to display the tab.



The 'Provenance field display' tab will scroll up.



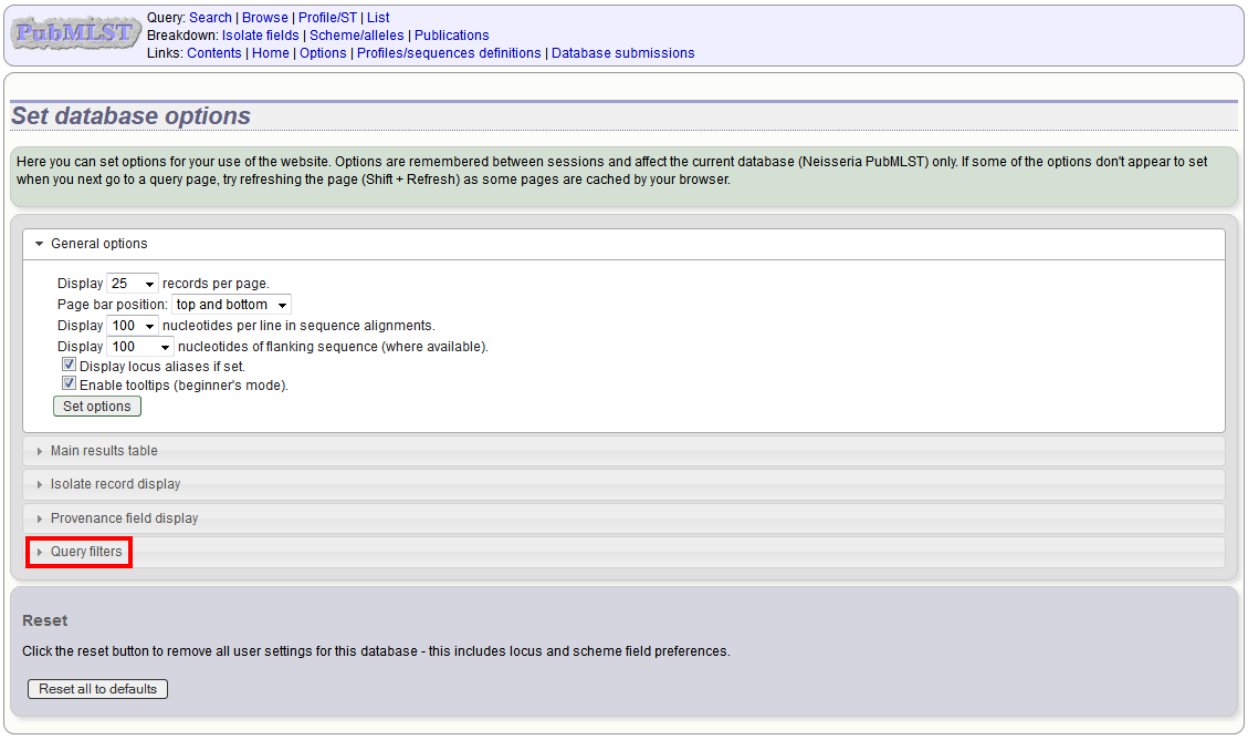
Some fields will be checked by default - these are defined during *database setup* (maindisplay option).

Check any fields that you wish to be displayed and then click 'Set options'. You can return to the default selection by clicking 'Default' followed by 'Set options'.

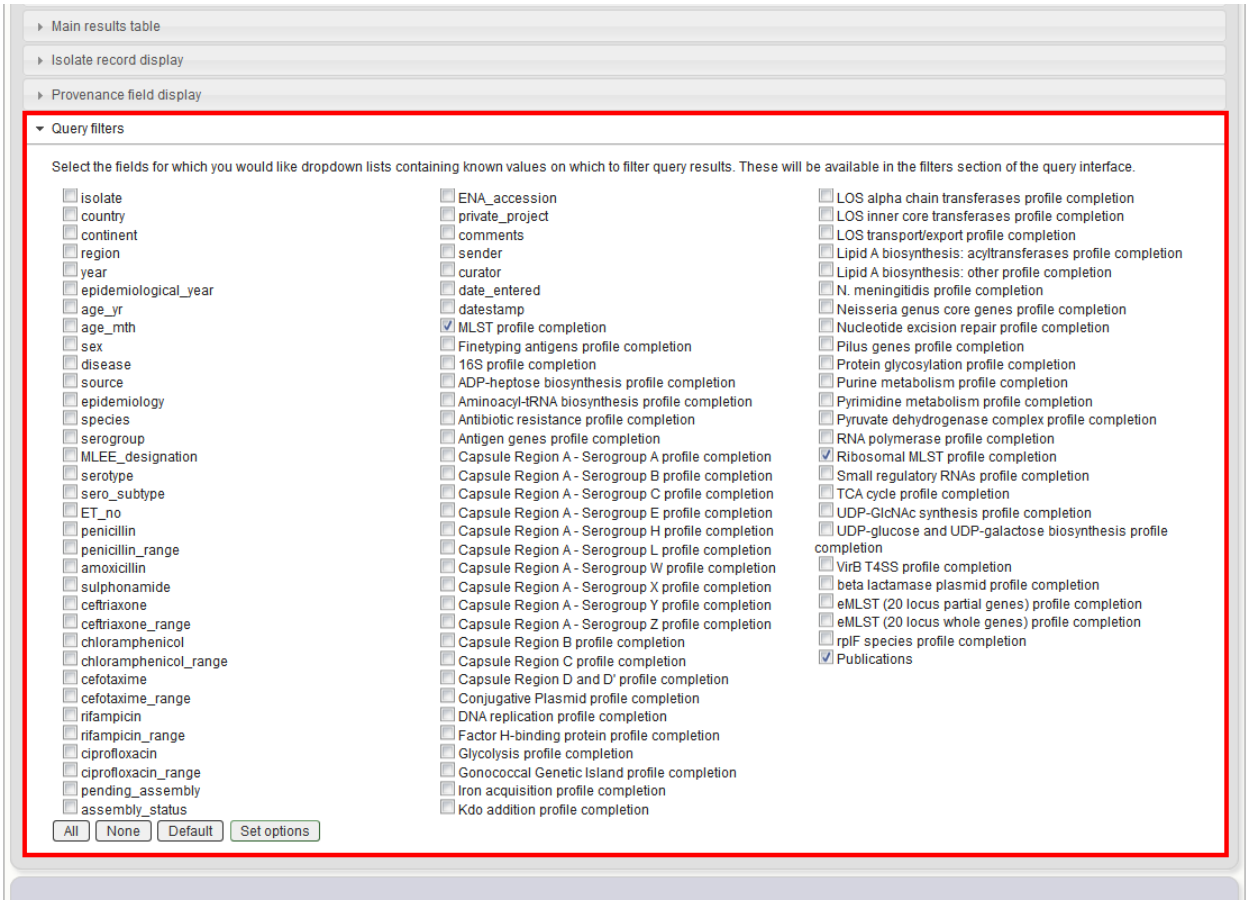
10.10.5 Query filters

The 'query filters' tab contains checkboxes for provenance fields and scheme completion status. Checking these results in drop-down list box filters appearing in the query page *filters fieldset*.

Click the 'Query filters' tab to display the tab.



The 'Query filters' tab will scroll up.



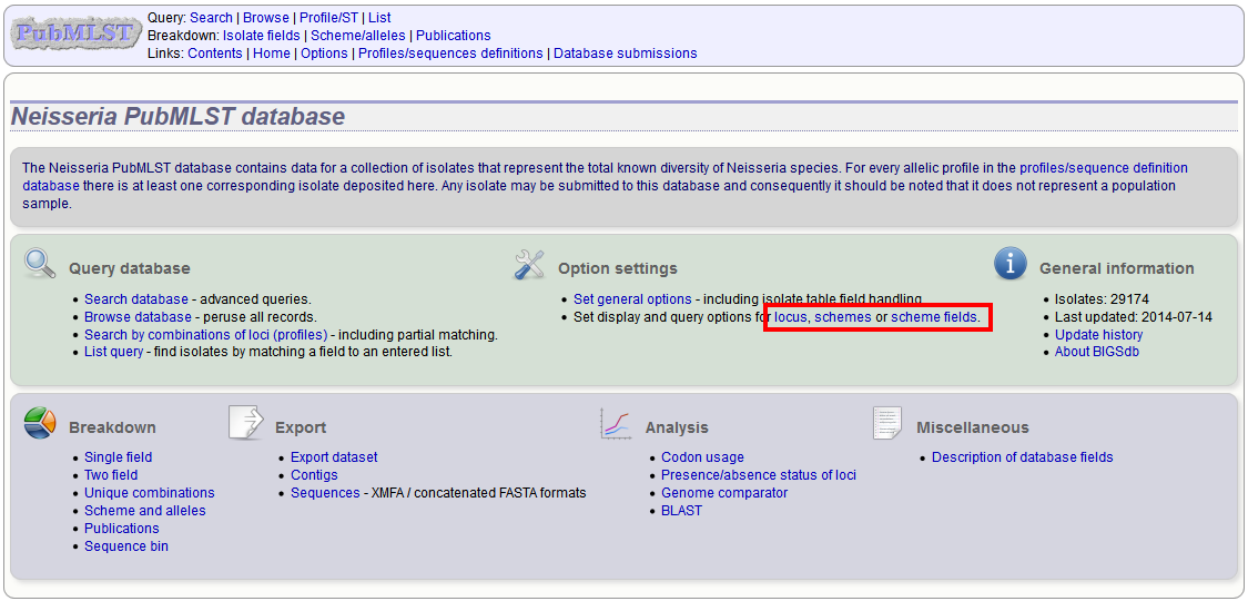
A list of possible filters appears. Click any checkbox for a filter you would like to make available. Click 'Set options' when done. You can return to the default selection by clicking 'Default' followed by 'Set options'.

10.10.6 Modifying locus and scheme display options

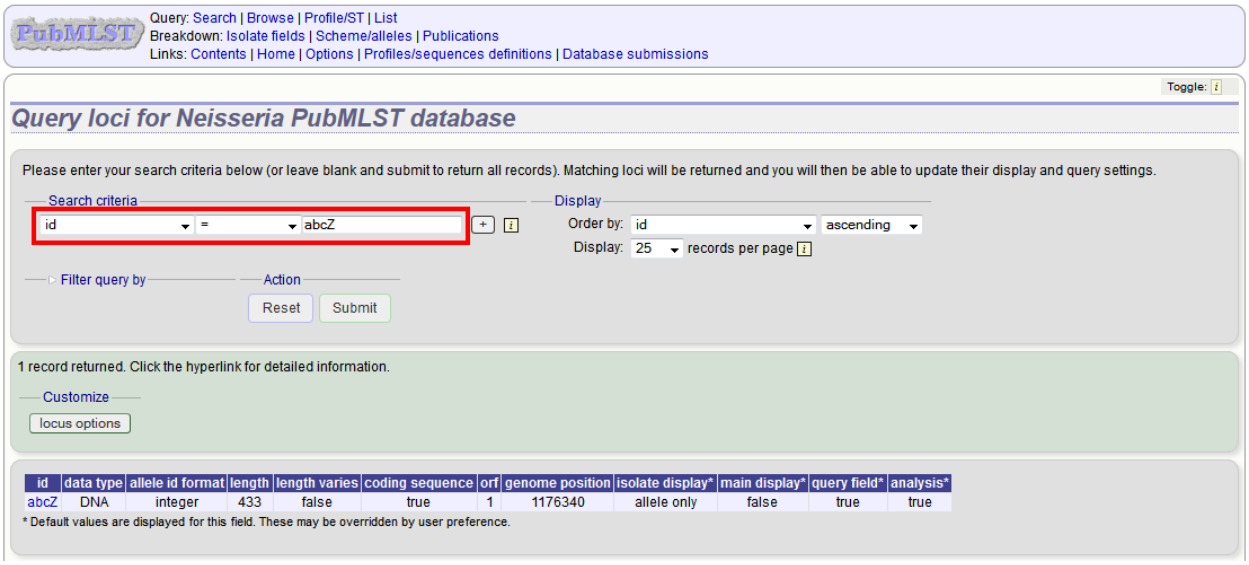
Whether or not loci, schemes or scheme fields are displayed in result tables, isolate records, or within query dropdown boxes can all be set with default options when first defined. These attributes can, however, be overridden by a user, and these selections will be remembered between sessions.

The procedure to modify these attributes is the same for locus, schemes or scheme fields, so the steps for loci will be demonstrated only.

Click the appropriate link on the isolate contents page.

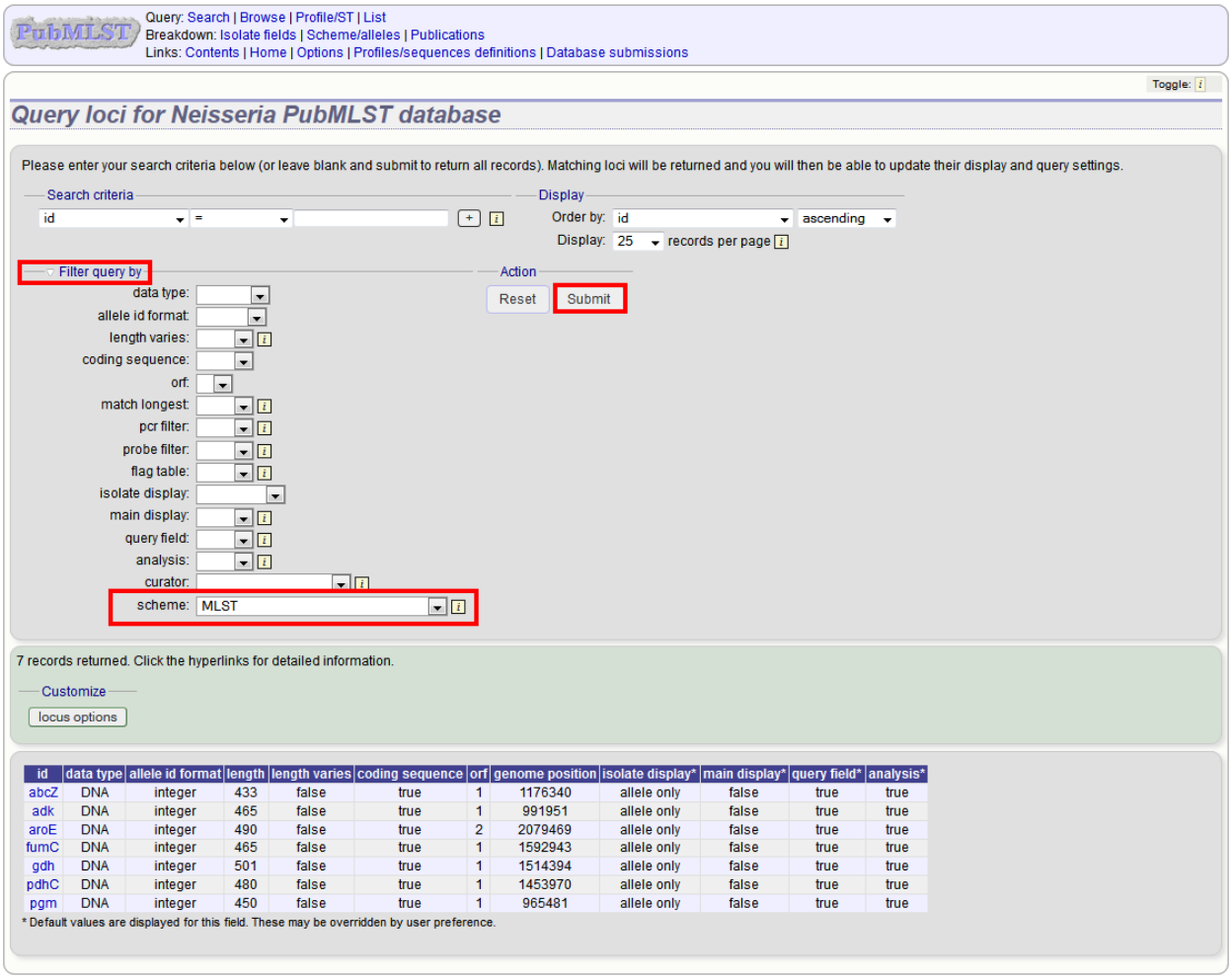


Either select the locus id by querying for it directly.

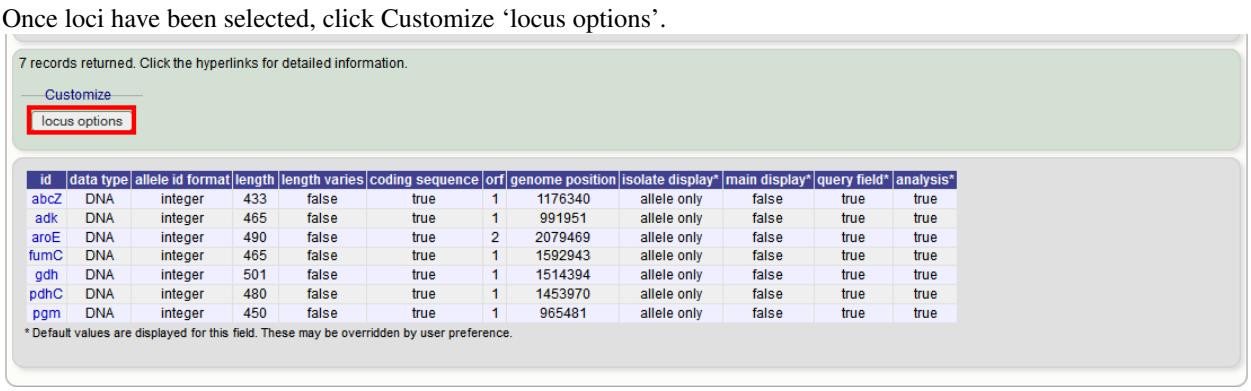


Designations can be queried using *standard operators*.

Alternatively, you can search by filtering loci by schemes. Click the 'Filter query by' header and select the scheme in the dropdown box.



Once loci have been selected, click Customize 'locus options'.



You can then choose to add or remove individual loci from the selection by clicking the appropriate checkboxes. At the bottom of the page are a number of attributes that you can change - clicking 'Change' will affect all selected loci.

Possible options for loci are:

- isolate_display - Sets how the locus is displayed within an isolate record:
  - allele only - display only identifier
  - sequence - display the full sequence
  - hide - don't show at all

- main_display - Sets whether the locus is displayed in the main results table following a query.
- query_field - Sets whether the locus appears in dropdown list boxes to be used within queries.
- analysis - Sets whether the locus can be used in data analysis functions.

Note: Settings for loci can be overridden by those set for schemes that they are members of. For example, if you set a locus to be displayed within a main results table, but that locus is a member of a scheme and you set that scheme not to be displayed, then the locus will not be shown. Conversely, if you set a scheme to be displayed, but set its member locus not to be shown, then that locus will not be displayed (but other loci and scheme fields may be, depending on their independent settings).

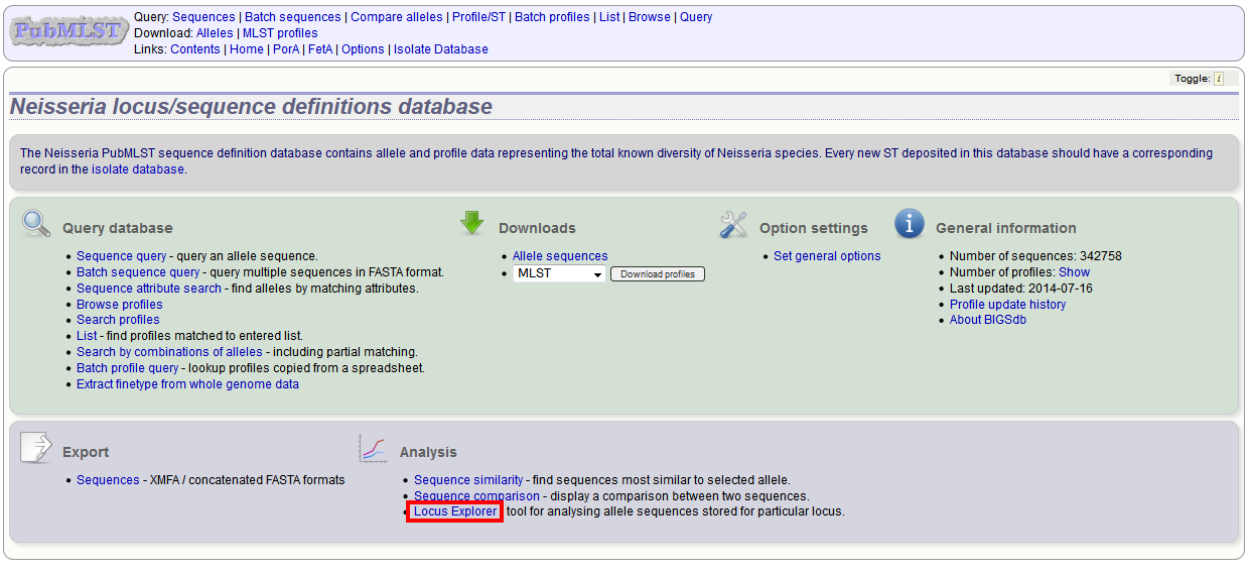
CHAPTER 11

Data analysis plugins

11.1 Locus explorer

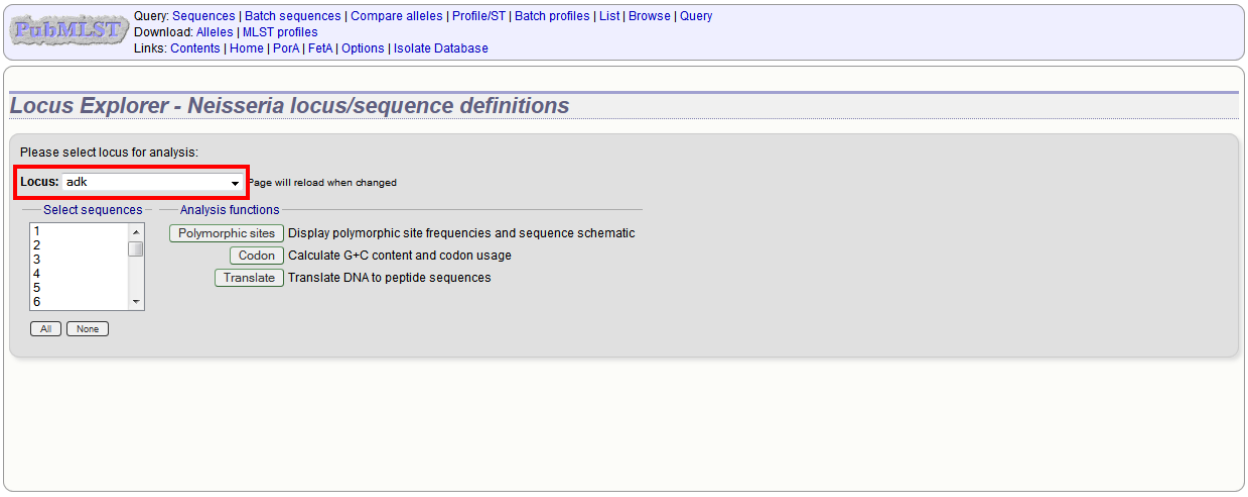
The locus explorer is a sequence definition database plugin. It can create schematics showing the polymorphic sites within a locus, calculate the GC content and generate aligned translated sequences.

Click 'Locus Explorer' from the sequence definition database contents page.



11.1.1 Polymorphic site analysis

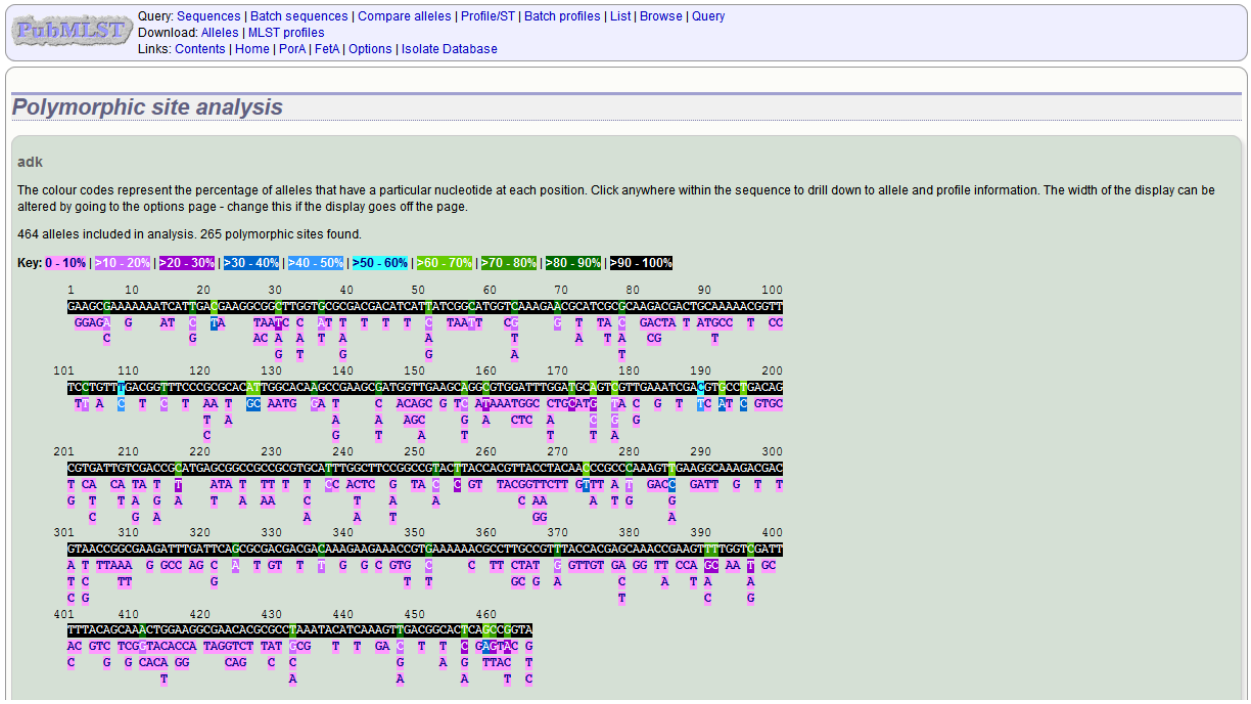
Select the locus you would like to analyse in the Locus dropdown box. The page will reload.



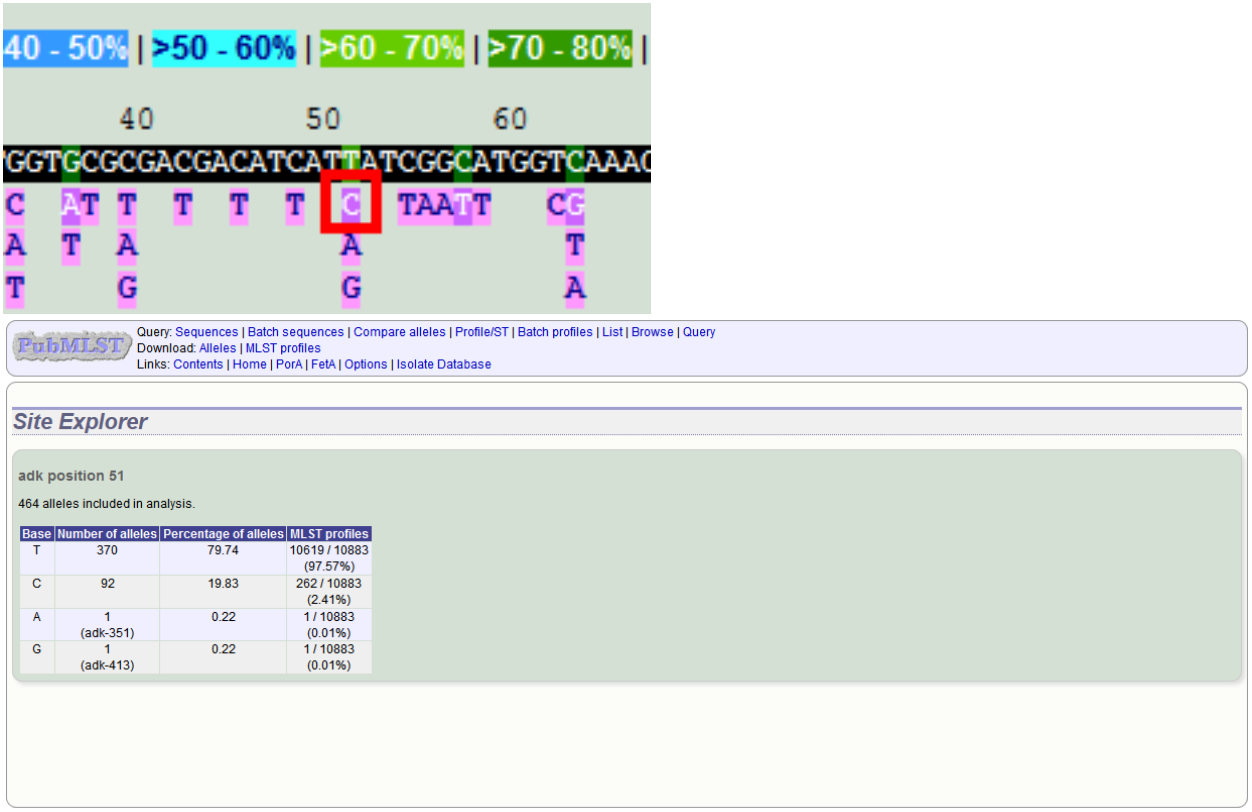
Select the alleles that you would like to include in the analysis. Variable length loci are limited to 200 sequences or fewer since these need to be aligned. Click 'Polymorphic sites'.

If an alignment is necessary, the job will be submitted to the job queue and the analysis performed. If no alignment is necessary, then the analysis is shown immediately.

The first part of the page shows the schematic.

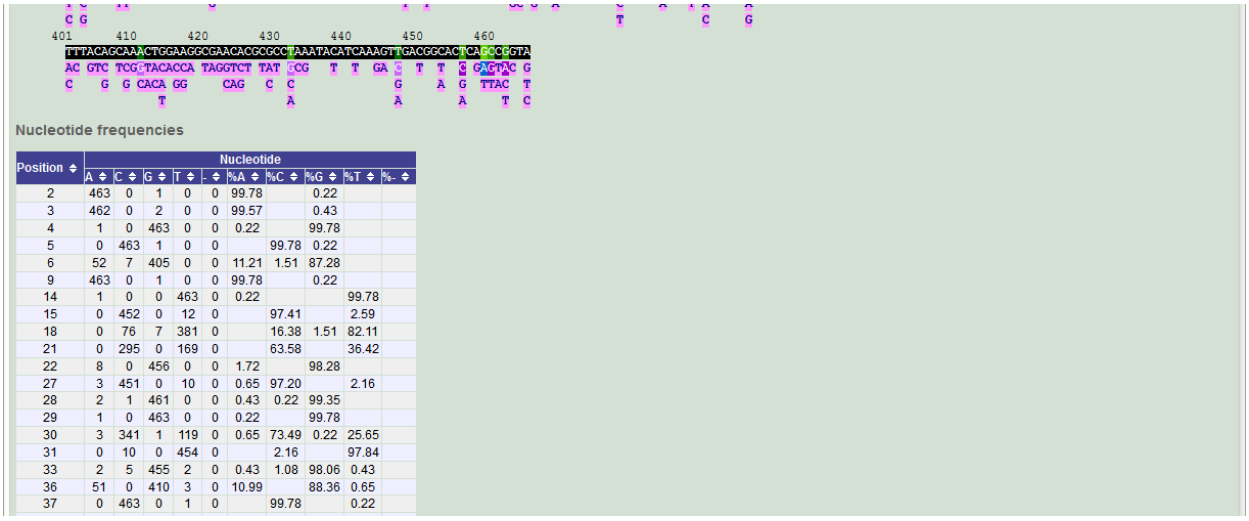


Clicking any of the sequence bases will calculate the exact frequencies of the different nucleotides at that position.



Base	Number of alleles	Percentage of alleles	MLST profiles
T	370	79.74	10619 / 10883 (97.57%)
C	92	19.83	262 / 10883 (2.41%)
A	1 (adk-351)	0.22	1 / 10883 (0.01%)
G	1 (adk-413)	0.22	1 / 10883 (0.01%)

The second part of the page shows a table listing nucleotide frequencies at each of the variable positions.



Nucleotide frequencies

Position	Nucleotide									
	A	C	G	T	-	%A	%C	%G	%T	%-
2	463	0	1	0	0	99.78		0.22		
3	462	0	2	0	0	99.57		0.43		
4	1	0	463	0	0	0.22		99.78		
5	0	463	1	0	0		99.78	0.22		
6	52	7	405	0	0	11.21	1.51	87.28		
9	463	0	1	0	0	99.78		0.22		
14	1	0	0	463	0	0.22			99.78	
15	0	452	0	12	0		97.41		2.59	
18	0	76	7	381	0		16.38	1.51	82.11	
21	0	295	0	169	0		63.58		36.42	
22	8	0	456	0	0	1.72		98.28		
27	3	451	0	10	0	0.65	97.20		2.16	
28	2	1	461	0	0	0.43	0.22	99.35		
29	1	0	463	0	0	0.22		99.78		
30	3	341	1	119	0	0.65	73.49	0.22	25.65	
31	0	10	0	454	0		2.16		97.84	
33	2	5	455	2	0	0.43	1.08	98.06	0.43	
36	51	0	410	3	0	10.99		88.36	0.65	
37	0	463	0	1	0		99.78		0.22	

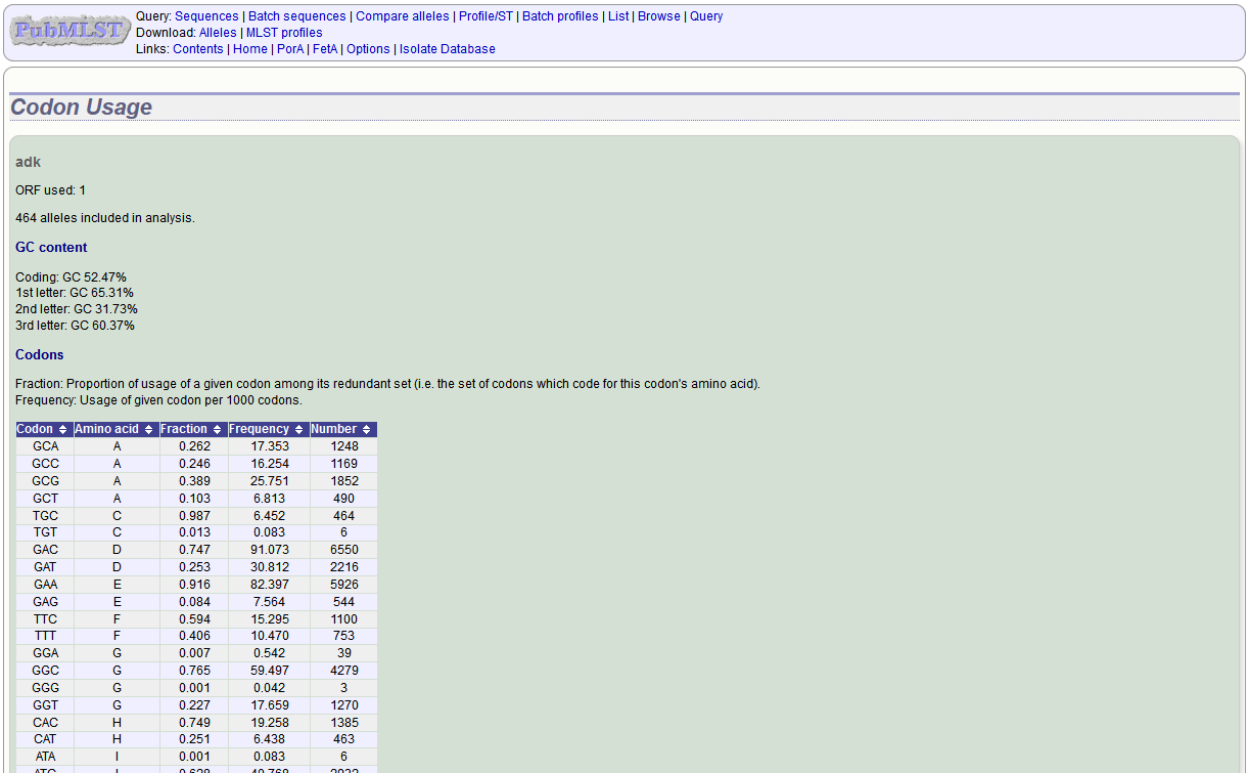
See also:

- *Investigating allele differences*.
- *Polymorphism analysis following isolate query*.

11.1.2 Codon usage

Select the alleles that you would like to include in the analysis. Again, variable length loci are limited to 200 sequences or fewer since these need to be aligned. Click 'Codon'.

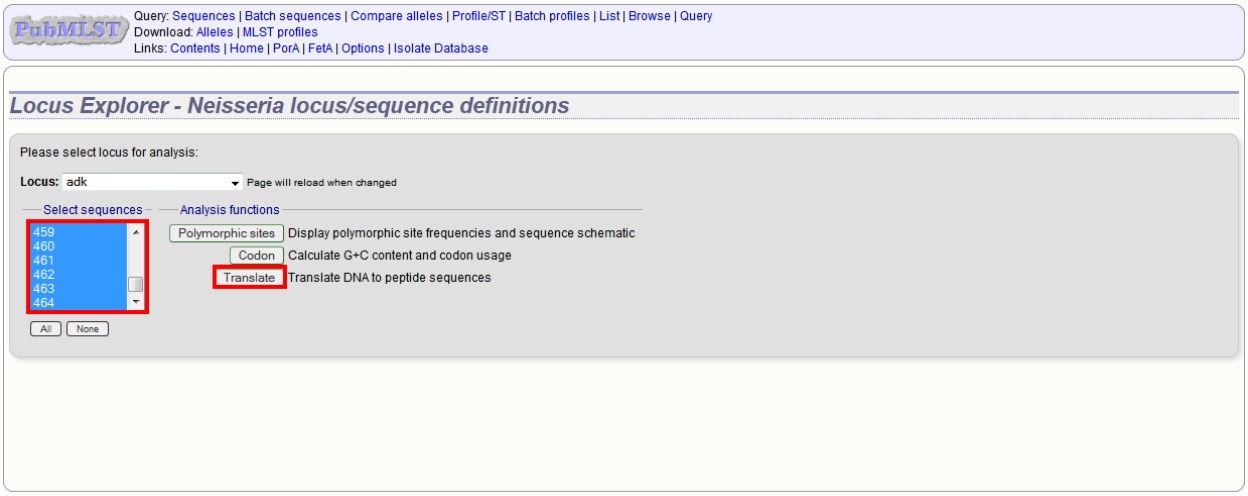
The GC content of the alleles will be determined and a table of the codon frequencies displayed.



11.1.3 Aligned translations

If a DNA coding sequence locus is selected, an aligned translation can be produced.

Select the alleles that you would like to include in the analysis. Again, variable length loci are limited to 200 sequences or fewer since these need to be aligned. Click 'Translate'.



An aligned amino acid sequence will be displayed.

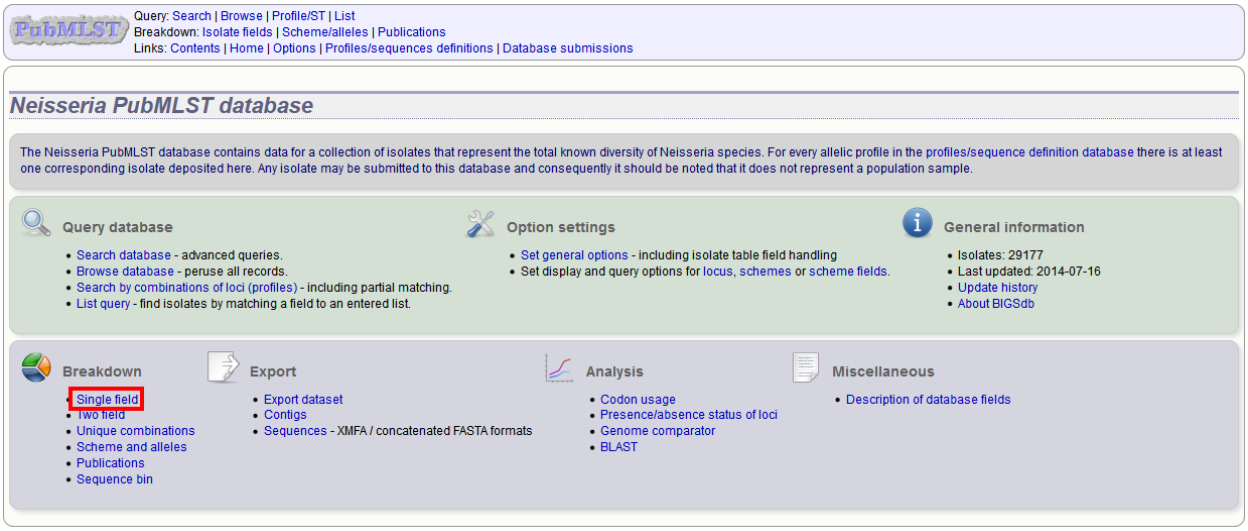
```
433_1     .........S.......................................................................................
434_1     ...............................................................L...............................
435_1     ...............................................................................T.......
436_1     ..................................................................................................
437_1     ..................................................................................................
438_1     ..................................................................................................
439_1     ..................................................................................................
440_1     .......K..........................................................................................
441_1     ..................................................................................................
442_1     ..................................................................................................
443_1     ...................................L..............................................................
444_1     ..................................................................................................
445_1     ..................................................................................................
446_1     ..................................................................................................
447_1     ..................................................................................................
448_1     ..................................................................................................
449_1     ..................................................................................................
450_1     ..................................................................................................
451_1     ..................................................................................................
452_1     .......K.......................................................T..................................
453_1     ..................................................................................................
454_1     ...................................................................................IA.....T.....
455_1     ..................................................................................................
456_1     ..................................................................................................
457_1     ..............................G...................................A...N.........P......IAF....T.....
458_1     ..................................................................................................
459_1     ..................................................................................................
460_1     ...................................................................................S..............
461_1     ..................................................................................................
462_1     ..................................................................................................
463_1     ..................................................................................................
464_1     ...............................................................................I..................
Consensus EAKKIIDEGGLVRDDIIIGMVKERIAQDDCKNGFLFDGFPRTLAQAEAMVEAGVDLDAVVEIDVPDSVIVDRMSGRRVHLASGRTYHVTYNPPKVEGKDD

                    110       120       130       140       150
          ----:----|----:----|----:----|----:----|----:----|----:
1_1       ..................................................
2_1       ..................................................
3_1       ..................................................
4_1       ..................................................
5_1       ..................................................
6_1       ..................................................
7_1       ..................................................
8_1       ..................................................
```

If there appear to be a lot of stop codons in the translation, it is possible that the orf value in the *locus definition* is not set correctly.

11.2 Field breakdown

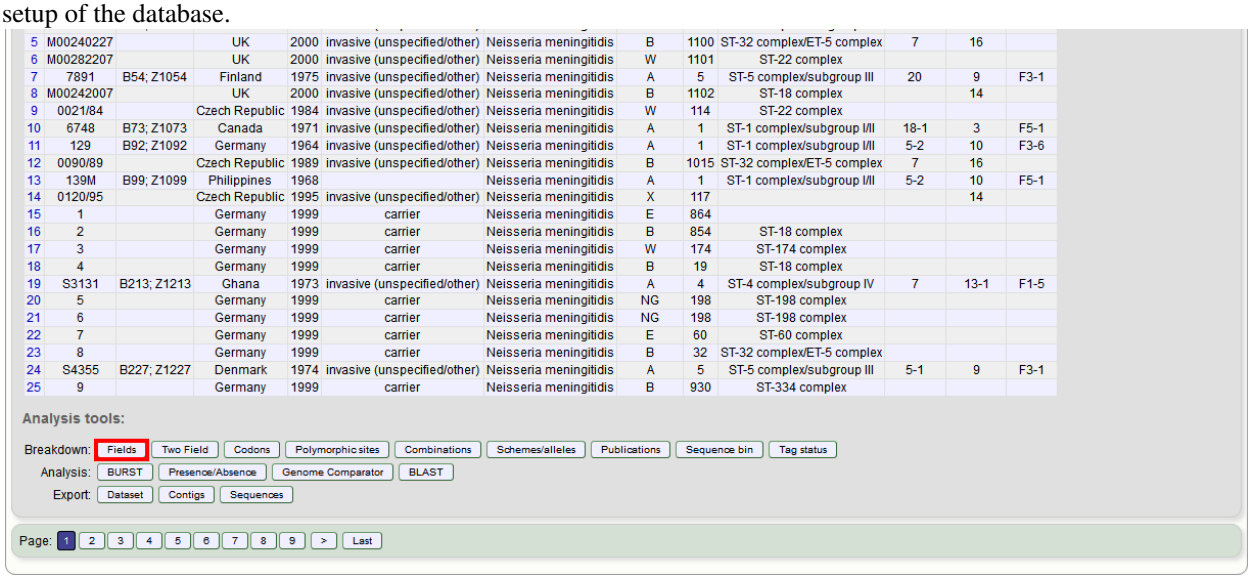
The field breakdown plugin for isolate databases displays the frequency of each value for fields stored in the isolates table. *Allele and scheme field breakdowns* are handled by a different plugin.

The breakdown function can be selected for the whole database by clicking the 'Single field' link in the Breakdown section of the main contents page.



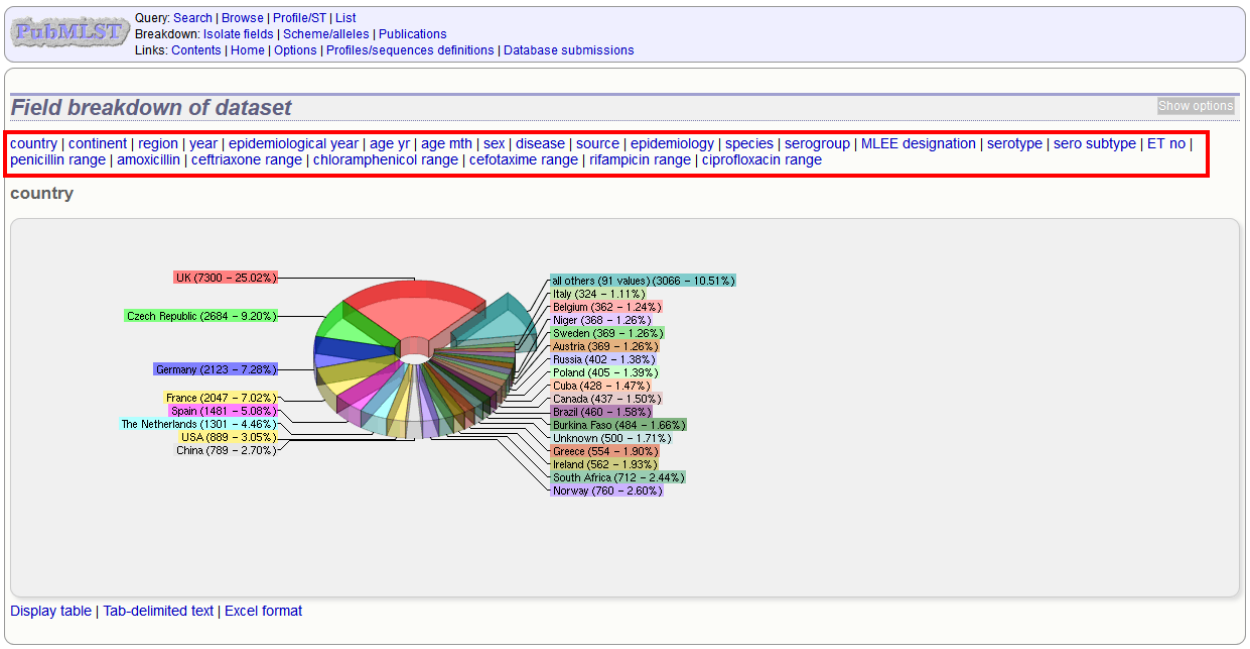
Alternatively, a breakdown can be displayed of the dataset returned from a query by clicking the 'Fields' button in the Breakdown list at the bottom of the results table. Please note that the list of functions here may vary depending on the

setup of the database.

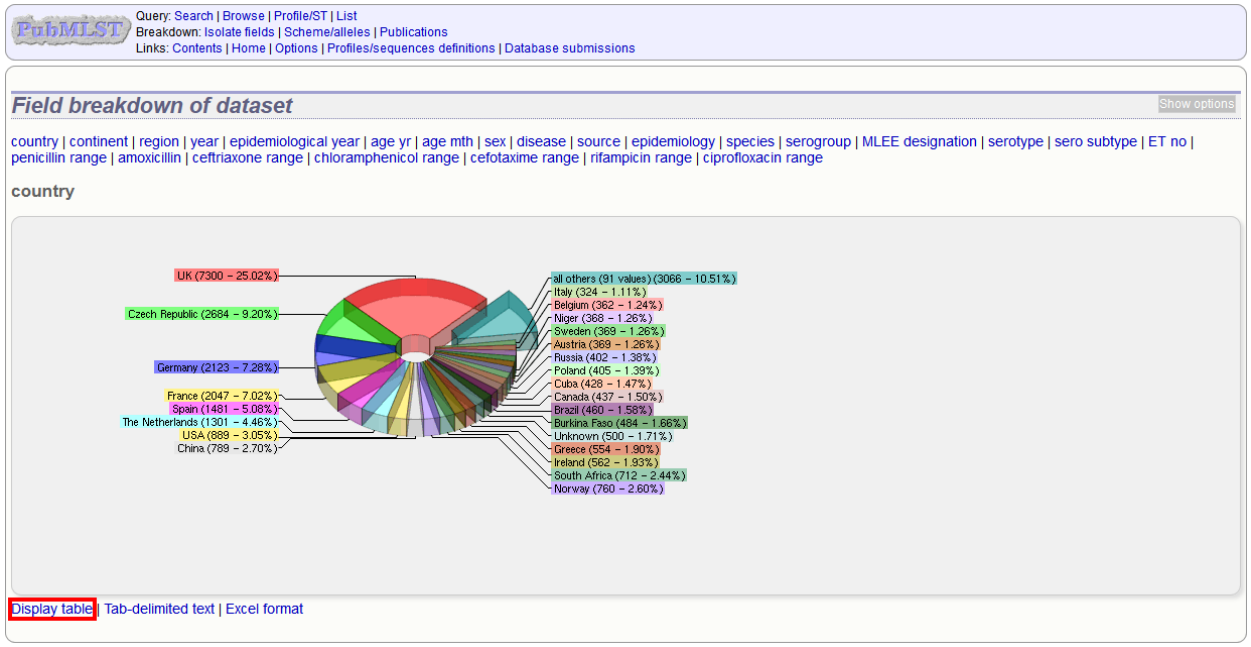


5	M00240227		UK	2000	invasive (unspecified/other)	Neisseria meningitidis	B	1100	ST-32 complex/ET-5 complex	7	16	
6	M00282207		UK	2000	invasive (unspecified/other)	Neisseria meningitidis	W	1101	ST-22 complex			
7	7891	B54; Z1054	Finland	1975	invasive (unspecified/other)	Neisseria meningitidis	A	5	ST-5 complex/subgroup III	20	9	F3-1
8	M00242007		UK	2000	invasive (unspecified/other)	Neisseria meningitidis	B	1102	ST-18 complex		14	
9	0021/84		Czech Republic	1984	invasive (unspecified/other)	Neisseria meningitidis	W	114	ST-22 complex			
10	6748	B73; Z1073	Canada	1971	invasive (unspecified/other)	Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	18-1	3	F5-1
11	129	B92; Z1092	Germany	1964	invasive (unspecified/other)	Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	5-2	10	F3-6
12	0090/89		Czech Republic	1989	invasive (unspecified/other)	Neisseria meningitidis	B	1015	ST-32 complex/ET-5 complex	7	16	
13	139M	B99; Z1099	Philippines	1968		Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	5-2	10	F5-1
14	0120/95		Czech Republic	1995	invasive (unspecified/other)	Neisseria meningitidis	X	117			14	
15	1		Germany	1999	carrier	Neisseria meningitidis	E	864				
16	2		Germany	1999	carrier	Neisseria meningitidis	B	854	ST-18 complex			
17	3		Germany	1999	carrier	Neisseria meningitidis	W	174	ST-174 complex			
18	4		Germany	1999	carrier	Neisseria meningitidis	B	19	ST-18 complex			
19	S3131	B213; Z1213	Ghana	1973	invasive (unspecified/other)	Neisseria meningitidis	A	4	ST-4 complex/subgroup IV	7	13-1	F1-5
20	5		Germany	1999	carrier	Neisseria meningitidis	NG	198	ST-198 complex			
21	6		Germany	1999	carrier	Neisseria meningitidis	NG	198	ST-198 complex			
22	7		Germany	1999	carrier	Neisseria meningitidis	E	60	ST-60 complex			
23	8		Germany	1999	carrier	Neisseria meningitidis	B	32	ST-32 complex/ET-5 complex			
24	S4355	B227; Z1227	Denmark	1974	invasive (unspecified/other)	Neisseria meningitidis	A	5	ST-5 complex/subgroup III	5-1	9	F3-1
25	9		Germany	1999	carrier	Neisseria meningitidis	B	930	ST-334 complex			

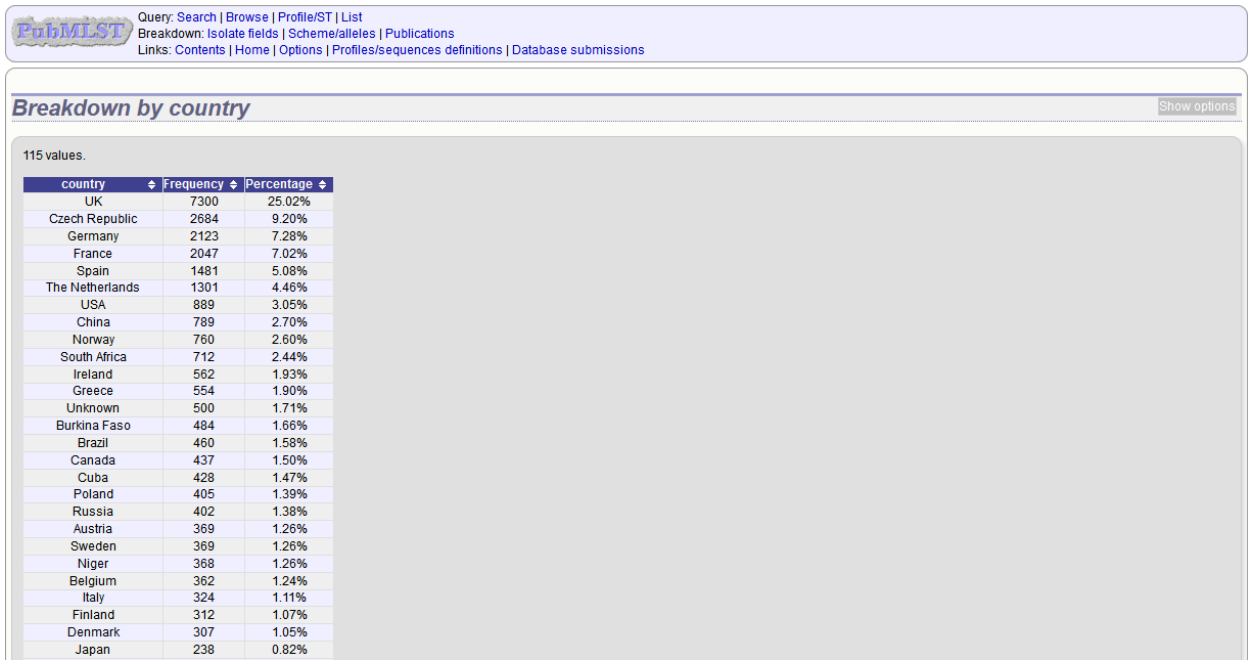
A series of charts will be displayed. Pick the field to display from the list at the top.



The values used to generate the chart can be displayed or extracted by clicking the 'Display table' link at the bottom of the page.

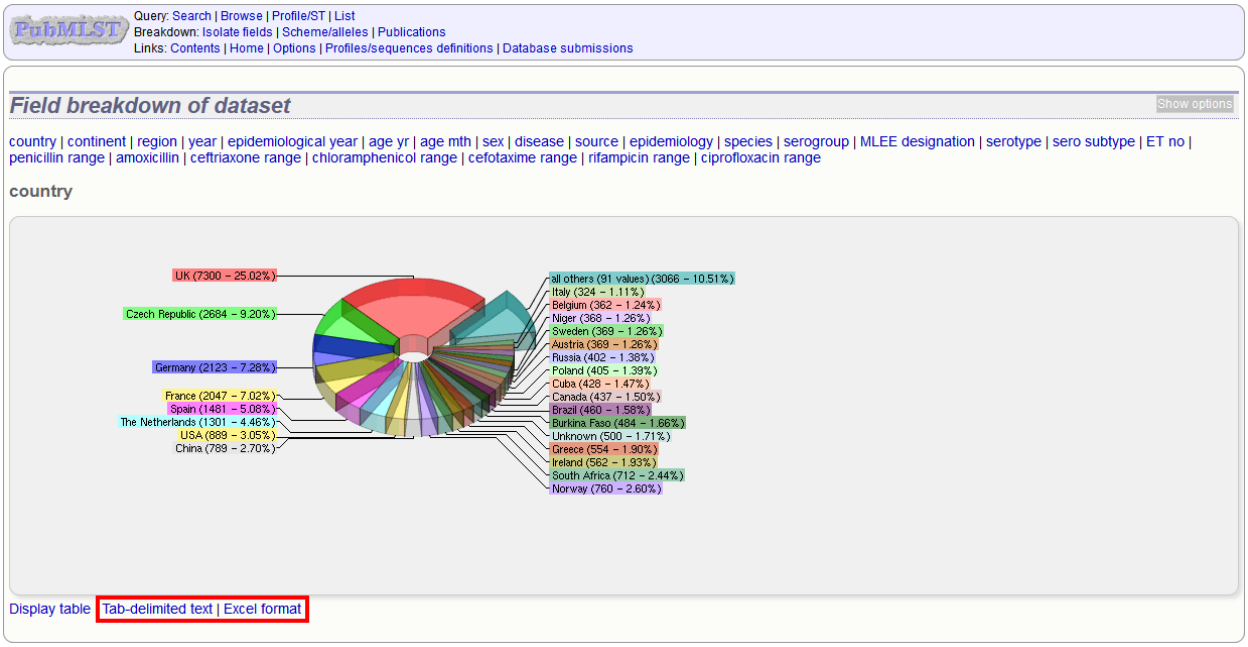


This displays a table that can be ordered by clicking the appropriate header.



country	Frequency	Percentage
UK	7300	25.02%
Czech Republic	2684	9.20%
Germany	2123	7.28%
France	2047	7.02%
Spain	1481	5.08%
The Netherlands	1301	4.46%
USA	889	3.05%
China	789	2.70%
Norway	760	2.60%
South Africa	712	2.44%
Ireland	562	1.93%
Greece	554	1.90%
Unknown	500	1.71%
Burkina Faso	484	1.66%
Brazil	460	1.58%
Canada	437	1.50%
Cuba	428	1.47%
Poland	405	1.39%
Russia	402	1.38%
Austria	369	1.26%
Sweden	369	1.26%
Niger	368	1.26%
Belgium	362	1.24%
Italy	324	1.11%
Finland	312	1.07%
Denmark	307	1.05%
Japan	238	0.82%

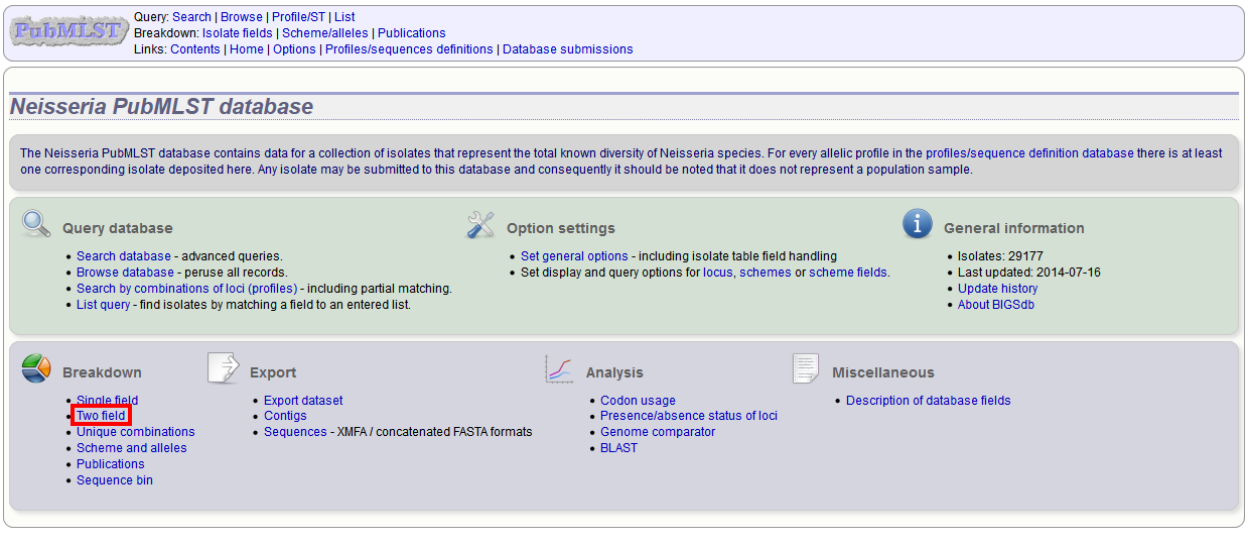
The data can also be downloaded in tab-delimited text or Excel formats by clicking the appropriate links.



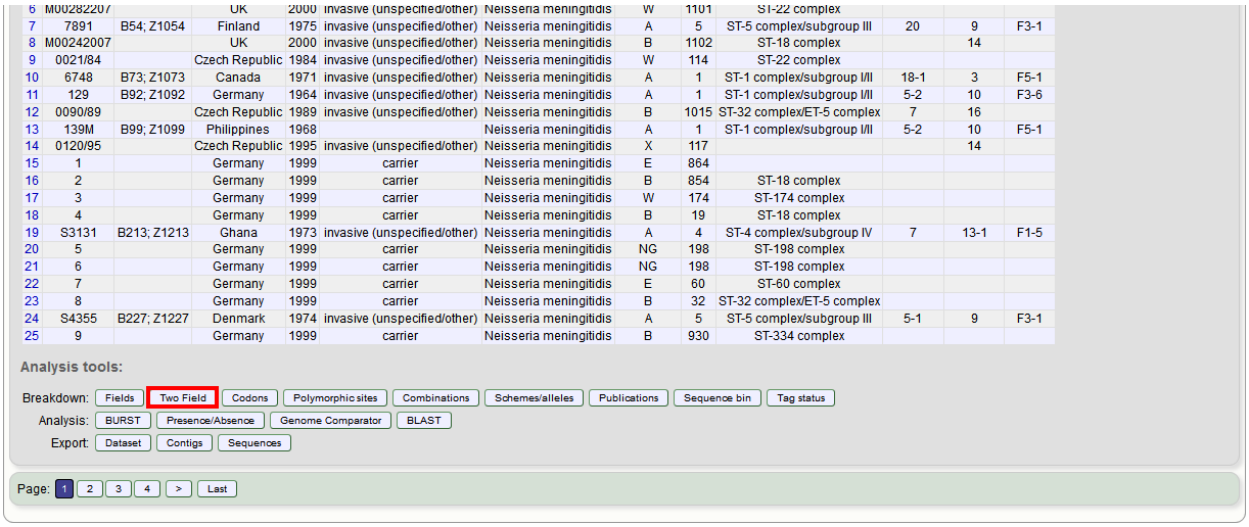
11.3 Two field breakdown

The two field breakdown plugin displays a table breaking down one field against another, e.g. breakdown of serogroup by year.

The analysis can be selected for the whole database by clicking the 'Two field breakdown' link on the main contents page.

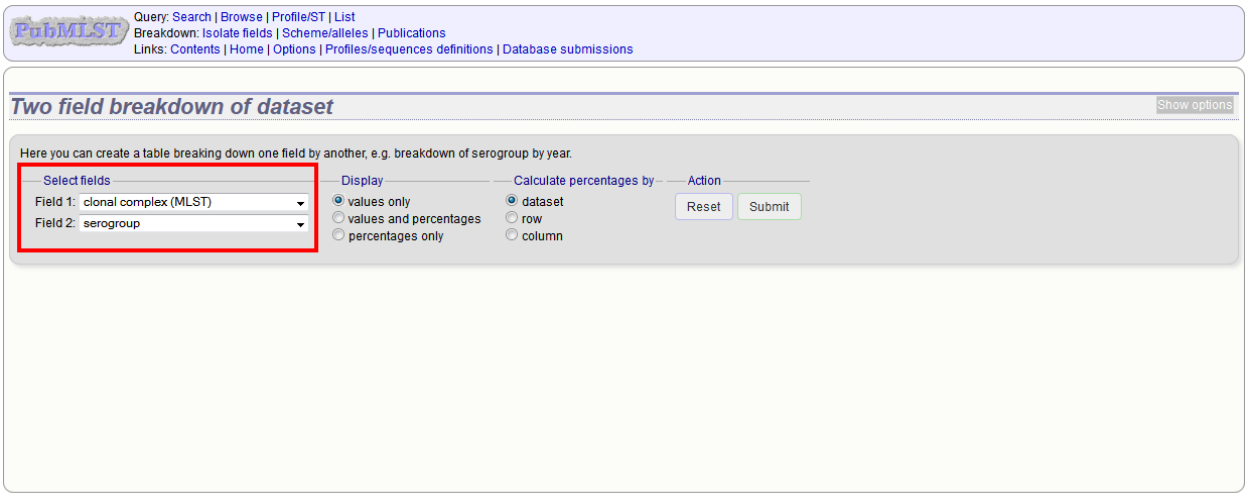


Alternatively, a two field breakdown can be displayed of the dataset returned from a query by clicking the 'Two field' button in the Breakdown list at the bottom of the results table. Please note that the list of functions here may vary depending on the setup of the database.

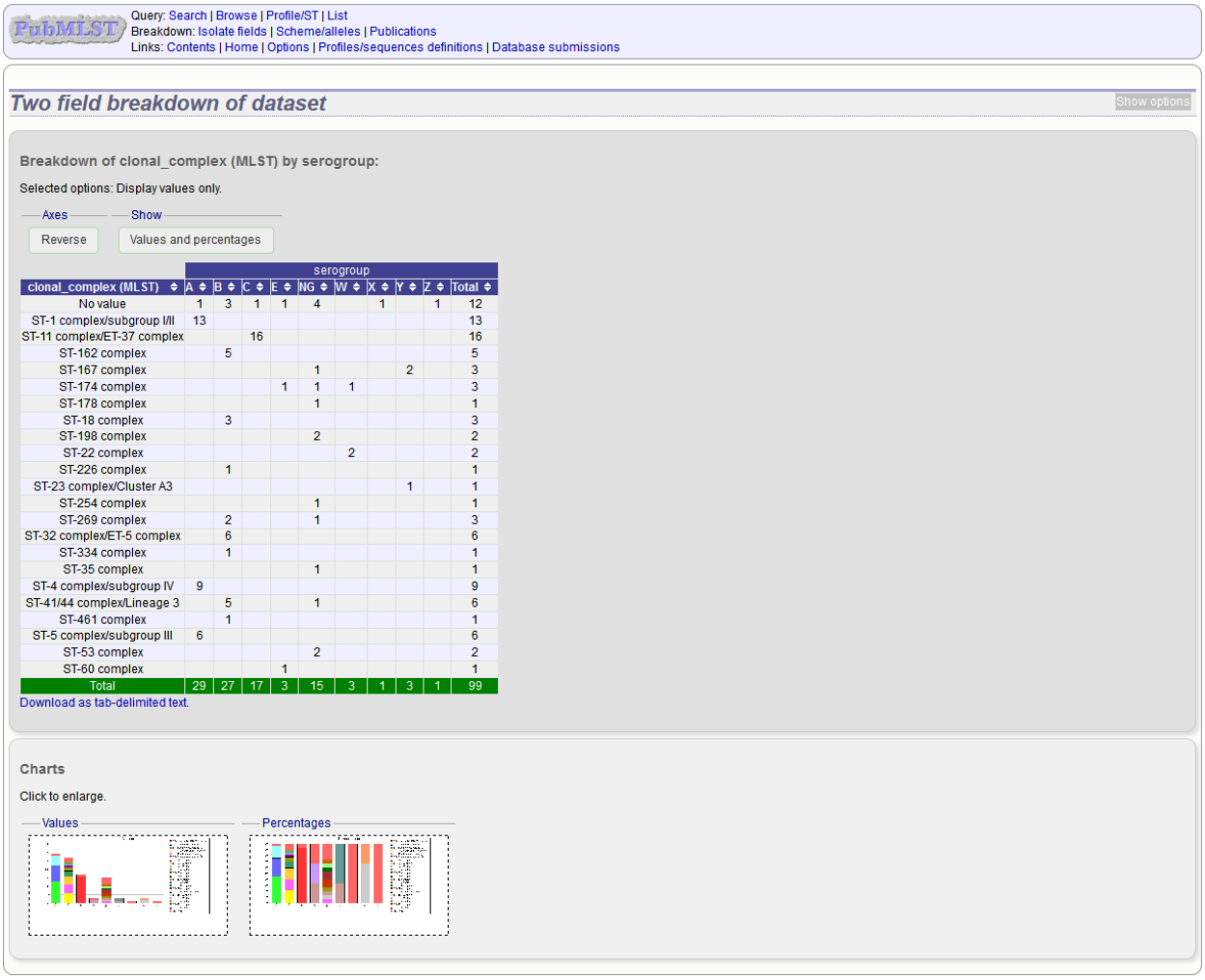


6	M00282207		UK	2000	invasive (unspecified/other)	Neisseria meningitidis	W	1101	ST-22 complex			
7	7891	B54; Z1054	Finland	1975	invasive (unspecified/other)	Neisseria meningitidis	A	5	ST-5 complex/subgroup III	20	9	F3-1
8	M00242007		UK	2000	invasive (unspecified/other)	Neisseria meningitidis	B	1102	ST-18 complex		14	
9	0021/84		Czech Republic	1984	invasive (unspecified/other)	Neisseria meningitidis	W	114	ST-22 complex			
10	6748	B73; Z1073	Canada	1971	invasive (unspecified/other)	Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	18-1	3	F5-1
11	129	B92; Z1092	Germany	1964	invasive (unspecified/other)	Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	5-2	10	F3-6
12	0090/89		Czech Republic	1989	invasive (unspecified/other)	Neisseria meningitidis	B	1015	ST-32 complex/ET-5 complex	7	16	
13	139M	B99; Z1099	Philippines	1968		Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	5-2	10	F5-1
14	0120/95		Czech Republic	1995	invasive (unspecified/other)	Neisseria meningitidis	X	117			14	
15	1		Germany	1999	carrier	Neisseria meningitidis	E	864				
16	2		Germany	1999	carrier	Neisseria meningitidis	B	854	ST-18 complex			
17	3		Germany	1999	carrier	Neisseria meningitidis	W	174	ST-174 complex			
18	4		Germany	1999	carrier	Neisseria meningitidis	B	19	ST-18 complex			
19	S3131	B213; Z1213	Ghana	1973	invasive (unspecified/other)	Neisseria meningitidis	A	4	ST-4 complex/subgroup IV	7	13-1	F1-5
20	5		Germany	1999	carrier	Neisseria meningitidis	NG	198	ST-198 complex			
21	6		Germany	1999	carrier	Neisseria meningitidis	NG	198	ST-198 complex			
22	7		Germany	1999	carrier	Neisseria meningitidis	E	60	ST-60 complex			
23	8		Germany	1999	carrier	Neisseria meningitidis	B	32	ST-32 complex/ET-5 complex			
24	S4355	B227; Z1227	Denmark	1974	invasive (unspecified/other)	Neisseria meningitidis	A	5	ST-5 complex/subgroup III	5-1	9	F3-1
25	9		Germany	1999	carrier	Neisseria meningitidis	B	930	ST-334 complex			

Select the two fields you wish to breakdown and how you would like the values displayed (percentage/absolute values and totaling options).



Click submit. The breakdown will be displayed as a table. Bar charts will also be displayed provided the number of returned values for both fields are less than 30.



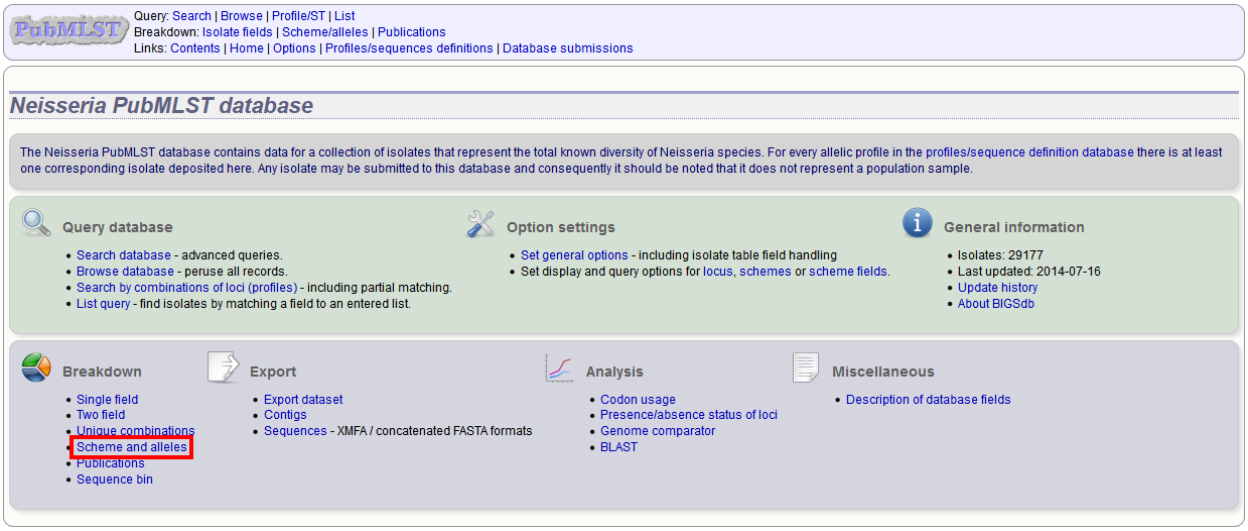
	serogroup									
clonal_complex (MLST)	A	B	C	E	NG	W	X	Y	Z	Total
No value	1	3	1	1	4		1		1	12
ST-1 complex/subgroup I/II	13									13
ST-11 complex/ET-37 complex			16							16
ST-162 complex		5								5
ST-167 complex					1			2		3
ST-174 complex				1	1	1				3
ST-178 complex					1					1
ST-18 complex		3								3
ST-198 complex					2					2
ST-22 complex						2				2
ST-226 complex		1								1
ST-23 complex/Cluster A3								1		1
ST-254 complex					1					1
ST-269 complex		2			1					3
ST-32 complex/ET-5 complex		6								6
ST-334 complex		1								1
ST-35 complex					1					1
ST-4 complex/subgroup IV	9									9
ST-41/44 complex/Lineage 3		5			1					6
ST-461 complex		1								1
ST-5 complex/subgroup III	6									6
ST-53 complex					2					2
ST-60 complex				1						1
Total	29	27	17	3	15	3	1	3	1	99

The table values can be exported in a format suitable for copying in to a spreadsheet by clicking 'Download as tab-delimited text' underneath the table.

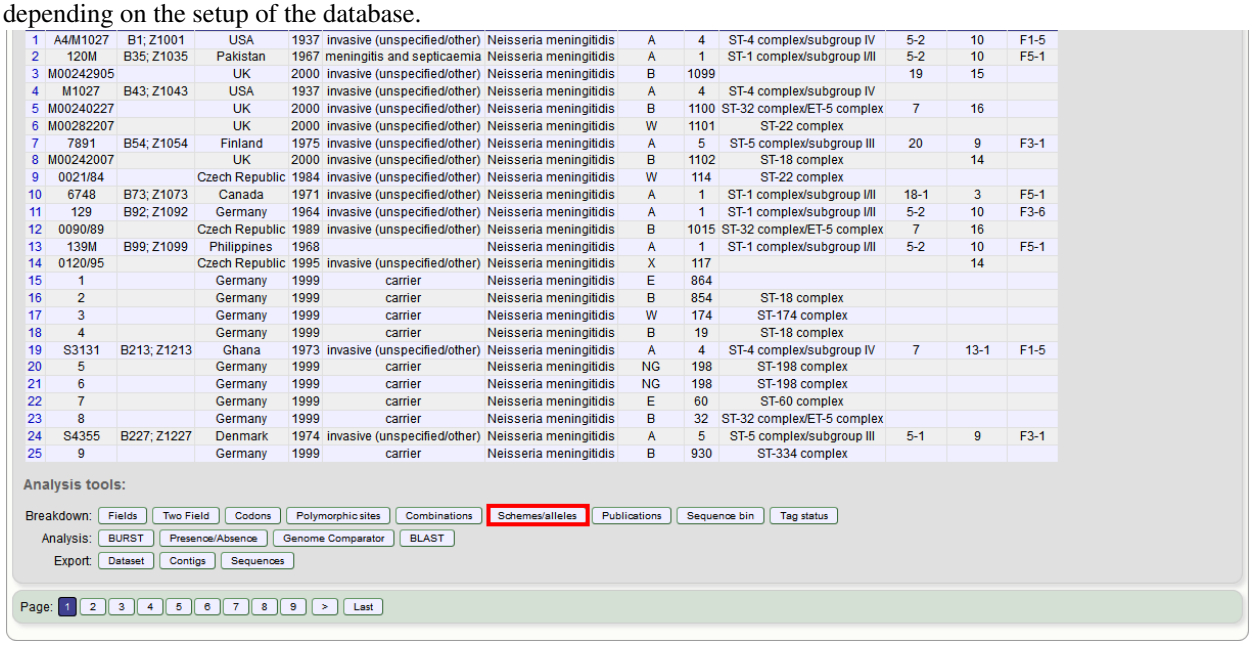
11.4 Scheme and allele breakdown

The scheme and allele breakdown plugin displays the frequency of each allele and scheme field (e.g. ST or clonal complex).

The function can be selected for the whole database by clicking the 'Scheme and allele breakdown' link on the main contents page.



Alternatively, a breakdown can be displayed of the dataset returned from a query by clicking the 'Schemes/alleles' button in the Breakdown list at the bottom of the results table. Please note that the list of functions here may vary depending on the setup of the database.

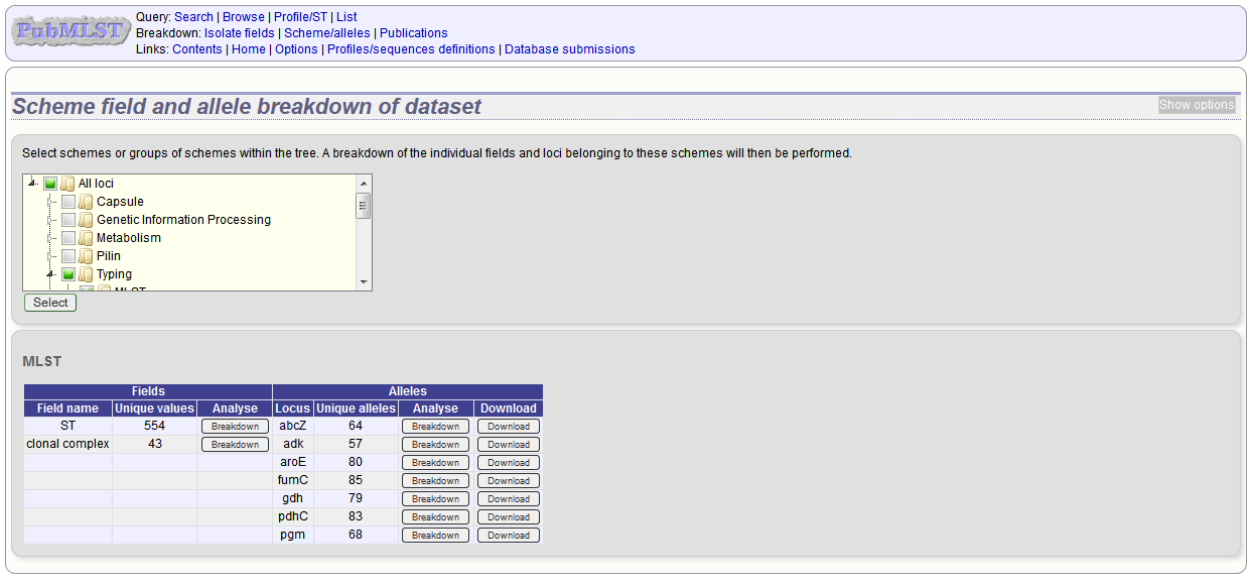


1	A4/M1027	B1; Z1001	USA	1937	invasive (unspecified/other)	Neisseria meningitidis	A	4	ST-4 complex/subgroup IV	5-2	10	F1-5
2	120M	B35; Z1035	Pakistan	1967	meningitis and septicaemia	Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	5-2	10	F5-1
3	M00242905		UK	2000	invasive (unspecified/other)	Neisseria meningitidis	B	1099		19	15	
4	M1027	B43; Z1043	USA	1937	invasive (unspecified/other)	Neisseria meningitidis	A	4	ST-4 complex/subgroup IV			
5	M00240227		UK	2000	invasive (unspecified/other)	Neisseria meningitidis	B	1100	ST-32 complex/ET-5 complex	7	16	
6	M00282207		UK	2000	invasive (unspecified/other)	Neisseria meningitidis	W	1101	ST-22 complex			
7	7891	B54; Z1054	Finland	1975	invasive (unspecified/other)	Neisseria meningitidis	A	5	ST-5 complex/subgroup III	20	9	F3-1
8	M00242007		UK	2000	invasive (unspecified/other)	Neisseria meningitidis	B	1102	ST-18 complex		14	
9	0021/84		Czech Republic	1984	invasive (unspecified/other)	Neisseria meningitidis	W	114	ST-22 complex			
10	6748	B73; Z1073	Canada	1971	invasive (unspecified/other)	Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	18-1	3	F5-1
11	129	B92; Z1092	Germany	1964	invasive (unspecified/other)	Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	5-2	10	F3-6
12	0090/89		Czech Republic	1989	invasive (unspecified/other)	Neisseria meningitidis	B	1015	ST-32 complex/ET-5 complex	7	16	
13	139M	B99; Z1099	Philippines	1968		Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	5-2	10	F5-1
14	0120/95		Czech Republic	1995	invasive (unspecified/other)	Neisseria meningitidis	X	117			14	
15	1		Germany	1999	carrier	Neisseria meningitidis	E	864				
16	2		Germany	1999	carrier	Neisseria meningitidis	B	854	ST-18 complex			
17	3		Germany	1999	carrier	Neisseria meningitidis	W	174	ST-174 complex			
18	4		Germany	1999	carrier	Neisseria meningitidis	B	19	ST-18 complex			
19	S3131	B213; Z1213	Ghana	1973	invasive (unspecified/other)	Neisseria meningitidis	A	4	ST-4 complex/subgroup IV	7	13-1	F1-5
20	5		Germany	1999	carrier	Neisseria meningitidis	NG	198	ST-198 complex			
21	6		Germany	1999	carrier	Neisseria meningitidis	NG	198	ST-198 complex			
22	7		Germany	1999	carrier	Neisseria meningitidis	E	60	ST-60 complex			
23	8		Germany	1999	carrier	Neisseria meningitidis	B	32	ST-32 complex/ET-5 complex			
24	S4355	B227; Z1227	Denmark	1974	invasive (unspecified/other)	Neisseria meningitidis	A	5	ST-5 complex/subgroup III	5-1	9	F3-1
25	9		Germany	1999	carrier	Neisseria meningitidis	B	930	ST-334 complex			

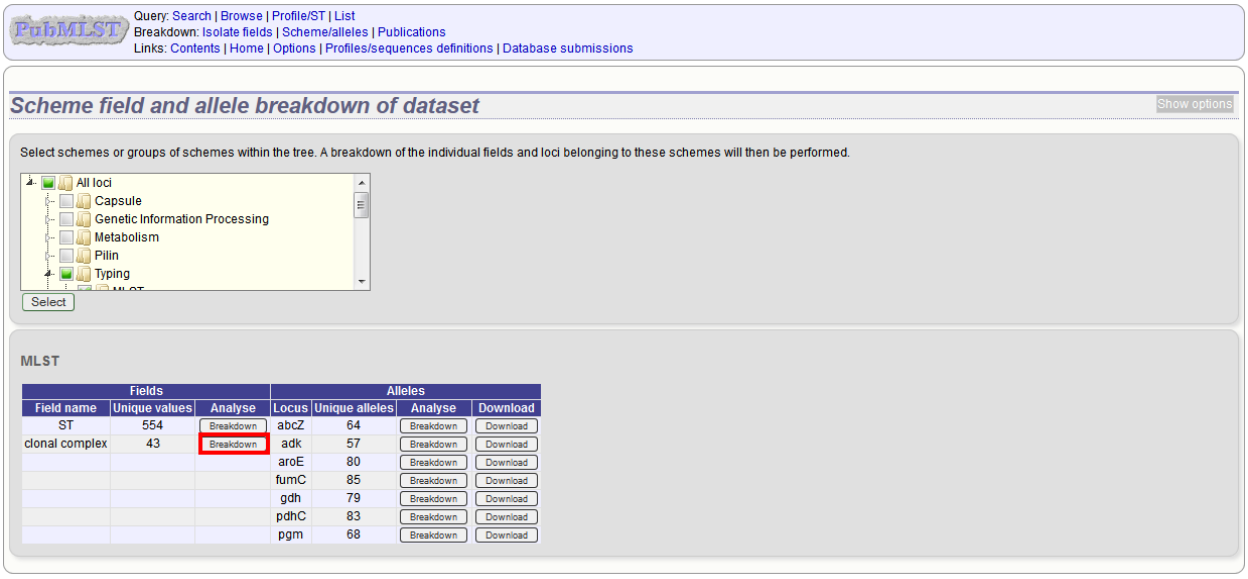
A scheme tree is shown. Select any combination of schemes to analyse.

Click 'Select'.

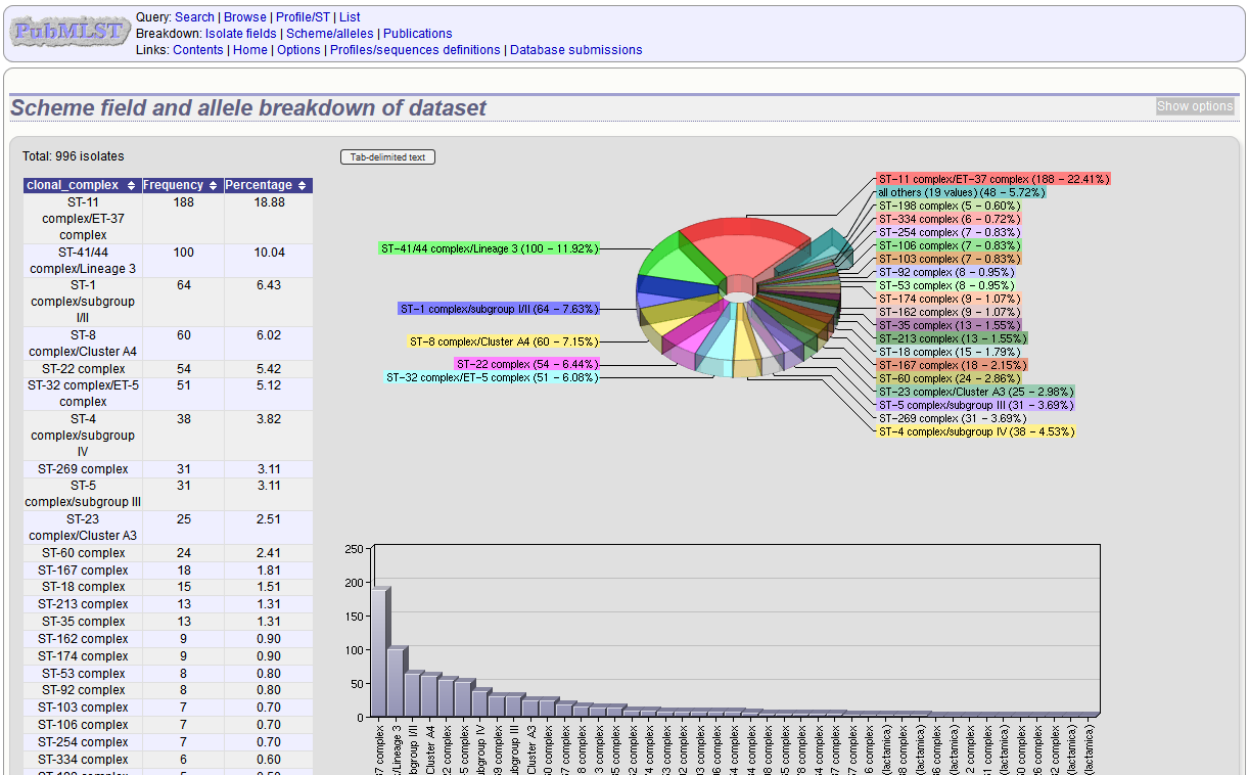
A table showing the number of unique values for each locus and scheme field will be displayed.



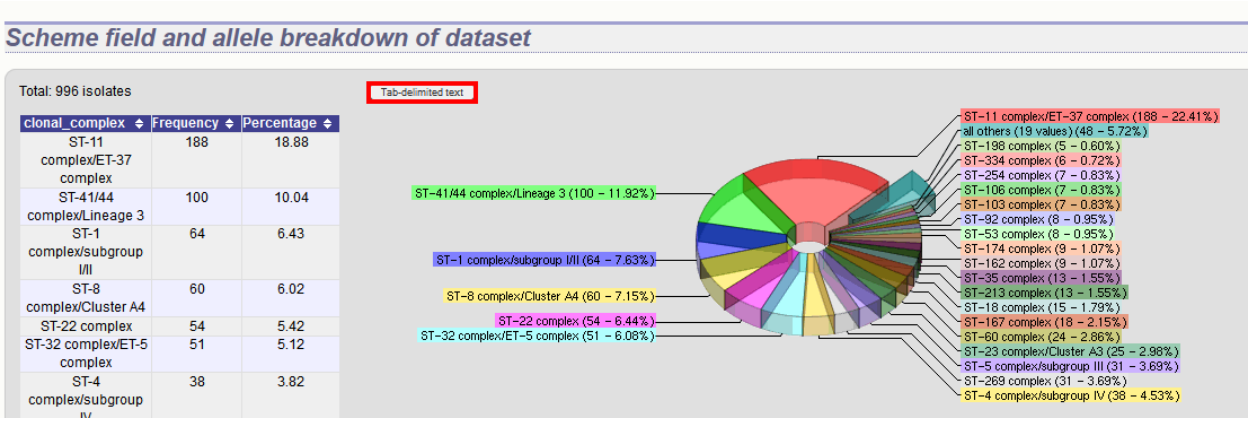
A detailed display of allele or field frequencies can be displayed by clicking the appropriate 'Breakdown' button.



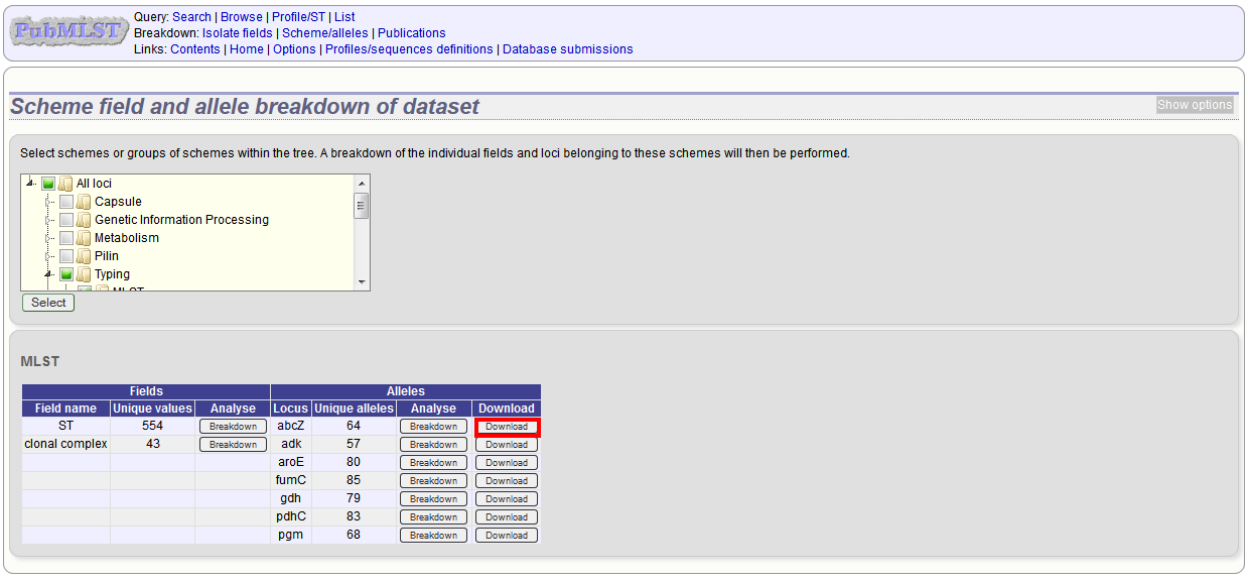
The sorting of the table can be changed by clicking the appropriate header - this toggles between ascending and descending order.



The table values can be exported in a format suitable for copying in to a spreadsheet by clicking the 'Tab-delimited text' button.



You can also download the sequeneces for alleles designated in the dataset for the loci belonging to the scheme by clicking the appropriate 'Download' button in the first results table.



Sequences will be served in FASTA format in order of frequency.

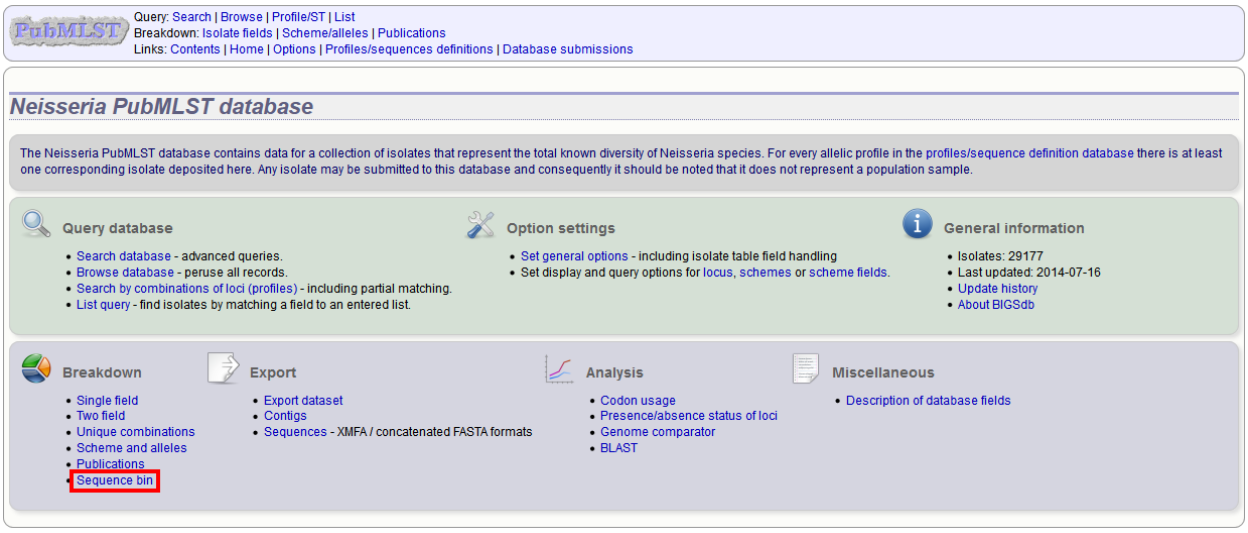
```
>2
TTTGATACCGTTGCCGAAGGTTTGGGTGAAATTCGCGATTTATTGCGCCGTTACCACCGC
GTCGGCCATGAGTTGGAAAACGGTTCGGGTGAGGCTTTGTTGAAAGAACTCAACGAATTA
CAACTTGAAATCGAAGCGAAGGACGGCTGGAAGCTGGATGCGGCAGTCAAGCAGACTTTG
GGGGAACTCGGTTTGCCGGAAAACGAAAAAATCGGCAACCTTTCCGGCGGTCAGAAAAAG
CGTGTCGCCTTGGCGCAGGCTTGGGTGCAGAAGCCCGACGTATTGCTGCTGGACGAACCG
ACCAACCATTTGGATATCGACGCGATTATTTGGCTGGAAAATCTGCTCAAAGCGTTTGAA
GGCAGCTTGGTTGTGATTACCCACGACCGCCGTTTTTTGGACAATATCGCCACGCGGATT
GTCGAACTCGATC
>1
TTTGATACTGTTGCCGAAGGTTTGGGCGAAATTCGCGATTTATTGCGCCGTTATCATCAT
GTCAGCCATGAGTTGGAAAATGGTTCGAGTGAGGCCTTATTGAAAGAGCTCAACGAATTG
CAACTTGAGATCGAAGCGAAGGACGGCTGGAAGTTGGATGCGGCGGTGAAGCAGACTTTG
GGCGAACTCGGTTTGCCGGAAAACGAAAAAATCGGCAACCTCTCCGGCGGTCAGAAAAAG
CGCGTCGCCTTGGCGCAGGCTTGGGTGCAGAAGCCCGACGTATTGCTGCTCGATGAACCG
ACCAACCATTTGGACATCGACGCGATTATTTGGTTGGAAAACCTGCTCAAAGCGTTTGAA
GGCAGCCTGGTTGTGATTACCCACGACCGCCGTTTTTTGGACAATATCGCCACGCGGATT
GTCGAACTCGATC
>4
```

```
TTTGATACCGTTGCCGAAGGTTTGGGCGAAATTCGTGATTTATTGCGCCGTTATCATCAT
GTCAGCCATGAGTTGGAAAATGGTTCGAGTGAGGCTTTGTTGAAAGAACTCAACGAATTG
CAACTTGAAATCGAAGCGAAGGACGGCTGGAAACTGGATGCGGCAGTCAAGCAGACTTTG
GGGGAACTCGGTTTGCCGGAAAATGAAAAAATCGGCAACCTTTCCGGCGGTCAGAAAAAG
CGCGTCGCCTTGGCTCAGGCTTGGGTGCAAAAGCCCGACGTATTGCTGCTGGACGAGCCG
ACCAACCATTTGGATATCGACGCGATTATTTGGCTGGAAAATCTGCTCAAAGCGTTTGAA
GGCAGCTTGGTTGTGATTACCCACGACCGCCGTTTTTTGGACAATATCGCCACGCGGATT
GTCGAACTCGATC
```

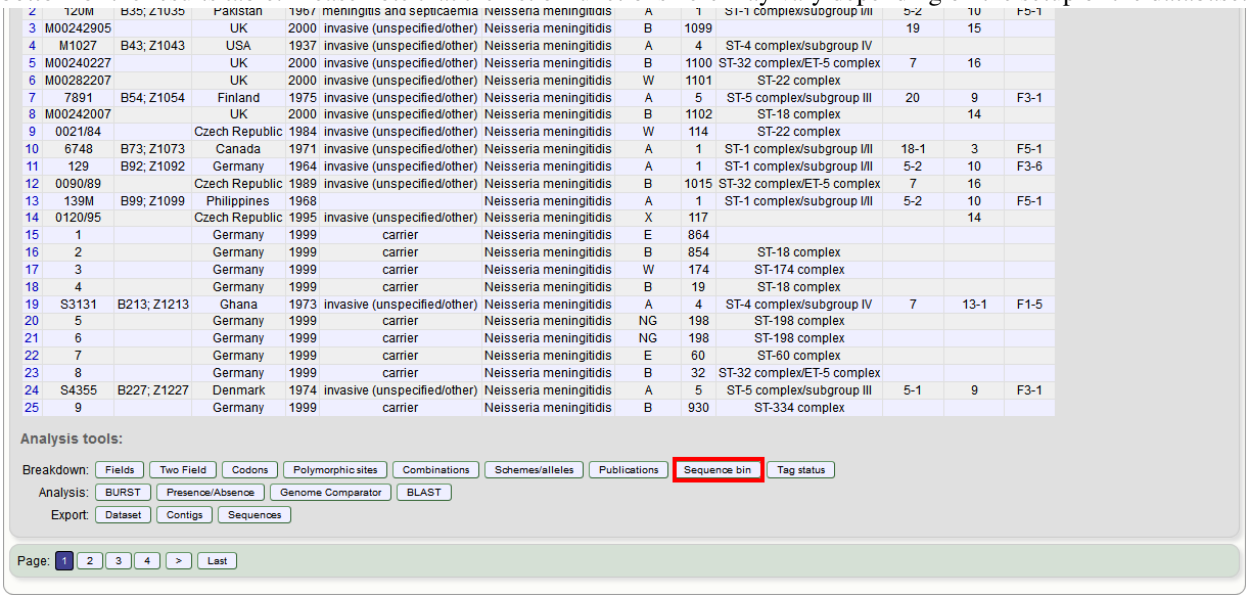
11.5 Sequence bin breakdown

The sequence bin breakdown plugin calculates statistics based on the number and length of contigs in the sequence bin as well as the number of loci tagged for an isolate record.

The function can be selected by clicking the 'Sequence bin' link on the Breakdown section of the main contents page.

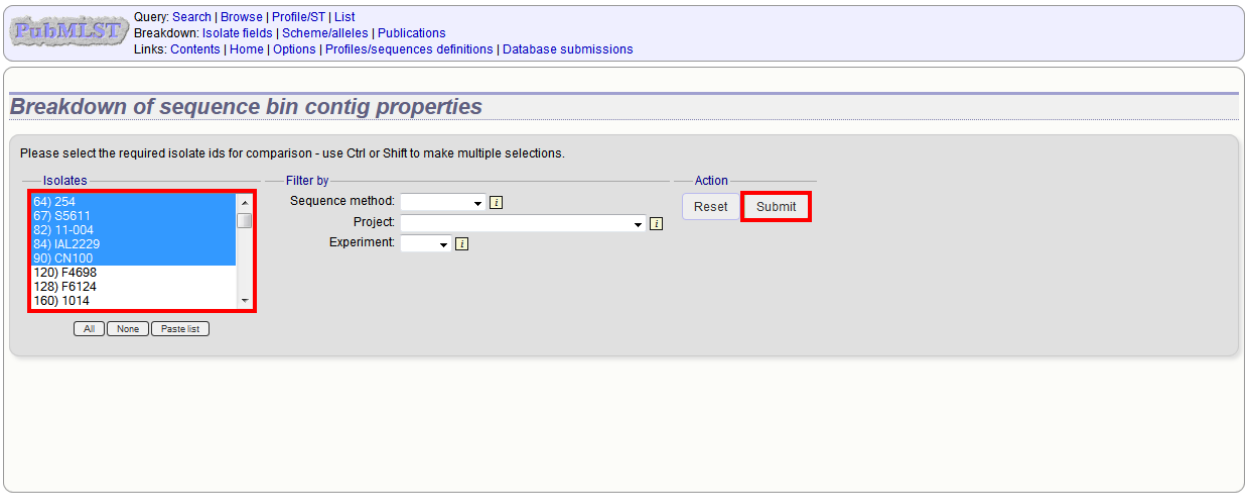


Alternatively, it can be accessed following a query by clicking the 'Sequence bin' button in the Breakdown list at the bottom of the results table. Please note that the list of functions here may vary depending on the setup of the database.



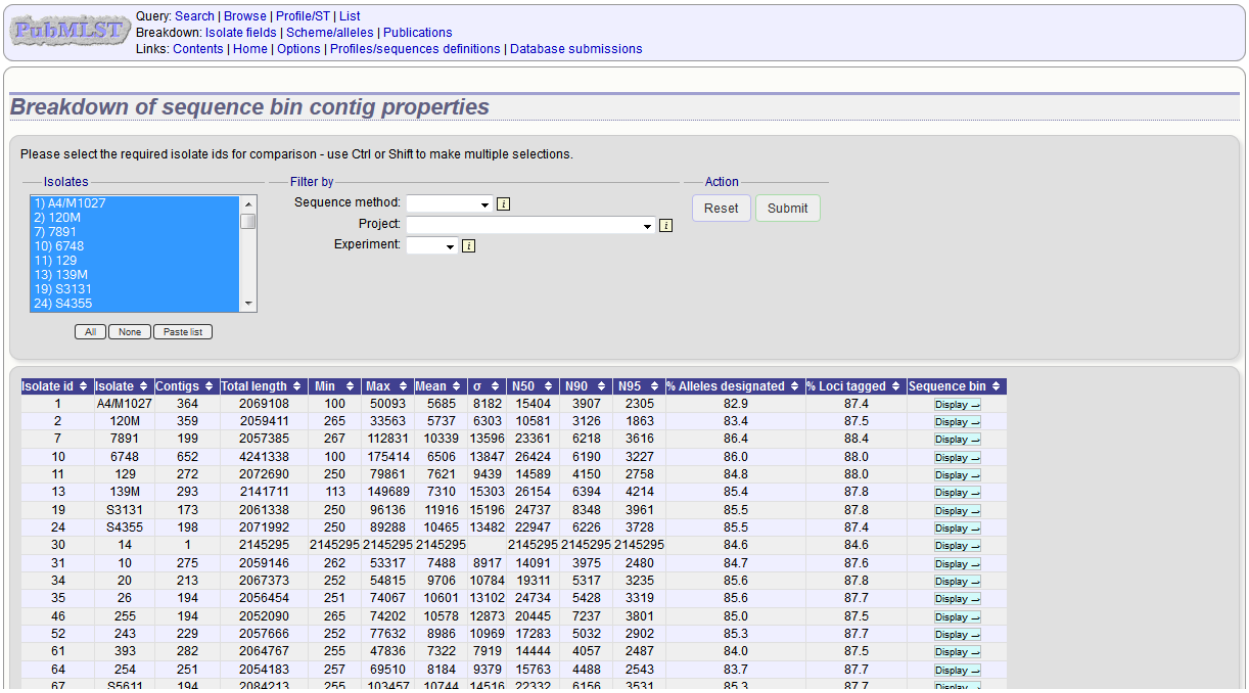
2	120M	B35; Z1035	Pakistan	1967	meningitis and septicaemia	Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	5-2	10	F5-1
3	M00242905		UK	2000	invasive (unspecified/other)	Neisseria meningitidis	B	1099		19	15	
4	M1027	B43; Z1043	USA	1937	invasive (unspecified/other)	Neisseria meningitidis	A	4	ST-4 complex/subgroup IV			
5	M00240227		UK	2000	invasive (unspecified/other)	Neisseria meningitidis	B	1100	ST-32 complex/ET-5 complex	7	16	
6	M00282207		UK	2000	invasive (unspecified/other)	Neisseria meningitidis	W	1101	ST-22 complex			
7	7891	B54; Z1054	Finland	1975	invasive (unspecified/other)	Neisseria meningitidis	A	5	ST-5 complex/subgroup III	20	9	F3-1
8	M00242007		UK	2000	invasive (unspecified/other)	Neisseria meningitidis	B	1102	ST-18 complex		14	
9	0021/84		Czech Republic	1984	invasive (unspecified/other)	Neisseria meningitidis	W	114	ST-22 complex			
10	6748	B73; Z1073	Canada	1971	invasive (unspecified/other)	Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	18-1	3	F5-1
11	129	B92; Z1092	Germany	1964	invasive (unspecified/other)	Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	5-2	10	F3-6
12	0090/89		Czech Republic	1989	invasive (unspecified/other)	Neisseria meningitidis	B	1015	ST-32 complex/ET-5 complex	7	16	
13	139M	B99; Z1099	Philippines	1968		Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	5-2	10	F5-1
14	0120/95		Czech Republic	1995	invasive (unspecified/other)	Neisseria meningitidis	X	117			14	
15	1		Germany	1999	carrier	Neisseria meningitidis	E	864				
16	2		Germany	1999	carrier	Neisseria meningitidis	B	854	ST-18 complex			
17	3		Germany	1999	carrier	Neisseria meningitidis	W	174	ST-174 complex			
18	4		Germany	1999	carrier	Neisseria meningitidis	B	19	ST-18 complex			
19	S3131	B213; Z1213	Ghana	1973	invasive (unspecified/other)	Neisseria meningitidis	A	4	ST-4 complex/subgroup IV	7	13-1	F1-5
20	5		Germany	1999	carrier	Neisseria meningitidis	NG	198	ST-198 complex			
21	6		Germany	1999	carrier	Neisseria meningitidis	NG	198	ST-198 complex			
22	7		Germany	1999	carrier	Neisseria meningitidis	E	60	ST-60 complex			
23	8		Germany	1999	carrier	Neisseria meningitidis	B	32	ST-32 complex/ET-5 complex			
24	S4355	B227; Z1227	Denmark	1974	invasive (unspecified/other)	Neisseria meningitidis	A	5	ST-5 complex/subgroup III	5-1	9	F3-1
25	9		Germany	1999	carrier	Neisseria meningitidis	B	930	ST-334 complex			

Select the isolate records to analyse - these will be pre-selected if you accessed the plugin following a query. Click submit.



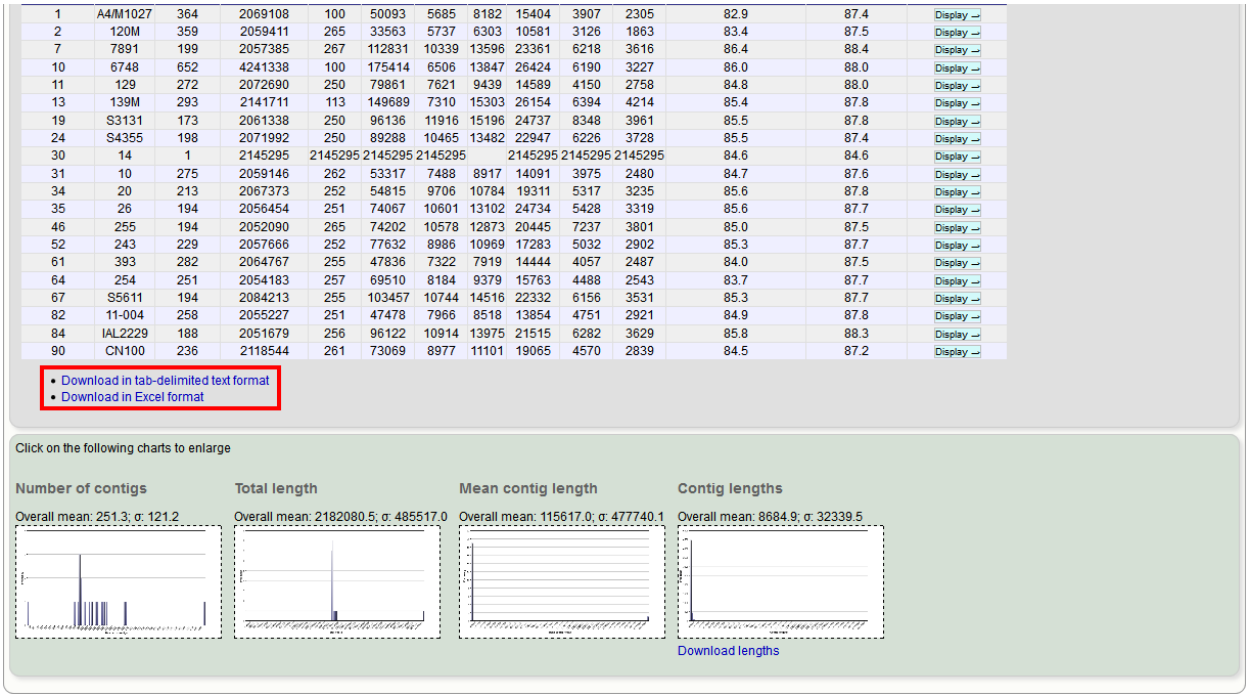
If there are fewer than 100 isolates selected, the table will be generated immediately. Otherwise it will be submitted to the job queue.

A table of sequence bin stats will be generated.



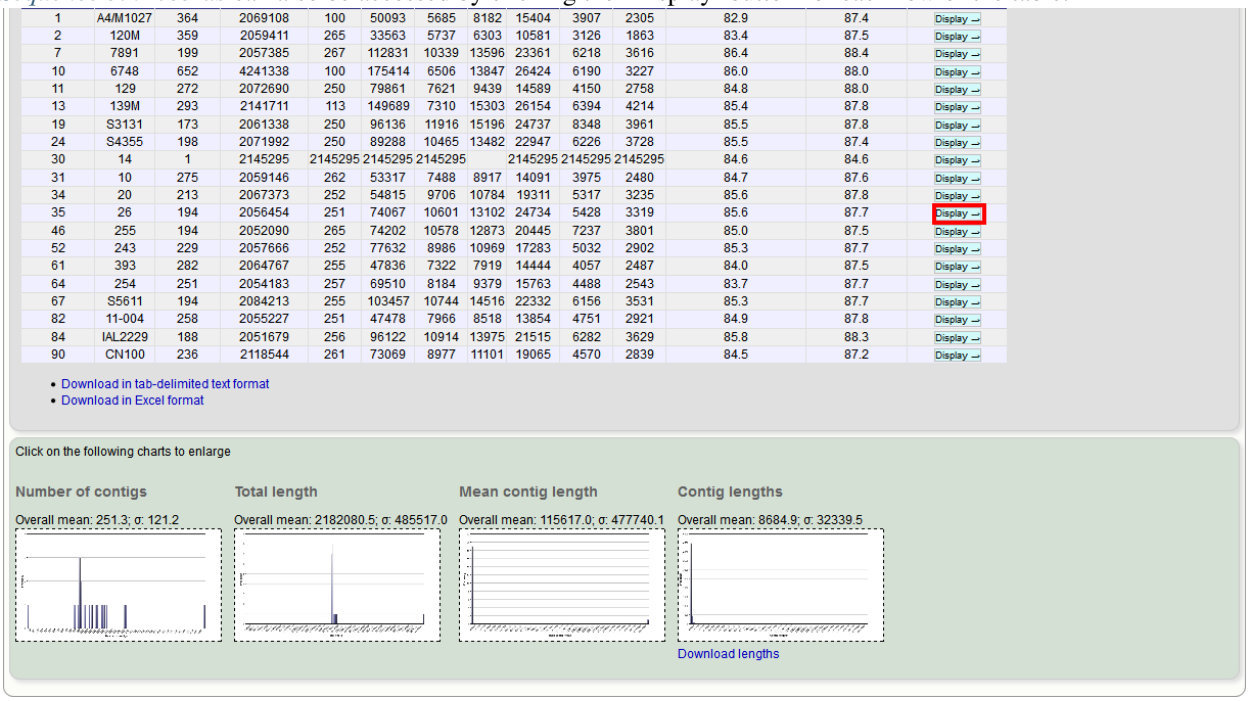
Isolate id	Isolate	Contigs	Total length	Min	Max	Mean	σ	N50	N90	N95	% Alleles designated	% Loci tagged	Sequence bin
1	A4/M1027	364	2069108	100	50093	5685	8182	15404	3907	2305	82.9	87.4	Display
2	120M	359	2059411	265	33563	5737	6303	10581	3126	1863	83.4	87.5	Display
7	7891	199	2057385	267	112831	10339	13596	23361	6218	3616	86.4	88.4	Display
10	6748	652	4241338	100	175414	6506	13847	26424	6190	3227	86.0	88.0	Display
11	129	272	2072690	250	79861	7621	9439	14589	4150	2758	84.8	88.0	Display
13	139M	293	2141711	113	149689	7310	15303	26154	6394	4214	85.4	87.8	Display
19	S3131	173	2061338	250	96136	11916	15196	24737	8348	3961	85.5	87.8	Display
24	S4355	198	2071992	250	89288	10465	13482	22947	6226	3728	85.5	87.4	Display
30	14	1	2145295	2145295	2145295	2145295		2145295	2145295	2145295	84.6	84.6	Display
31	10	275	2059146	262	53317	7488	8917	14091	3975	2480	84.7	87.6	Display
34	20	213	2067373	252	54815	9706	10784	19311	5317	3235	85.6	87.8	Display
35	26	194	2056454	251	74067	10601	13102	24734	5428	3319	85.6	87.7	Display
46	255	194	2052090	265	74202	10578	12873	20445	7237	3801	85.0	87.5	Display
52	243	229	2057666	252	77632	8986	10969	17283	5032	2902	85.3	87.7	Display
61	393	282	2064767	255	47836	7322	7919	14444	4057	2487	84.0	87.5	Display
64	254	251	2054183	257	69510	8184	9379	15763	4488	2543	83.7	87.7	Display
67	S5611	194	2084213	255	103457	10744	14516	22332	6156	3531	85.3	87.7	Display

You can choose to export the data in tab-delimited text or Excel formats by clicking the appropriate link at the bottom of the table.



1	A4/M1027	364	2069108	100	50093	5685	8182	15404	3907	2305	82.9	87.4	Display
2	120M	359	2059411	265	33563	5737	6303	10581	3126	1863	83.4	87.5	Display
7	7891	199	2057385	267	112831	10339	13596	23361	6218	3616	86.4	88.4	Display
10	6748	652	4241338	100	175414	6506	13847	26424	6190	3227	86.0	88.0	Display
11	129	272	2072690	250	79861	7621	9439	14589	4150	2758	84.8	88.0	Display
13	139M	293	2141711	113	149689	7310	15303	26154	6394	4214	85.4	87.8	Display
19	S3131	173	2061338	250	96136	11916	15196	24737	8348	3961	85.5	87.8	Display
24	S4355	198	2071992	250	89288	10465	13482	22947	6226	3728	85.5	87.4	Display
30	14	1	2145295	2145295	2145295	2145295		2145295	2145295	2145295	84.6	84.6	Display
31	10	275	2059146	262	53317	7488	8917	14091	3975	2480	84.7	87.6	Display
34	20	213	2067373	252	54815	9706	10784	19311	5317	3235	85.6	87.8	Display
35	26	194	2056454	251	74067	10601	13102	24734	5428	3319	85.6	87.7	Display
46	255	194	2052090	265	74202	10578	12873	20445	7237	3801	85.0	87.5	Display
52	243	229	2057666	252	77632	8986	10969	17283	5032	2902	85.3	87.7	Display
61	393	282	2064767	255	47836	7322	7919	14444	4057	2487	84.0	87.5	Display
64	254	251	2054183	257	69510	8184	9379	15763	4488	2543	83.7	87.7	Display
67	S5611	194	2084213	255	103457	10744	14516	22332	6156	3531	85.3	87.7	Display
82	11-004	258	2055227	251	47478	7966	8518	13854	4751	2921	84.9	87.8	Display
84	IAL2229	188	2051679	256	96122	10914	13975	21515	6282	3629	85.8	88.3	Display
90	CN100	236	2118544	261	73069	8977	11101	19065	4570	2839	84.5	87.2	Display

Sequence bin records can also be accessed by clicking the 'Display' button for each row of the table.



1	A4/M1027	364	2069108	100	50093	5685	8182	15404	3907	2305	82.9	87.4	Display
2	120M	359	2059411	265	33563	5737	6303	10581	3126	1863	83.4	87.5	Display
7	7891	199	2057385	267	112831	10339	13596	23361	6218	3616	86.4	88.4	Display
10	6748	652	4241338	100	175414	6506	13847	26424	6190	3227	86.0	88.0	Display
11	129	272	2072690	250	79861	7621	9439	14589	4150	2758	84.8	88.0	Display
13	139M	293	2141711	113	149689	7310	15303	26154	6394	4214	85.4	87.8	Display
19	S3131	173	2061338	250	96136	11916	15196	24737	8348	3961	85.5	87.8	Display
24	S4355	198	2071992	250	89288	10465	13482	22947	6226	3728	85.5	87.4	Display
30	14	1	2145295	2145295	2145295	2145295		2145295	2145295	2145295	84.6	84.6	Display
31	10	275	2059146	262	53317	7488	8917	14091	3975	2480	84.7	87.6	Display
34	20	213	2067373	252	54815	9706	10784	19311	5317	3235	85.6	87.8	Display
35	26	194	2056454	251	74067	10601	13102	24734	5428	3319	85.6	87.7	Display
46	255	194	2052090	265	74202	10578	12873	20445	7237	3801	85.0	87.5	Display
52	243	229	2057666	252	77632	8986	10969	17283	5032	2902	85.3	87.7	Display
61	393	282	2064767	255	47836	7322	7919	14444	4057	2487	84.0	87.5	Display
64	254	251	2054183	257	69510	8184	9379	15763	4488	2543	83.7	87.7	Display
67	S5611	194	2084213	255	103457	10744	14516	22332	6156	3531	85.3	87.7	Display
82	11-004	258	2055227	251	47478	7966	8518	13854	4751	2921	84.9	87.8	Display
84	IAL2229	188	2051679	256	96122	10914	13975	21515	6282	3629	85.8	88.3	Display
90	CN100	236	2118544	261	73069	8977	11101	19065	4570	2839	84.5	87.2	Display

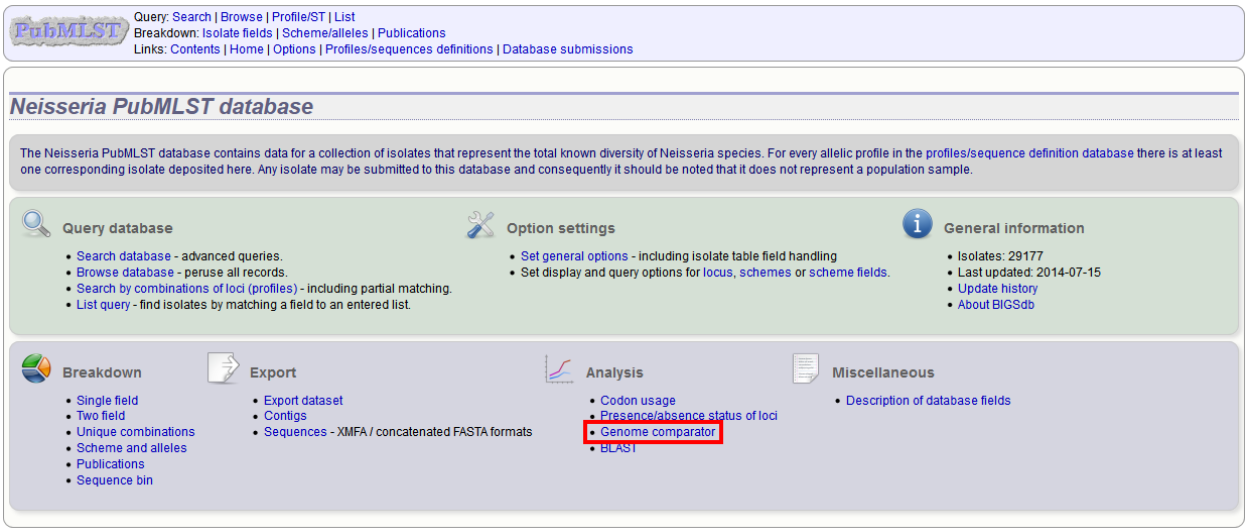
11.6 Genome comparator

Genome Comparator is an optional plugin that can be enabled for specific databases. It is used to compare whole genome data of isolates within the database using either the database defined loci or the coding sequences of an annotated genome as the comparator.

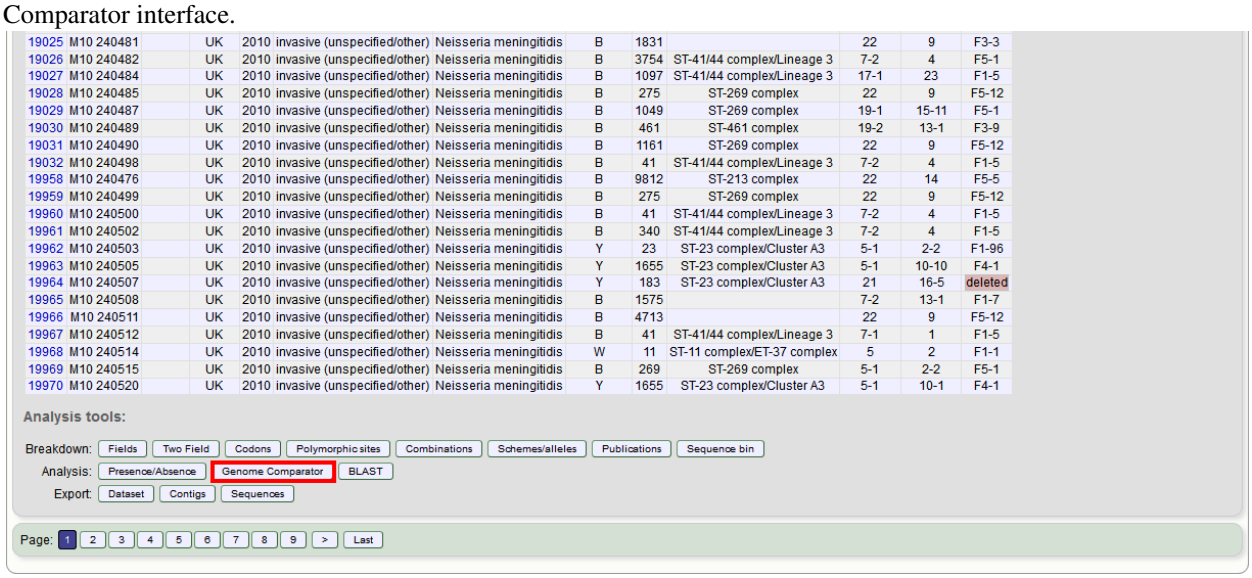
Output is equivalent to a whole genome MLST profile, a distance matrix calculated based on allelic differences and a

NeighborNet graph generated from this distance matrix.

Genome Comparator can be accessed on databases where it is enabled from the contents page by clicking the 'Genome Comparator' link.



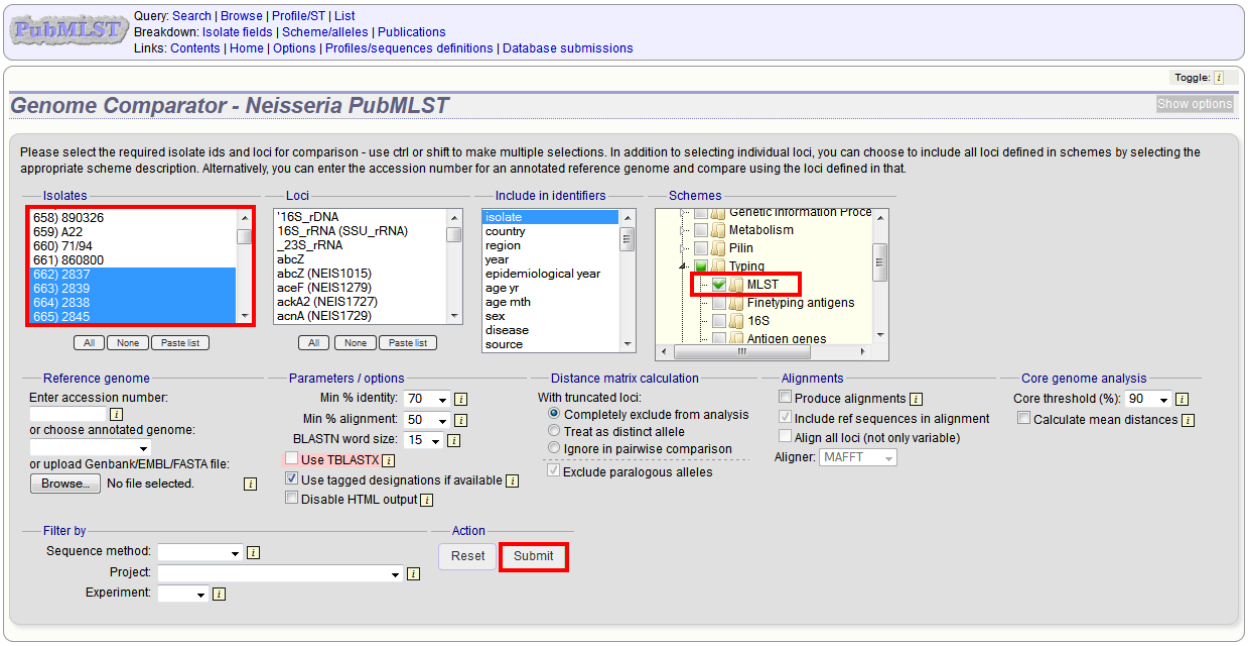
Alternatively, it can be accessed following a query by clicking the 'Genome Comparator' button at the bottom of the results table. Isolates with sequence data returned in the query will be automatically selected within the Genome Comparator interface.



19025	M10 240481	UK	2010	invasive (unspecified/other)	Neisseria meningitidis	B	1831		22	9	F3-3
19026	M10 240482	UK	2010	invasive (unspecified/other)	Neisseria meningitidis	B	3754	ST-41/44 complex/Lineage 3	7-2	4	F5-1
19027	M10 240484	UK	2010	invasive (unspecified/other)	Neisseria meningitidis	B	1097	ST-41/44 complex/Lineage 3	17-1	23	F1-5
19028	M10 240485	UK	2010	invasive (unspecified/other)	Neisseria meningitidis	B	275	ST-269 complex	22	9	F5-12
19029	M10 240487	UK	2010	invasive (unspecified/other)	Neisseria meningitidis	B	1049	ST-269 complex	19-1	15-11	F5-1
19030	M10 240489	UK	2010	invasive (unspecified/other)	Neisseria meningitidis	B	461	ST-461 complex	19-2	13-1	F3-9
19031	M10 240490	UK	2010	invasive (unspecified/other)	Neisseria meningitidis	B	1161	ST-269 complex	22	9	F5-12
19032	M10 240498	UK	2010	invasive (unspecified/other)	Neisseria meningitidis	B	41	ST-41/44 complex/Lineage 3	7-2	4	F1-5
19958	M10 240476	UK	2010	invasive (unspecified/other)	Neisseria meningitidis	B	9812	ST-213 complex	22	14	F5-5
19959	M10 240499	UK	2010	invasive (unspecified/other)	Neisseria meningitidis	B	275	ST-269 complex	22	9	F5-12
19960	M10 240500	UK	2010	invasive (unspecified/other)	Neisseria meningitidis	B	41	ST-41/44 complex/Lineage 3	7-2	4	F1-5
19961	M10 240502	UK	2010	invasive (unspecified/other)	Neisseria meningitidis	B	340	ST-41/44 complex/Lineage 3	7-2	4	F1-5
19962	M10 240503	UK	2010	invasive (unspecified/other)	Neisseria meningitidis	Y	23	ST-23 complex/Cluster A3	5-1	2-2	F1-96
19963	M10 240505	UK	2010	invasive (unspecified/other)	Neisseria meningitidis	Y	1655	ST-23 complex/Cluster A3	5-1	10-10	F4-1
19964	M10 240507	UK	2010	invasive (unspecified/other)	Neisseria meningitidis	Y	183	ST-23 complex/Cluster A3	21	16-5	deleted
19965	M10 240508	UK	2010	invasive (unspecified/other)	Neisseria meningitidis	B	1575		7-2	13-1	F1-7
19966	M10 240511	UK	2010	invasive (unspecified/other)	Neisseria meningitidis	B	4713		22	9	F5-12
19967	M10 240512	UK	2010	invasive (unspecified/other)	Neisseria meningitidis	B	41	ST-41/44 complex/Lineage 3	7-1	1	F1-5
19968	M10 240514	UK	2010	invasive (unspecified/other)	Neisseria meningitidis	W	11	ST-11 complex/ET-37 complex	5	2	F1-1
19969	M10 240515	UK	2010	invasive (unspecified/other)	Neisseria meningitidis	B	269	ST-269 complex	5-1	2-2	F5-1
19970	M10 240520	UK	2010	invasive (unspecified/other)	Neisseria meningitidis	Y	1655	ST-23 complex/Cluster A3	5-1	10-1	F4-1

11.6.1 Analysis using defined loci

Select the isolate genomes that you wish to analyse and then either the loci from the list or a set of schemes. Press submit.



The job will be submitted to the job queue and will start running shortly. Click the link to follow the job progress and view the output.

There will be a series of tables displaying variable loci, colour-coded to indicate allelic differences. Finally, there will be links to a distance matrix which can be loaded in to SplitsTree for further analysis and to a NeighborNet chart showing relatedness of isolates. Due to processing constraints on the web server, this NeighborNet is only calculated if 200 or fewer genomes are selected for analysis, but this can be generated in the stand-alone version of SplitsTree using the distance matrix if required.

PubMLST
Query: Search | Browse | Profile/ST | List
Breakdown: Isolate fields | Scheme/alleles | Publications
Links: Contents | Home | Options | Profiles/sequences definitions | Database submissions

Job status viewer

Status

Job id:	BIGSdb_27748_1405410063_94241
Submit time:	2014-07-15 08:41:03
Status:	finished
Start time:	2014-07-15 08:41:05
Progress:	100%
Stop time:	2014-07-15 08:41:22
Total time:	17 seconds

Output

Analysis against defined loci

Allele numbers are used where these have been defined, otherwise sequences will be marked as 'New#1, 'New#2' etc. Missing alleles are marked as 'X'. Truncated alleles (located at end of contig) are marked as 'T'.

Locus	644 (L93/4286)	662 (2837)	663 (2839)	664 (2838)	665 (2845)	666 (2843)	667 (2842)	669 (2846)	670 (2840)	671 (2844)	672 (2847)	698 (FAM18)
abcZ	2	2	2	2	2	2	2	7	2	2	2	2
adk	3	3	3	3	3	3	3	3	3	3	3	3
aroE	4	19	4	4	4	4	4	4	19	19	19	4
fumC	3	3	3	3	24	23	23	3	3	3	3	3
gdh	8	8	8	8	8	8	8	8	8	8	8	8
pdhC	4	4	4	4	4	6	6	4	4	4	4	4
pgm	6	6	6	6	6	6	6	6	6	6	6	6

Loci with sequence differences among isolates:

Variable loci: 4

Locus	644 (L93/4286)	662 (2837)	663 (2839)	664 (2838)	665 (2845)	666 (2843)	667 (2842)	669 (2846)	670 (2840)	671 (2844)	672 (2847)	698 (FAM18)
abcZ	2	2	2	2	2	2	2	7	2	2	2	2
aroE	4	19	4	4	4	4	4	4	19	19	19	4
fumC	3	3	3	3	24	23	23	3	3	3	3	3
pdhC	4	4	4	4	4	6	6	4	4	4	4	4

Exactly matching loci

These loci are identical in all isolates.

Matches: 3

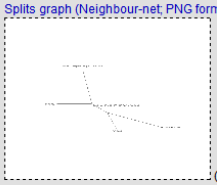
Locus	644 (L93/4286)	662 (2837)	663 (2839)	664 (2838)	665 (2845)	666 (2843)	667 (2842)	669 (2846)	670 (2840)	671 (2844)	672 (2847)	698 (FAM18)
adk	3	3	3	3	3	3	3	3	3	3	3	3
gdh	8	8	8	8	8	8	8	8	8	8	8	8
pgm	6	6	6	6	6	6	6	6	6	6	6	6

Unique strains

Unique strains: 5

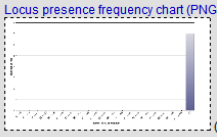
Strain 1	Strain 2	Strain 3	Strain 4	Strain 5
644 (L93/4286)	662 (2837)	666 (2843)	665 (2845)	669 (2846)
663 (2839)	670 (2840)	667 (2842)		
664 (2838)	671 (2844)			
698 (FAM18)	672 (2847)			

- Text output file
- Excel format
- Distance matrix (Nexus format) - Suitable for loading in to SplitsTree. Distances between taxa are calculated as the number of loci with different allele sequences
- Splits graph (Neighbour-net; PNG format)



(click to enlarge)

- Splits graph (Neighbour-net; SVG format) - This can be edited in Inkscape or other vector graphics editors
- Locus presence frequency
- Locus presence frequency chart (PNG format)



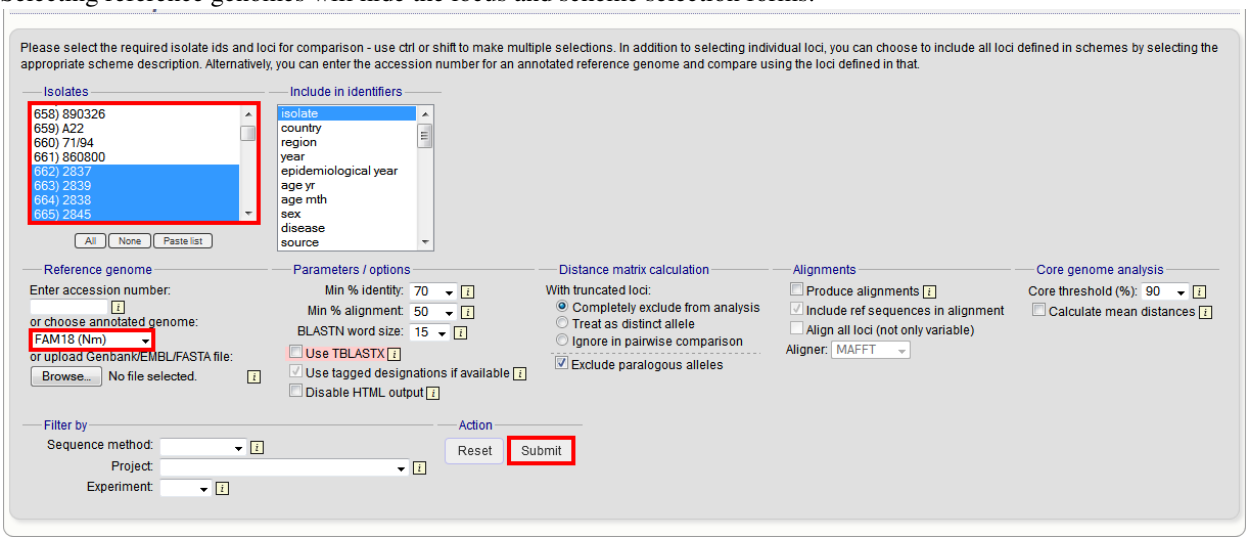
(click to enlarge)

- Tar file containing output files

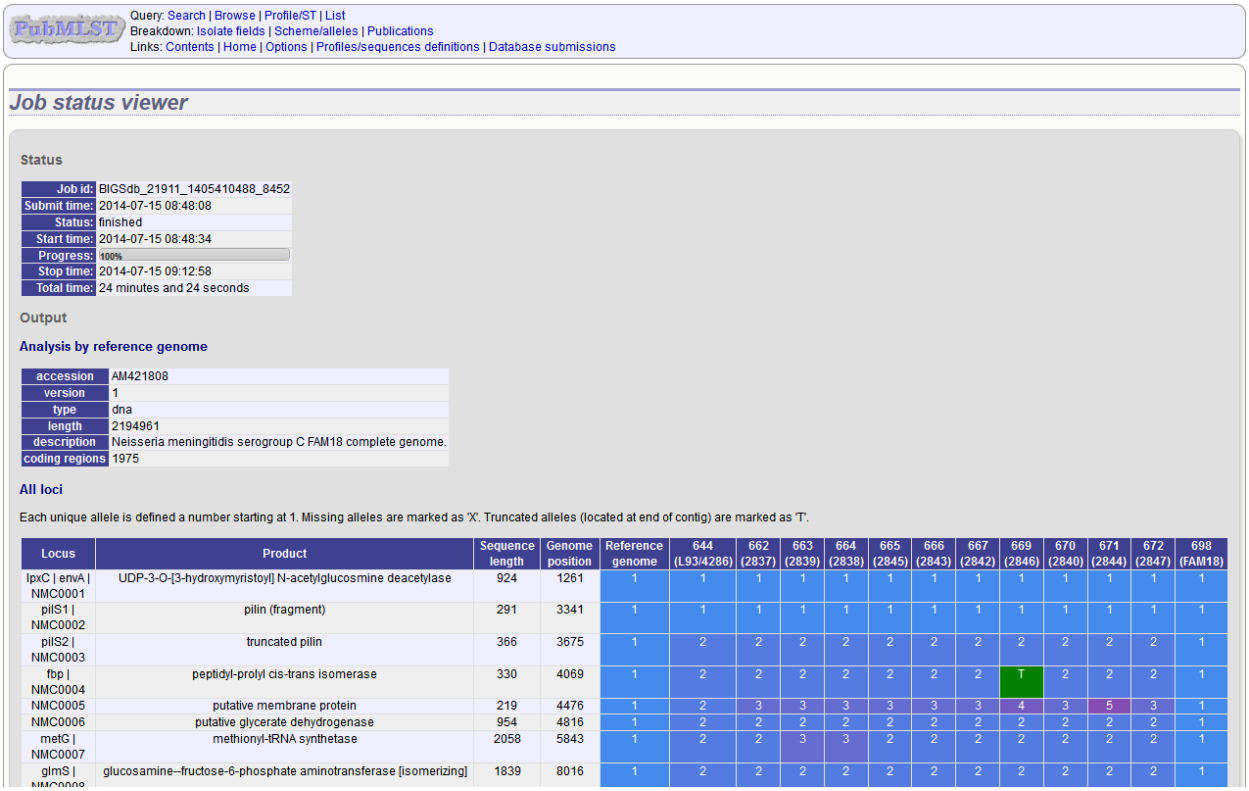
Please note that job results will remain on the server for 7 days.

11.6.2 Analysis using annotated reference genome

Select the isolate genomes that you wish to analyse and then either enter a Genbank accession number for the reference genome, or select from the list of reference genomes (this list will only be present if the administrator has *set it up*). Selecting reference genomes will hide the locus and scheme selection forms.



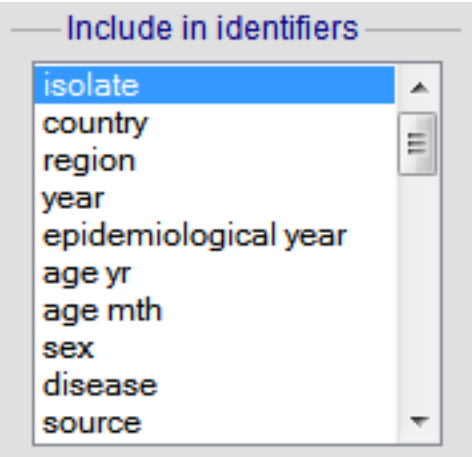
Output is similar to when comparing against defined loci, but this time every coding sequence in the annotated reference will be BLASTed against the selected genomes. Because allele designations are not defined, the allele found in the reference genome is designated allele 1, the next different sequence is allele 2 etc.



Locus	Product	Sequence length	Genome position	Reference genome	644 (L93/4286)	662 (2837)	663 (2839)	664 (2838)	665 (2845)	666 (2843)	667 (2842)	669 (2846)	670 (2840)	671 (2844)	672 (2847)	698 (FAM18)
lpxC | envA | NMC0001	UDP-3-O-[3-hydroxymyristoyl] N-acetylglucosmine deacetylase	924	1261	1	1	1	1	1	1	1	1	1	1	1	1	1
pilS1 | NMC0002	pilin (fragment)	291	3341	1	1	1	1	1	1	1	1	1	1	1	1	1
pilS2 | NMC0003	truncated pilin	366	3675	1	2	2	2	2	2	2	2	2	2	2	2	1
fbp | NMC0004	peptidyl-prolyl cis-trans isomerase	330	4069	1	2	2	2	2	2	2	2	T	2	2	2	1
NMC0005	putative membrane protein	219	4476	1	2	3	3	3	3	3	3	4	3	5	3	1
NMC0006	putative glycerate dehydrogenase	954	4816	1	2	2	2	2	2	2	2	2	2	2	2	1
metG | NMC0007	methionyl-tRNA synthetase	2058	5843	1	2	2	3	3	2	2	2	2	2	2	2	1
glmS | NMC0008	glucosamine--fructose-6-phosphate aminotransferase [isomerizing]	1839	8016	1	2	2	2	2	2	2	2	2	2	2	2	1

11.6.3 Include in identifiers fieldset

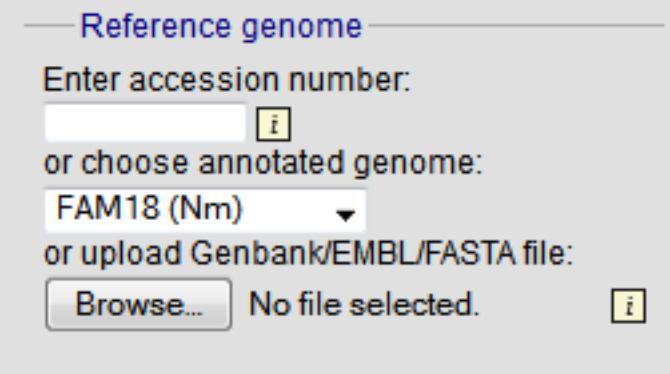
This selection box allows you to choose which isolate provenance fields will be included in the results table and sequence exports.



Multiple values can be selected by clicking while holding down Ctrl.

11.6.4 Reference genome fieldset

This section allows you to choose a reference genome to use as the source of comparator sequences.

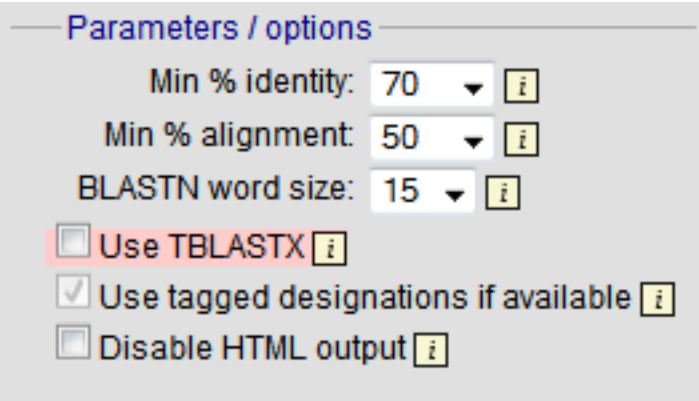


There are three possibilities here:

1. Enter accession number - Enter a Genbank accession number of an annotated reference and Genome Comparator will automatically retrieve this from Genbank.
2. Select from list - The administrator may have selected some genomes to offer for comparison. If these are present, simply select from the list.
3. Upload genome - Click 'Browse' and upload your own reference. This can either be in Genbank, EMBL or FASTA format. Ensure that the filename ends in the appropriate file extension (.gb, .embl, .fas) so that it is recognized.

11.6.5 Parameters/options fieldset

This section allows you to modify BLAST parameters. This affects sensitivity and speed.



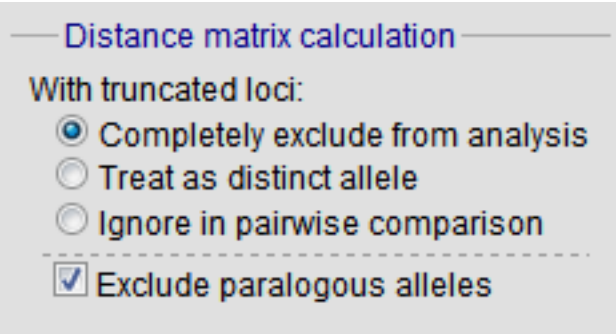
- Min % identity - This sets the threshold identity that a matching sequence has to be in order to be considered (default: 70%). Only the best match is used.
- Min % alignment - This sets the percentage of the length of reference allele sequence that the alignment has to cover in order to be considered (default: 50%).
- BLASTN word size - This is the length of the initial identical match that BLAST requires before extending a match (default: 15). Increasing this value improves speed at the expense of sensitivity. The default value gives good results in most cases, but increasing this to 20 is almost as good (there was 1 difference among 2000 loci in a test run) and will speed up the analysis approximately two-fold.
- Use TBLASTX - This compares the six-frame translation of your nucleotide query sequence against the six-frame translation of the contig sequences. Sequences will be classed as identical if they result in the same translated sequence even if the nucleotide sequence is different. This is significantly slower than using BLASTN.

Additionally, two other options are available in this fieldset:

- Use tagged designations - When analysing using defined loci, Genome Comparator can use the designations stored within the database (this is the default). This is much quicker since it doesn't need to run BLAST against these sequences. If a designation is missing, BLAST will be run for that locus anyway.
- Disable HTML output - If running Genome Comparator against a large number of genomes, the resulting table may get so large that your web browser struggles to render it properly and may use up too much memory on your computer. Clicking this button prevents this output - this output is not required for further analysis since everything present in it is also generated in Excel format at the end. HTML output is automatically disabled when more than 150 genomes are analysed.

11.6.6 Distance matrix calculation fieldset

This section provides options for the treatment of truncated and paralogous loci when generating the distance matrix.



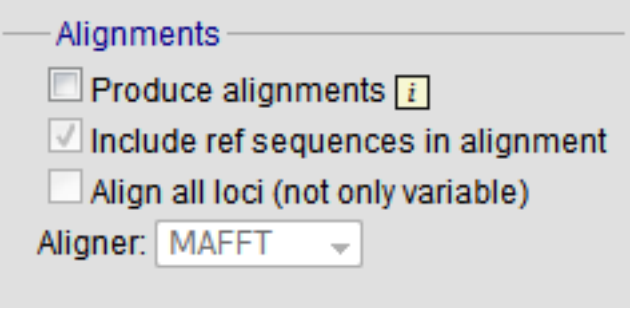
For truncated loci, i.e. those that continue beyond the end of a contig so are incomplete you can:

- Completely exclude from analysis - Any locus that is truncated in at least one isolate will be removed from the analysis completely (default). Using this option means that if there is one bad genome with a lot of truncated sequences in your analysis, a large proportion of the loci may not be used to calculate distances.
- Treat as a distinct allele - This treats all truncated sequences as a specific allele 'T'. This varies from any other allele, but all truncated sequences will be treated as though they were identical.
- Ignore in pairwise comparison - This is probably the best option (and will likely become the default). In this case, truncated alleles are only excluded from the analysis when comparing the particular isolate that has it. Other isolates with different alleles will be properly included. The affect of this option will be to shorten the distances of isolates with poorly sequenced genomes with the others.

Paralogous loci, i.e. those with multiple good matches, can be excluded from the analysis (default). This is the safest option since there is no guarantee that differences seen between isolates at paralogous loci are real if the alternative matches are equally good.

11.6.7 Alignments fieldset

This section enables you to choose to produce alignments of the sequences identified.

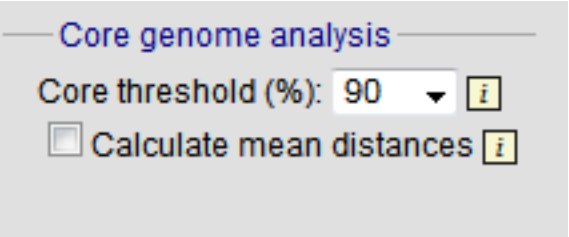


Available options are:

- Produce alignments - Selecting this will produce the alignment files, as well as XMFA and FASTA outputs of aligned sequences. This will result in the analysis taking approximately twice as long to run.
- Include ref sequences in alignment - When doing analysis using an annotated reference, selecting this will include the reference sequence in the alignment files.
- Align all loci - By default, only loci that vary among the isolates are aligned. You may however wish to align all if you would like the resultant XMFA and FASTA files to include all coding sequences.
- Aligner - There are currently two choices of alignment algorithm (provided they have both been installed)
  - MAFFT (default) - This is the preferred option as it is significantly quicker than MUSCLE, uses less memory, and produces comparable results.
  - MUSCLE - This was originally the only choice. It is still included to enable previous analyses to be re-run and compared but it is recommended that MAFFT isused otherwise.

11.6.8 Core genome analysis fieldset

This section enables you to modify the inclusion threshold used to calculate whether or not a locus is part of the core genome (of the dataset).

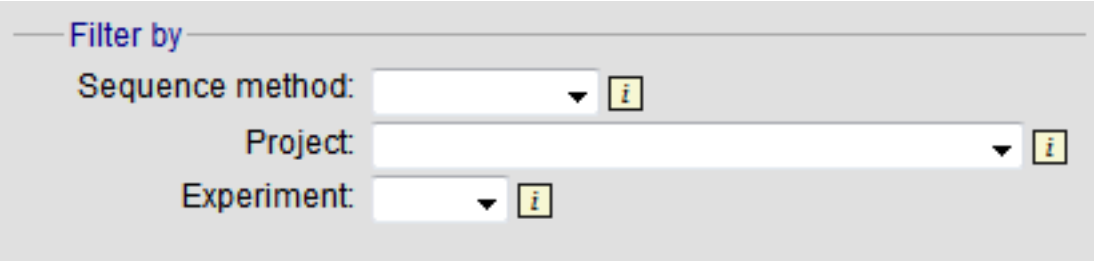


The default setting of 90% means that a locus is counted as core if it appears within 90% or more of the genomes in the dataset.

There is also an option to calculate the mean distance among sequences of the loci. Selecting this will also select the option to produce alignments.

11.6.9 Filter fieldset

This section allows you to further filter your collection of isolates and the contigs to include.



Available options are:

- Sequence method - Choose to only analyse contigs that have been generated using a particular method. This depends on the method being set when the contigs were uploaded.
- Project - Only include isolates belonging to the chosen project. This enables you to select all isolates and filter to a project.
- Experiment - Contig files can belong to an experiment. How this is used can vary between databases, but this enables you to only include contigs from a particular experiment.

11.6.10 Understanding the output

Distance matrix

The distance matrix is simply a count of the number of loci that differ between each pair of isolates. It is generated in NEXUS format which can be used as the input file for SplitsTree. This can be used to generate NeighborNet, Split decomposition graphs and trees offline. If 200 isolates or fewer are included in the analysis, a Neighbor network is automatically generated from this distance matrix.

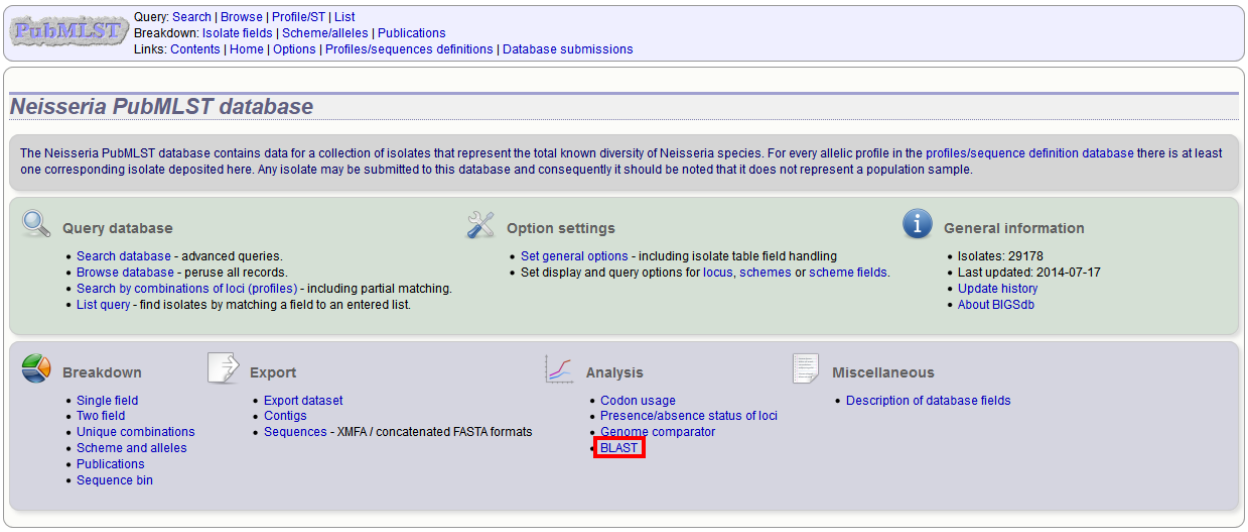
Unique strains

The table of unique strains is a list of isolates that are identical at every locus. Every isolate is likely to be classed as unique if a whole genome analysis is performed, but with a constrained set of loci, such as those for MLST, this will group isolates that are indistinguishable at that level of resolution.

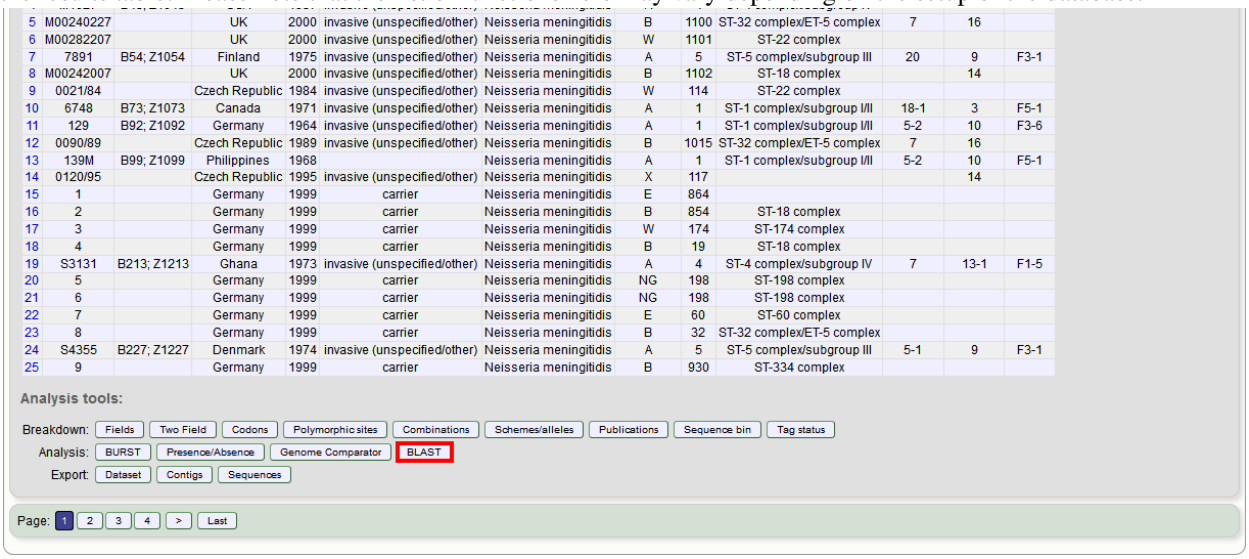
11.7 BLAST

The BLAST plugin enables you to BLAST a sequence against any of the genomes in the database, displaying a table of matches and extracting matching sequences.

The function can be accessed by selecting the 'BLAST' link on the Analysis section of the main contents page.

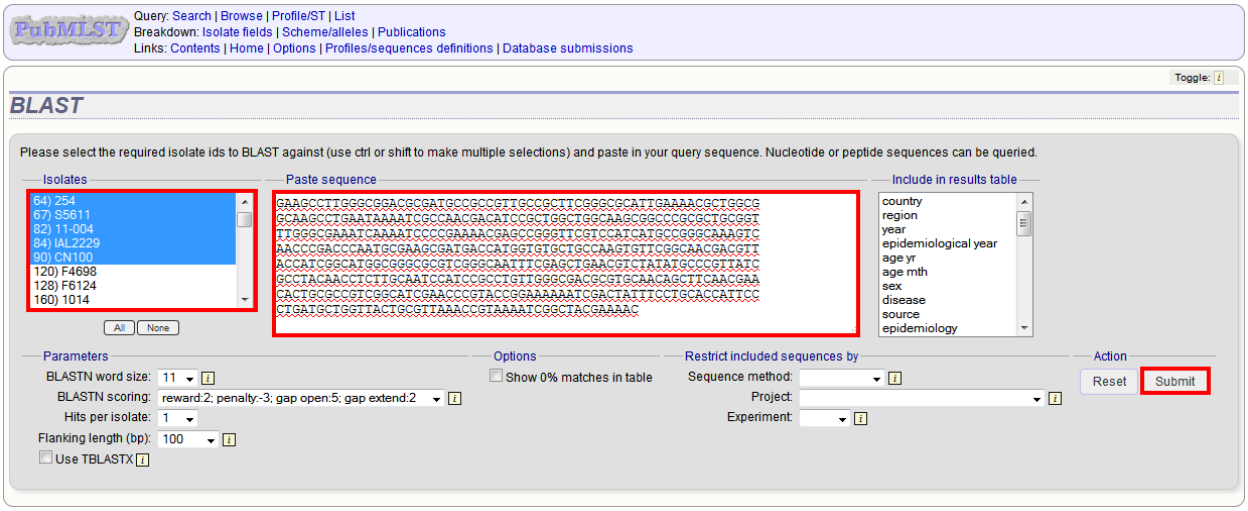


Alternatively,it can be accessed following a query by clicking the 'BLAST' button in the Analysis list at the bottom of the results table. Please note that the list of functions here may vary depending on the setup of the database.



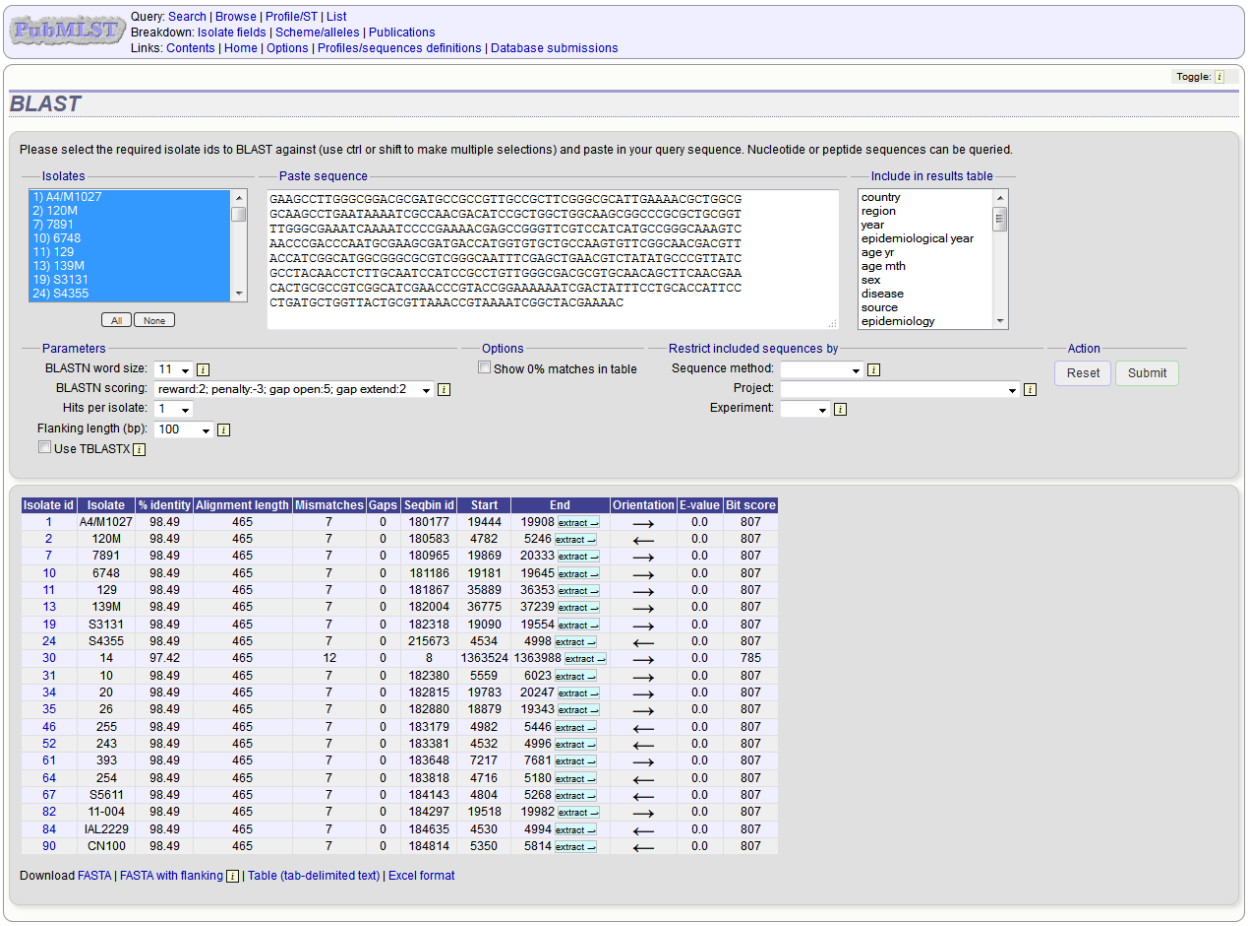
5	M00240227		UK	2000	invasive (unspecified/other)	Neisseria meningitidis	B	1100	ST-32 complex/ET-5 complex	7	16	
6	M00282207		UK	2000	invasive (unspecified/other)	Neisseria meningitidis	W	1101	ST-22 complex			
7	7891	B54; Z1054	Finland	1975	invasive (unspecified/other)	Neisseria meningitidis	A	5	ST-5 complex/subgroup III	20	9	F3-1
8	M00242007		UK	2000	invasive (unspecified/other)	Neisseria meningitidis	B	1102	ST-18 complex		14	
9	0021/84		Czech Republic	1984	invasive (unspecified/other)	Neisseria meningitidis	W	114	ST-22 complex			
10	6748	B73; Z1073	Canada	1971	invasive (unspecified/other)	Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	18-1	3	F5-1
11	129	B92; Z1092	Germany	1964	invasive (unspecified/other)	Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	5-2	10	F3-6
12	0090/89		Czech Republic	1989	invasive (unspecified/other)	Neisseria meningitidis	B	1015	ST-32 complex/ET-5 complex	7	16	
13	139M	B99; Z1099	Philippines	1968		Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	5-2	10	F5-1
14	0120/95		Czech Republic	1995	invasive (unspecified/other)	Neisseria meningitidis	X	117			14	
15	1		Germany	1999	carrier	Neisseria meningitidis	E	864				
16	2		Germany	1999	carrier	Neisseria meningitidis	B	854	ST-18 complex			
17	3		Germany	1999	carrier	Neisseria meningitidis	W	174	ST-174 complex			
18	4		Germany	1999	carrier	Neisseria meningitidis	B	19	ST-18 complex			
19	S3131	B213; Z1213	Ghana	1973	invasive (unspecified/other)	Neisseria meningitidis	A	4	ST-4 complex/subgroup IV	7	13-1	F1-5
20	5		Germany	1999	carrier	Neisseria meningitidis	NG	198	ST-198 complex			
21	6		Germany	1999	carrier	Neisseria meningitidis	NG	198	ST-198 complex			
22	7		Germany	1999	carrier	Neisseria meningitidis	E	60	ST-60 complex			
23	8		Germany	1999	carrier	Neisseria meningitidis	B	32	ST-32 complex/ET-5 complex			
24	S4355	B227; Z1227	Denmark	1974	invasive (unspecified/other)	Neisseria meningitidis	A	5	ST-5 complex/subgroup III	5-1	9	F3-1
25	9		Germany	1999	carrier	Neisseria meningitidis	B	930	ST-334 complex			

Select the isolate records to analyse - these will be pre-selected if you accessed the plugin following a query. Paste in a sequence to query - this be either a DNA or peptide sequence.



Click submit.

A table of BLAST results will be displayed.



Clicking any of the 'extract' buttons will display the matched sequence along with a translated sequence and flanking sequences.

181867	35889	36353	extract →	→	0.0	807
182004	36775	37239	extract →	→	0.0	807
182318	19090	19554	extract →	→	0.0	807
215673	4534	4998	extract →	←	0.0	807
8	1363524	1363988	extract →	→	0.0	785
182380	5559	6023	extract →	→	0.0	807
182815	19783	20247	extract →	→	0.0	807

PubMLST
Query: Search | Browse | Profile/ST | List
Breakdown: Isolate fields | Scheme/alleles | Publications
Links: Contents | Home | Options | Profiles/sequences definitions | Database submissions

Extracted sequence: Seqbin id#:182318 (19090-19554)

sequence bin id#182318

sequence	Solexa
method	
start	19090
end	19554
length	465
orientation	→
translation	

```
sequence   Solexa CGGCACGGGT TTGAACAGCC ATCCCGAATA CGCCGAAAAA GCCGCCGCCA AACTCGCCGA ATTGTCCGGC TTGCCGTTTG TCAGCGCGCC GAACAAATTT GAAGCCTTGG GCGGACGCGA TGCCGCCGTT GCCGCTTCGG
method             GCGCATTGAA AACGCTGGCG GCAAGCCTGA ATAAAATCGC CAACGACATC CGCTGGCTGG CAAGCGGCCC GCGCTGCGGT TTGGGCGAAA TCAAAATCCC CGAAAACGAG CCGGGTTCGT CCATCATGCC GGGCAAAGTC
start      19090   AACCCGACCC AATGCGAAGC GATGACCATG GTGTGCTGCC AAGTGTTCGG CAACGACGTT ACCATCGGTA TGGCGGGCGC GTCGGGCAAT TTCGAGCTGA ACGTCTATAT GCCCGTCATC GCCTACAACC TCTTGCAATC
end        19554   CATCCGCCTG TTGGGCGACG CGTGCAACAG CTTCAACGAA CACTGCGCCG TCGGCATTGA ACCCGTACCG GAAAAAATCG ACTATTTCCT GCACCATTCC CTGATGCTCG TTACCGCGTT AAACCGCAAA ATCGGTTACG
length     465     AAAACGCCGC CAAAGTCGCC AAAACCGCCT ACAAAAACAA CAAATCGTTG CGCGAAACCG CCGTTGAGTT GGGCTTGCTG ACGGGCGAAG AATTTGACGA ACTGG
orientation  →
translation

      R  H  G  F  E  Q  P  S  R  I  R  R  K  S  R  R  Q  T  R  R  I  V  R  L  A  V  C  Q  R  A  E  Q  I  *   F1
       G  T  G  L  N  S  H  P  E  Y  A  E  K  A  A  A  K  L  A  E  L  S  G  L  P  F  V  S  A  P  N  K  F     F2
        A  R  V  *  T  A  I  P  N  T  P  K  K  P  P  P  N  S  P  N  C  P  A  C  R  L  S  A  R  R  T  N  L     F3
    1 CGGCACGGGTTTGAACAGCCATCCCGAATACGCCGAAAAAGCCGCCGCCAAACTCGCCGAATTGTCCGGCTTGCCGTTTGTCAGCGCGCCGAACAAATTT 100
      ----:----|----:----|----:----|----:----|----:----|----:----|----:----|----:----|----:----|----:----|

       S  L  G  R  T  R  C  R  R  C  R  F  G  R  I  E  N  A  G  G  K  P  E  *  N  R  Q  R  H  P  L  A  G     F1
      E  A  L  G  G  R  D  A  A  V  A  A  S  G  A  L  K  T  L  A  A  S  L  N  K  I  A  N  D  I  R  W  L  A   F2
       K  P  W  A  D  A  M  P  P  L  P  L  R  A  H  *  K  R  W  R  Q  A  *  I  K  S  P  T  T  S  A  G  W     F3
  101 GAAGCCTTGGGCGGACGCGATGCCGCCGTTGCCGCTTCGGGCGCATTGAAAACGCTGGCGGCAAGCCTGAATAAAATCGCCAACGACATCCGCTGGCTGG 200
      ----:----|----:----|----:----|----:----|----:----|----:----|----:----|----:----|----:----|----:----|

       K  R  P  A  L  R  F  G  R  N  Q  N  P  R  K  R  A  G  F  V  H  H  A  G  Q  S  Q  P  D  P  M  R  S     F1
        S  G  P  R  C  G  L  G  E  I  K  I  P  E  N  E  P  G  S  S  I  M  P  G  K  V  N  P  T  Q  C  E  A    F2
      Q  A  A  R  A  A  V  W  A  K  S  K  S  P  K  T  S  R  V  R  P  S  C  R  A  K  S  T  R  P  N  A  K  R   F3
  201 CAAGCGGCCCGCGCTGCGGTTTGGGCGAAATCAAAATCCCCGAAAACGAGCCGGGTTCGTCCATCATGCCGGGCAAAGTCAACCCGACCCAATGCGAAGC 300
      ----:----|----:----|----:----|----:----|----:----|----:----|----:----|----:----|----:----|----:----|

      D  D  H  G  V  L  P  S  V  R  Q  R  R  Y  H  R  Y  G  G  R  V  G  Q  F  R  A  E  R  L  Y  A  R  H  R   F1
       M  T  M  V  C  C  Q  V  F  G  N  D  V  T  I  G  M  A  G  A  S  G  N  F  E  L  N  V  Y  M  P  V  I     F2
        *  P  W  C  A  A  K  C  S  A  T  T  L  P  S  V  W  R  A  R  R  A  I  S  S  *  T  S  I  C  P  S  S     F3
  301 GATGACCATGGTGTGCTGCCAAGTGTTCGGCAACGACGTTACCATCGGTATGGCGGGCGCGTCGGGCAATTTCGAGCTGAACGTCTATATGCCCGTCATC 400
      ----:----|----:----|----:----|----:----|----:----|----:----|----:----|----:----|----:----|----:----|

       L  Q  P  L  A  I  H  P  P  V  G  R  R  V  Q  Q  L  Q  R  T  L  R  R  R  H  *  T  R  T  G  K  N  R     F1
      A  Y  N  L  L  Q  S  I  R  L  L  G  D  A  C  N  S  F  N  E  H  C  A  V  G  I  E  P  V  P  E  K  I  D   F2
       P  T  T  S  C  N  P  S  A  C  W  A  T  R  A  T  A  S  T  N  T  A  P  S  A  L  N  P  Y  R  K  K  S     F3
  401 GCCTACAACCTCTTGCAATCCATCCGCCTGTTGGGCGACGCGTGCAACAGCTTCAACGAACACTGCGCCGTCGGCATTGAACCCGTACCGGAAAAAATCG 500
```

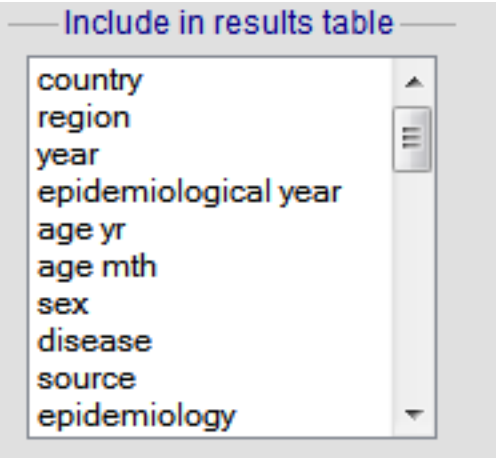
At the bottom of the results table are links to export the matching sequences in FASTA format, (optionall) including flanking sequnces. You can also export the table in tab-delimited text or Excel formats.

82	11-004	98.49	465	7	0	184297	19518	19982	extract →	→	0.0	807
84	IAL2229	98.49	465	7	0	184635	4530	4994	extract →	←	0.0	807
90	CN100	98.49	465	7	0	184814	5350	5814	extract →	←	0.0	807

Download FASTA | FASTA with flanking i | Table (tab-delimited text) | Excel format

11.7.1 Include in results table fieldset

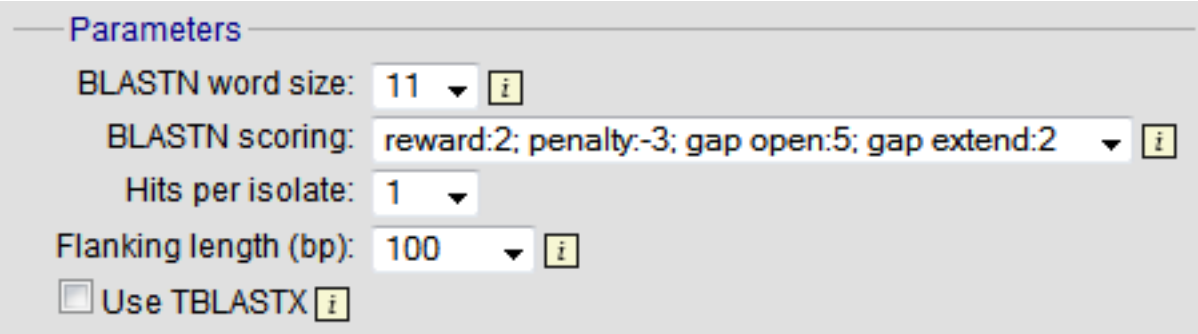
This selection box allows you to choose which isolate provenance fields will be included in the results table.



Multiple values can be selected by clicking while holding down Ctrl.

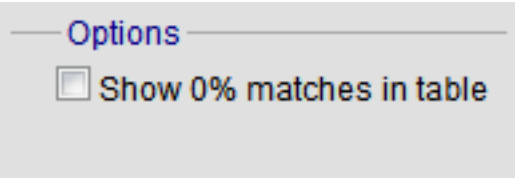
11.7.2 Parameters fieldset

This section allows you to modify BLAST parameters. This affects sensitivity and speed.



- BLASTN word size - This is the length of the initial identical match that BLAST requires before extending a match (default: 11). Increasing this value improves speed at the expense of sensitivity.
- BLASTN scoring - This is a dropdown box of combinations of identical base rewards; mismatch penalties; and gap open and extension penalties. BLASTN has a constrained list of allowed values which reflects the available options in the list.
- Hits per isolate - By default, only the best match is shown. Increase this value to the number of hits you'd like to see per isolate.
- Flanking length - Set the size of the upstream and downstream flanking sequences that you'd like to include.
- Use TBLASTX - This compares the six-frame translation of your nucleotide query sequence against the six-frame translation of the contig sequences. This is significantly slower than using BLASTN.

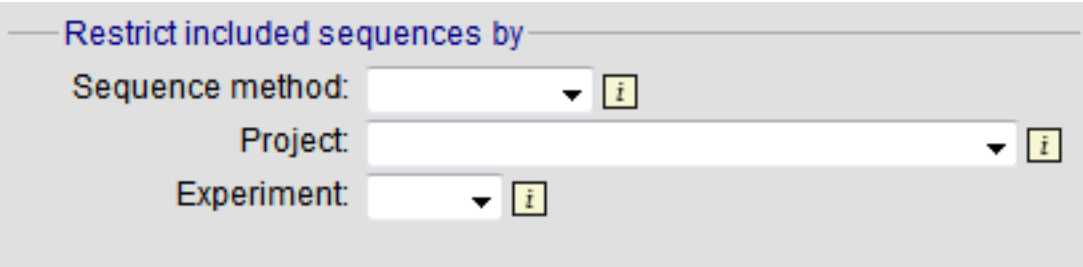
11.7.3 No matches



Click this option to create a row in the table indicating that a match was not found. This can be useful when screening a large number of isolates.

11.7.4 Filter fieldset

This section allows you to further filter your collection of isolates and the contig sequences to include.



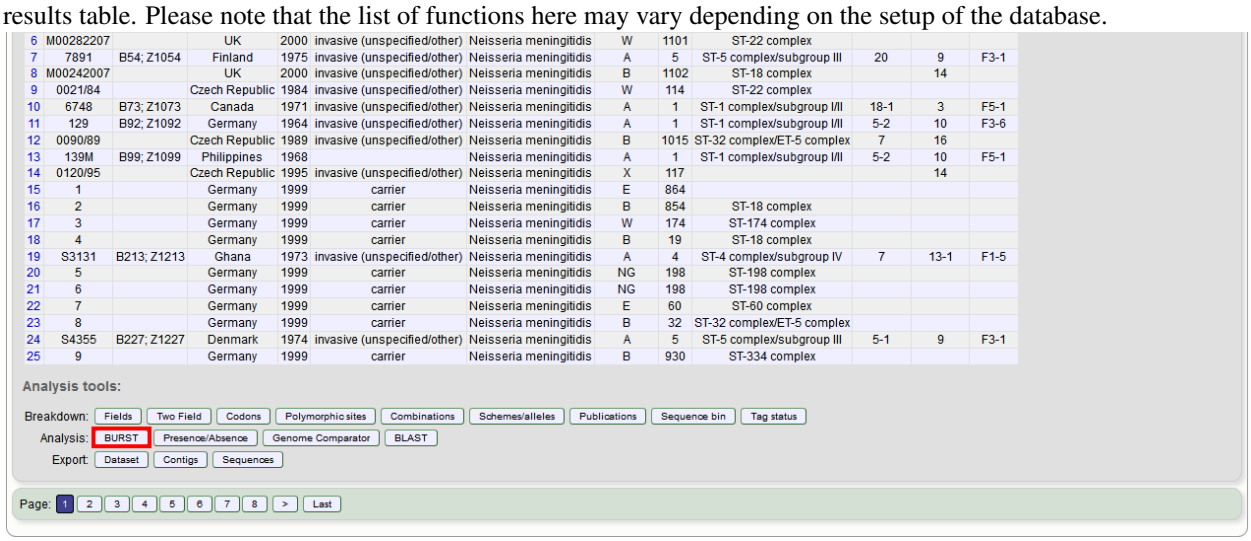
Available options are:

- Sequence method - Choose to only analyse contigs that have been generated using a particular method. This depends on the method being set when the contigs were uploaded.
- Project - Only include isolates belonging to the chosen project. This enables you to select all isolates and filter to a project.
- Experiment - Contig files can belong to an experiment. How this is used can vary between databases, but this enables you to only include contigs from a particular experiment.

11.8 BURST

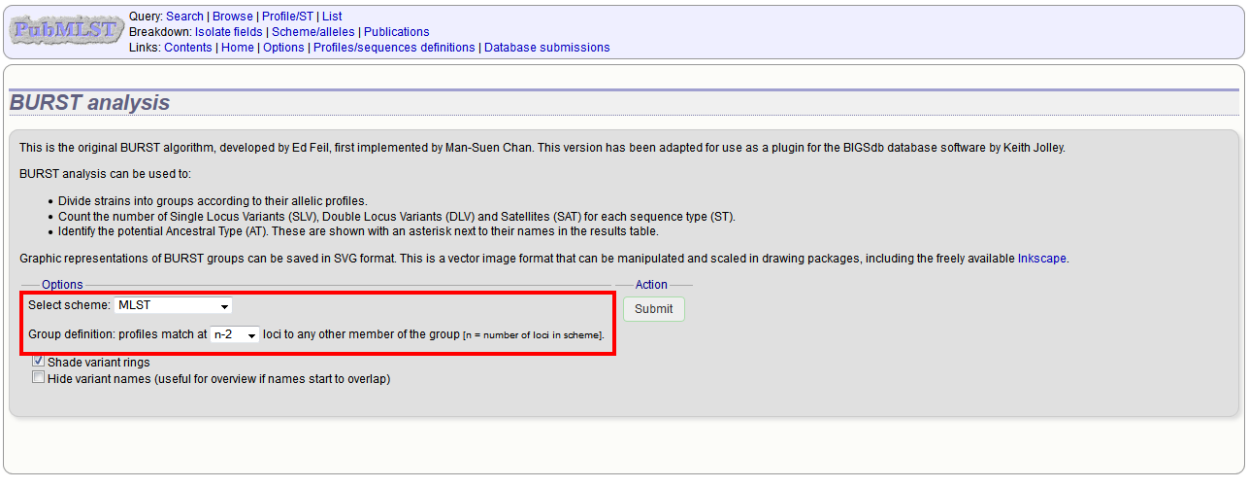
BURST is an algorithm used to group MLST-type data based on a count of the number of profiles that match each other at specified numbers of loci. The analysis is available for both sequence definition database and isolate database schemes that have primary key fields set. The algorithm has to be *specifically enabled* by an administrator. Analysis is limited to 1000 or fewer records.

The plugin can be accessed following a query by clicking the 'BURST' button in the Analysis list at the bottom of the results table. Please note that the list of functions here may vary depending on the setup of the database.



6	M00282207		UK	2000	invasive (unspecified/other)	Neisseria meningitidis	W	1101	ST-22 complex				
7	7891	B54; Z1054	Finland	1975	invasive (unspecified/other)	Neisseria meningitidis	A	5	ST-5 complex/subgroup III	20	9	F3-1
8	M00242007		UK	2000	invasive (unspecified/other)	Neisseria meningitidis	B	1102	ST-18 complex		14	
9	0021/84		Czech Republic	1984	invasive (unspecified/other)	Neisseria meningitidis	W	114	ST-22 complex			
10	6748	B73; Z1073	Canada	1971	invasive (unspecified/other)	Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	18-1	3	F5-1
11	129	B92; Z1092	Germany	1964	invasive (unspecified/other)	Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	5-2	10	F3-6
12	0090/89		Czech Republic	1989	invasive (unspecified/other)	Neisseria meningitidis	B	1015	ST-32 complex/ET-5 complex	7	16	
13	139M	B99; Z1099	Philippines	1968		Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	5-2	10	F5-1
14	0120/95		Czech Republic	1995	invasive (unspecified/other)	Neisseria meningitidis	X	117			14	
15	1		Germany	1999	carrier	Neisseria meningitidis	E	864				
16	2		Germany	1999	carrier	Neisseria meningitidis	B	854	ST-18 complex			
17	3		Germany	1999	carrier	Neisseria meningitidis	W	174	ST-174 complex			
18	4		Germany	1999	carrier	Neisseria meningitidis	B	19	ST-18 complex			
19	S3131	B213; Z1213	Ghana	1973	invasive (unspecified/other)	Neisseria meningitidis	A	4	ST-4 complex/subgroup IV	7	13-1	F1-5
20	5		Germany	1999	carrier	Neisseria meningitidis	NG	198	ST-198 complex			
21	6		Germany	1999	carrier	Neisseria meningitidis	NG	198	ST-198 complex			
22	7		Germany	1999	carrier	Neisseria meningitidis	E	60	ST-60 complex			
23	8		Germany	1999	carrier	Neisseria meningitidis	B	32	ST-32 complex/ET-5 complex			
24	S4355	B227; Z1227	Denmark	1974	invasive (unspecified/other)	Neisseria meningitidis	A	5	ST-5 complex/subgroup III	5-1	9	F3-1
25	9		Germany	1999	carrier	Neisseria meningitidis	B	930	ST-334 complex			

If there multiple schemes that can be analysed, these can then be selected along with the group definition.

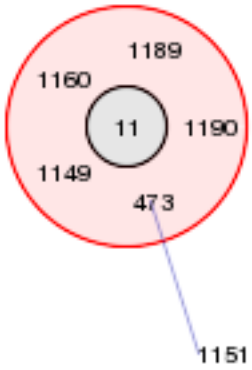


Modifying the group definition affects the size of groups and how they link together. By default, the definition is n-2 (where n is the number of loci), so for example on a 7 locus MLST scheme groups contain STs that match at 5 or more loci to any other member of the group.

Click Submit.

A series of tables will be displayed indicating the groups of profiles. Where one profile can be identified as a central genotype, i.e. the profile that has the greatest number of other profiles that are single locus variants (SLV), double locus variants (DLV) and so on, a graphical representation will be displayed. The central profile is indicated with an asterisk.

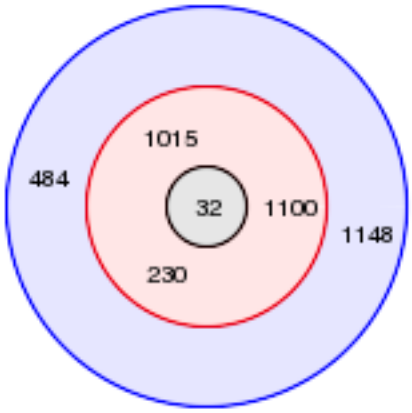
group: 2				
ST	Frequency	SLV	DLV	SAT
11*	37	5		1
473	1	2	4	
1149	19	1	4	1
1151	1	0	1	5
1160	1	2	3	1
1189	1	1	4	1
1190	1	1	4	1



SVG file (right click to save)

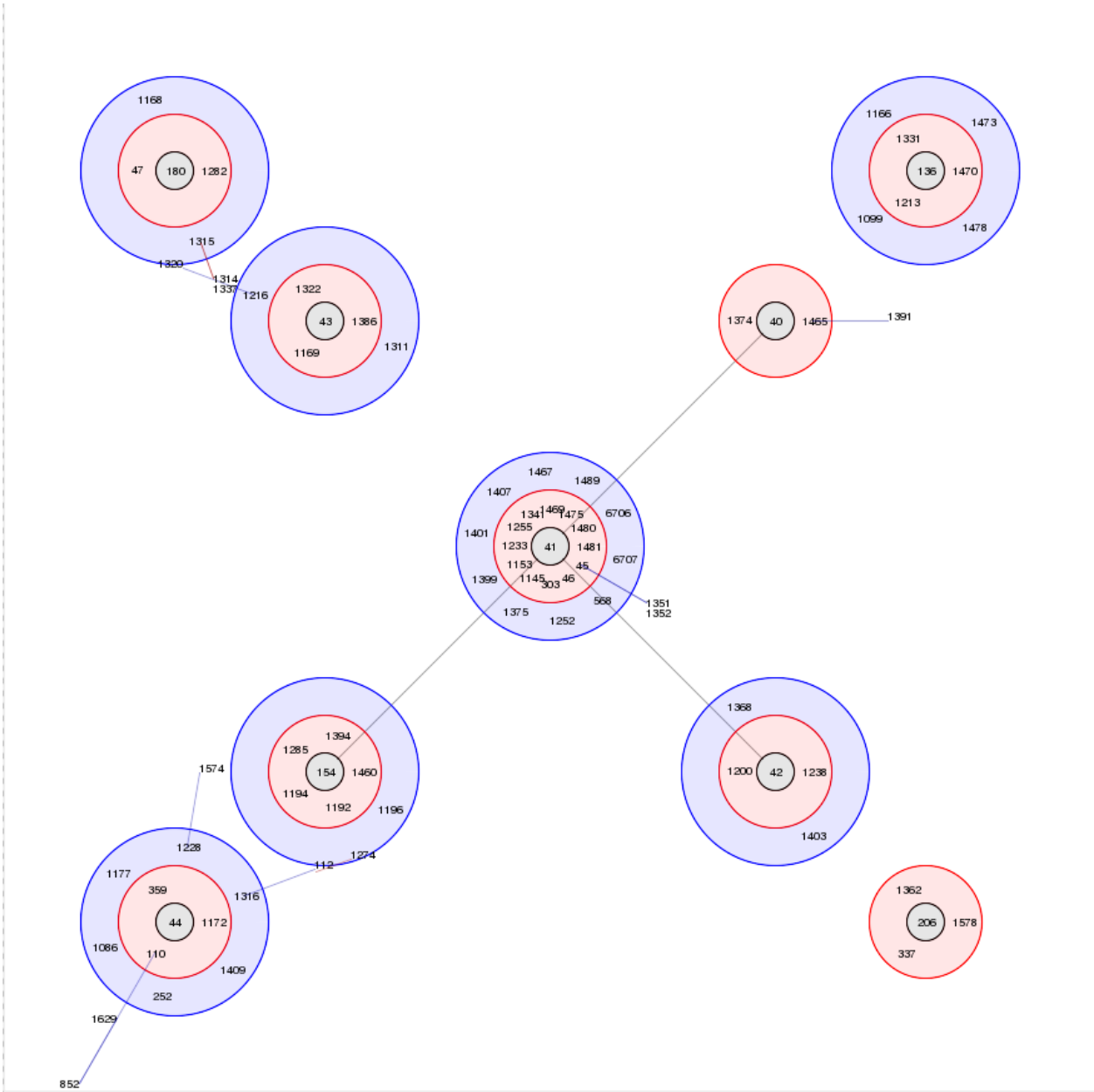
SLV profiles that match the central profile are shown within a red circle surrounding the central profile. Most distant profiles (triple locus variants) may be linked with a line. Larger groups may additionally have DLV profiles. These are shown in a blue circle.

group: 6				
ST	Frequency	SLV	DLV	SAT
32*	2	3	2	
230	1	1	3	1
484	1	0	3	2
1015	1	1	4	
1100	1	1	2	2
1148	1	0	4	1



SVG file (right click to save)

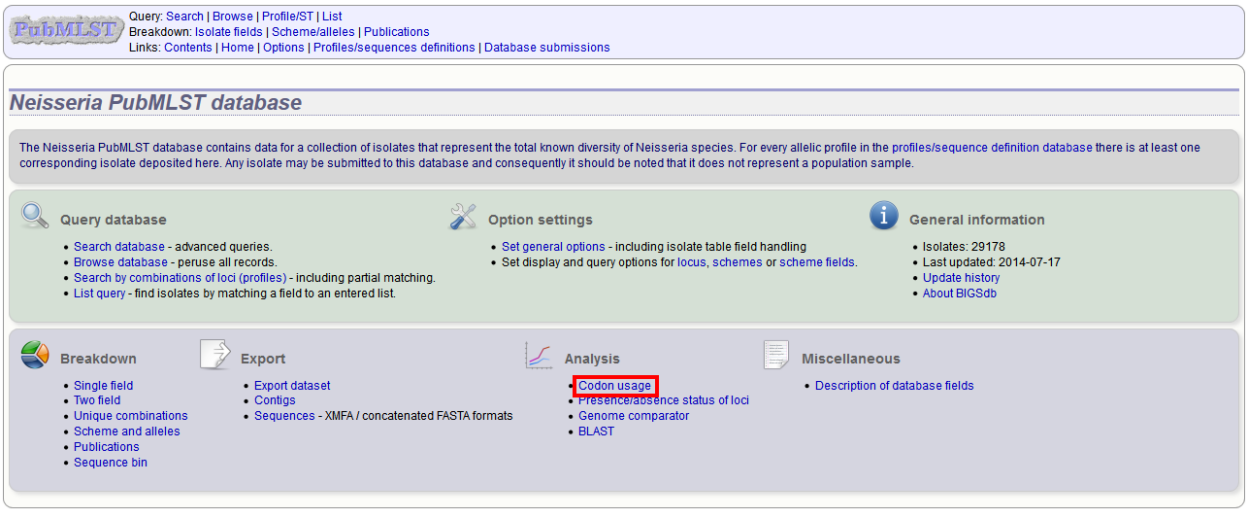
Groups can get very large, where linked profiles form sub-groups and an attempt is made to depict these.



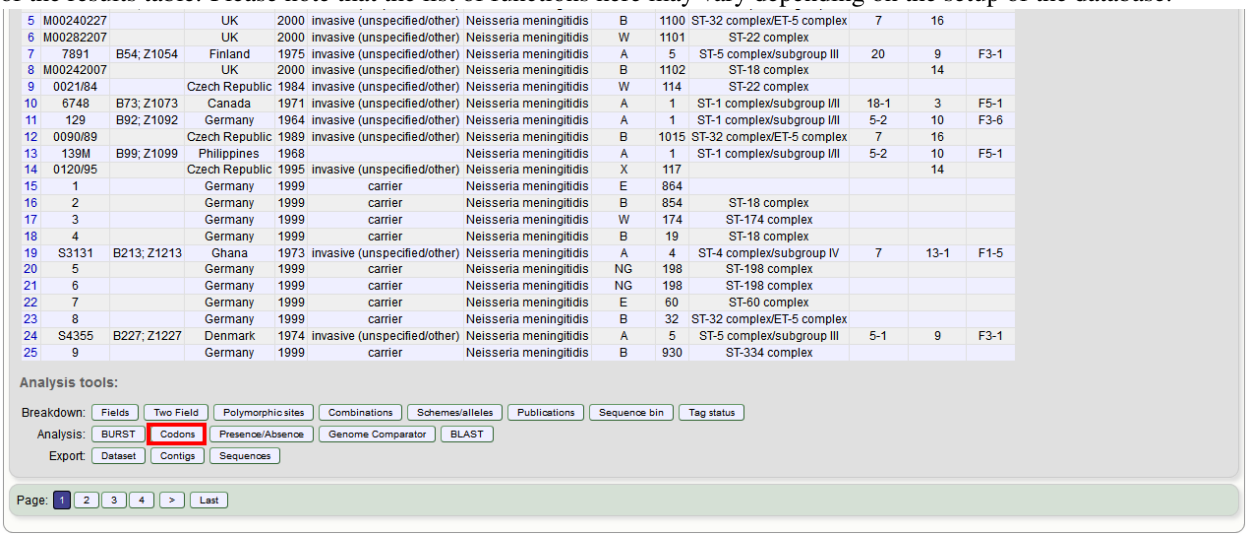
11.9 Codon usage

The codon usage plugin for isolate databases calculates the absolute and relative synonymous codon usage by isolate and by locus.

The function can be selected by clicking the 'Codon usage' link in the Analysis section of the main contents page.

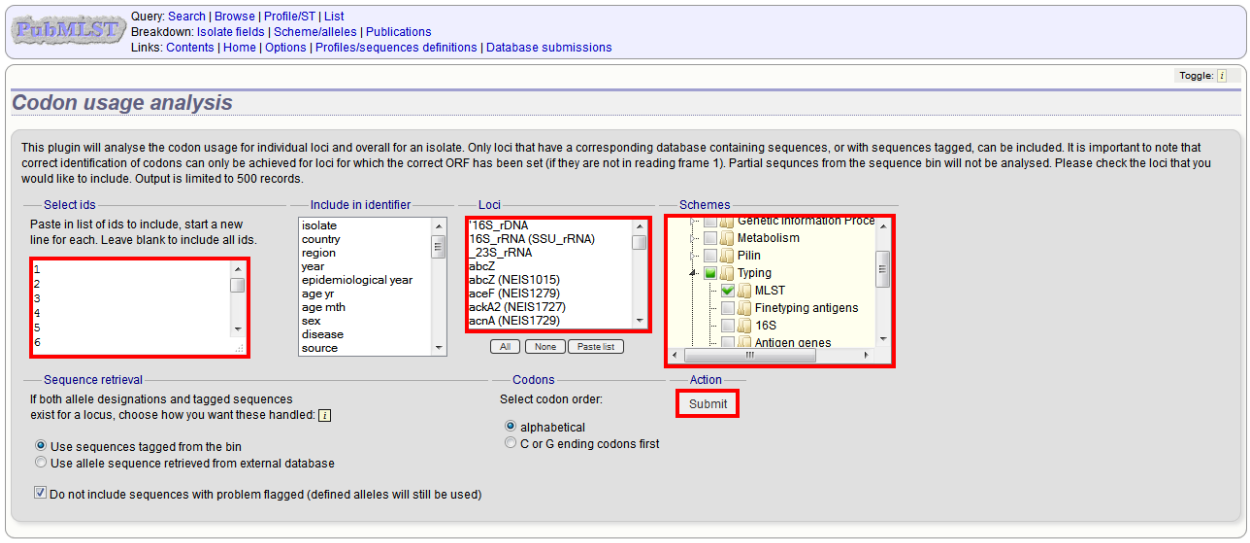


Alternatively, it can be accessed following a query by clicking the 'Codons' button in the Analysis list at the bottom of the results table. Please note that the list of functions here may vary depending on the setup of the database.

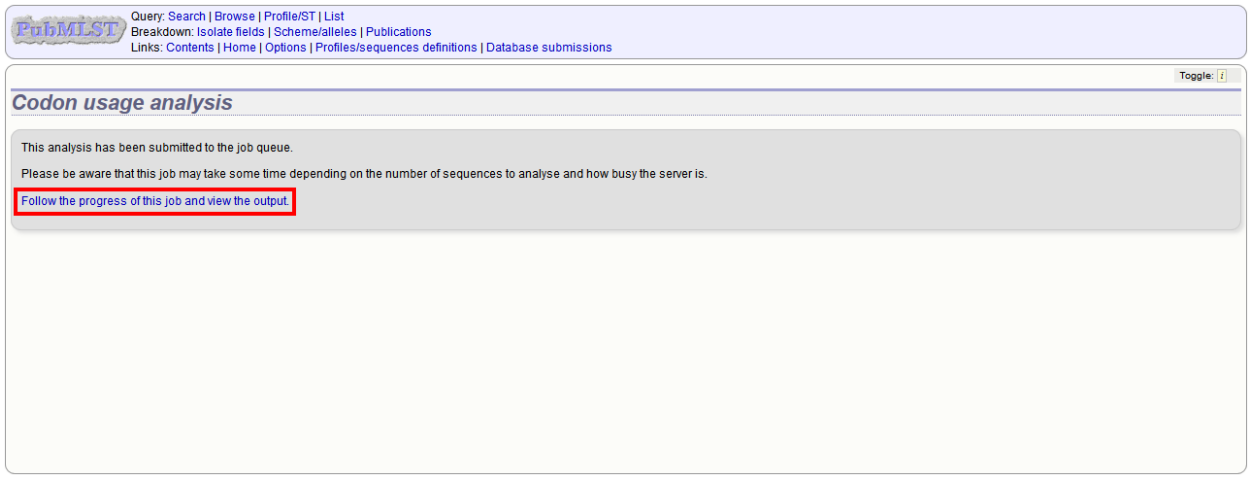


5	M00240227		UK	2000	invasive (unspecified/other)	Neisseria meningitidis	B	1100	ST-32 complex/ET-5 complex	7	16	
6	M00282207		UK	2000	invasive (unspecified/other)	Neisseria meningitidis	W	1101	ST-22 complex			
7	7891	B54; Z1054	Finland	1975	invasive (unspecified/other)	Neisseria meningitidis	A	5	ST-5 complex/subgroup III	20	9	F3-1
8	M00242007		UK	2000	invasive (unspecified/other)	Neisseria meningitidis	B	1102	ST-18 complex		14	
9	0021/84		Czech Republic	1984	invasive (unspecified/other)	Neisseria meningitidis	W	114	ST-22 complex			
10	6748	B73; Z1073	Canada	1971	invasive (unspecified/other)	Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	18-1	3	F5-1
11	129	B92; Z1092	Germany	1964	invasive (unspecified/other)	Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	5-2	10	F3-6
12	0090/89		Czech Republic	1989	invasive (unspecified/other)	Neisseria meningitidis	B	1015	ST-32 complex/ET-5 complex	7	16	
13	139M	B99; Z1099	Philippines	1968		Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	5-2	10	F5-1
14	0120/95		Czech Republic	1995	invasive (unspecified/other)	Neisseria meningitidis	X	117			14	
15	1		Germany	1999	carrier	Neisseria meningitidis	E	864				
16	2		Germany	1999	carrier	Neisseria meningitidis	B	854	ST-18 complex			
17	3		Germany	1999	carrier	Neisseria meningitidis	W	174	ST-174 complex			
18	4		Germany	1999	carrier	Neisseria meningitidis	B	19	ST-18 complex			
19	S3131	B213; Z1213	Ghana	1973	invasive (unspecified/other)	Neisseria meningitidis	A	4	ST-4 complex/subgroup IV	7	13-1	F1-5
20	5		Germany	1999	carrier	Neisseria meningitidis	NG	198	ST-198 complex			
21	6		Germany	1999	carrier	Neisseria meningitidis	NG	198	ST-198 complex			
22	7		Germany	1999	carrier	Neisseria meningitidis	E	60	ST-60 complex			
23	8		Germany	1999	carrier	Neisseria meningitidis	B	32	ST-32 complex/ET-5 complex			
24	S4355	B227; Z1227	Denmark	1974	invasive (unspecified/other)	Neisseria meningitidis	A	5	ST-5 complex/subgroup III	5-1	9	F3-1
25	9		Germany	1999	carrier	Neisseria meningitidis	B	930	ST-334 complex			

Enter the ids of the isolate records to analyse - these will be already entered if you accessed the plugin following a query. Select the loci you would like to analyse, either from the dropdown loci list, and/or by selecting one or more schemes.



Click submit. The job will be submitted to the queue and will start running shortly. Click the link to follow the job progress and view the output.



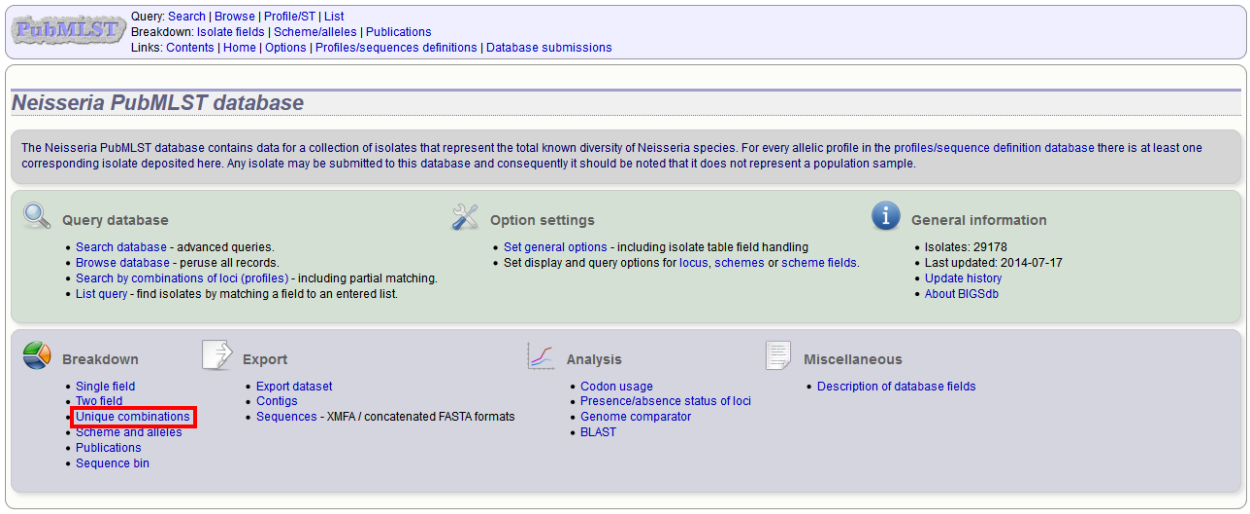
Four tab-delimited text files will be created.

- Absolute frequency of codon usage by isolate
- Absolute frequency of codon usage by locus
- Relative synonymous codon usage by isolate
- Relative synonymous codon usage by locus

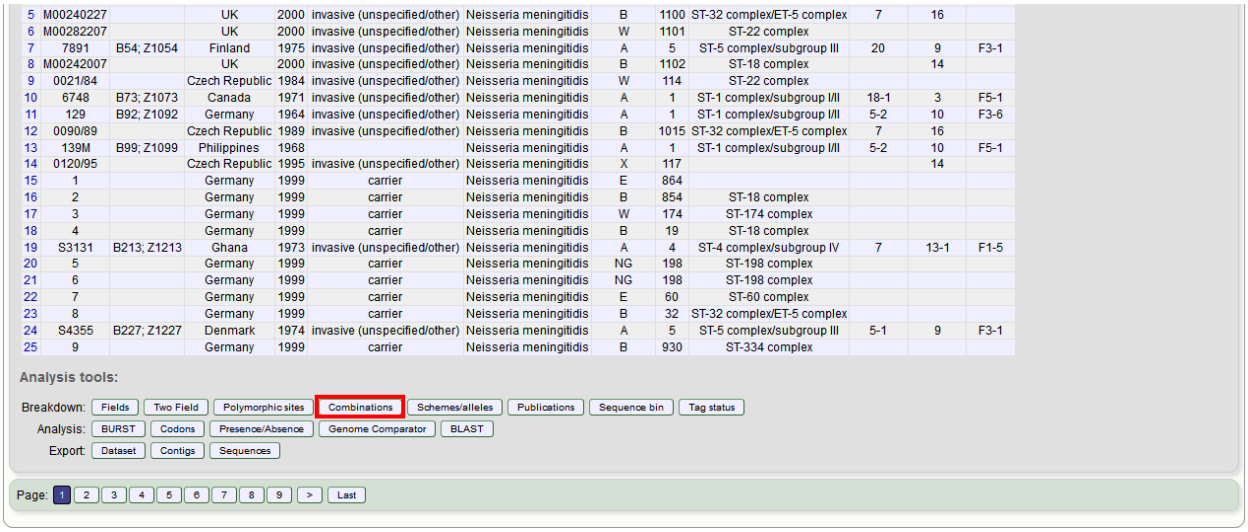
11.10 Unique combinations

The Unique Combinations plugin calculates the frequencies of unique file combinations within an isolate dataset. Provenance fields, composite fields, allele designations and scheme fields can be combined.

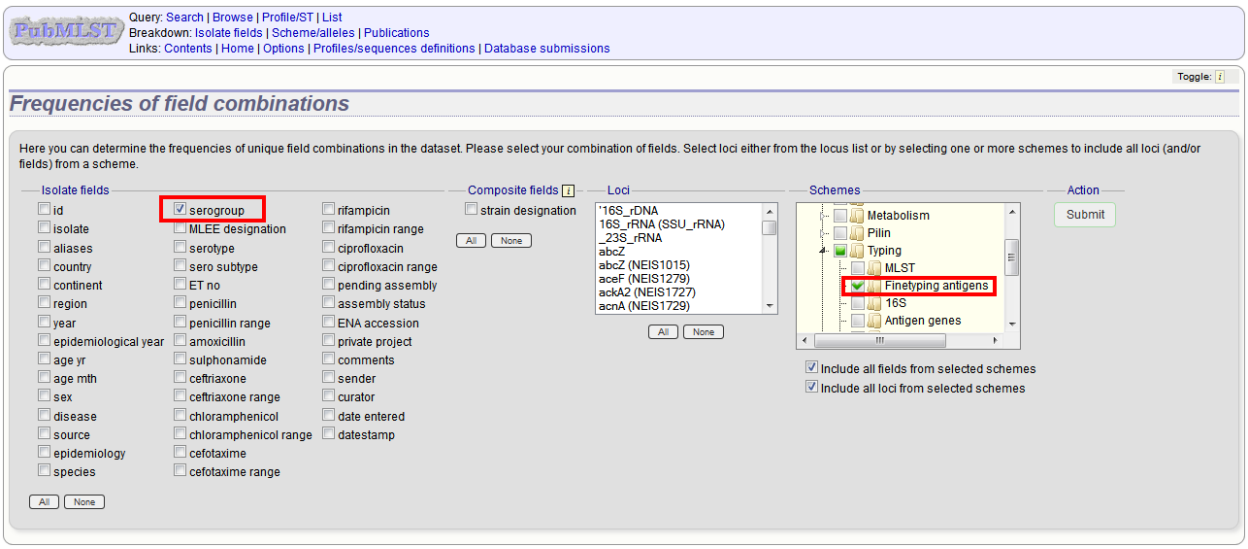
The function can be selected by clicking the 'Unique combinations' link in the Breakdown section of the main contents page. This will run the analysis on the entire database.



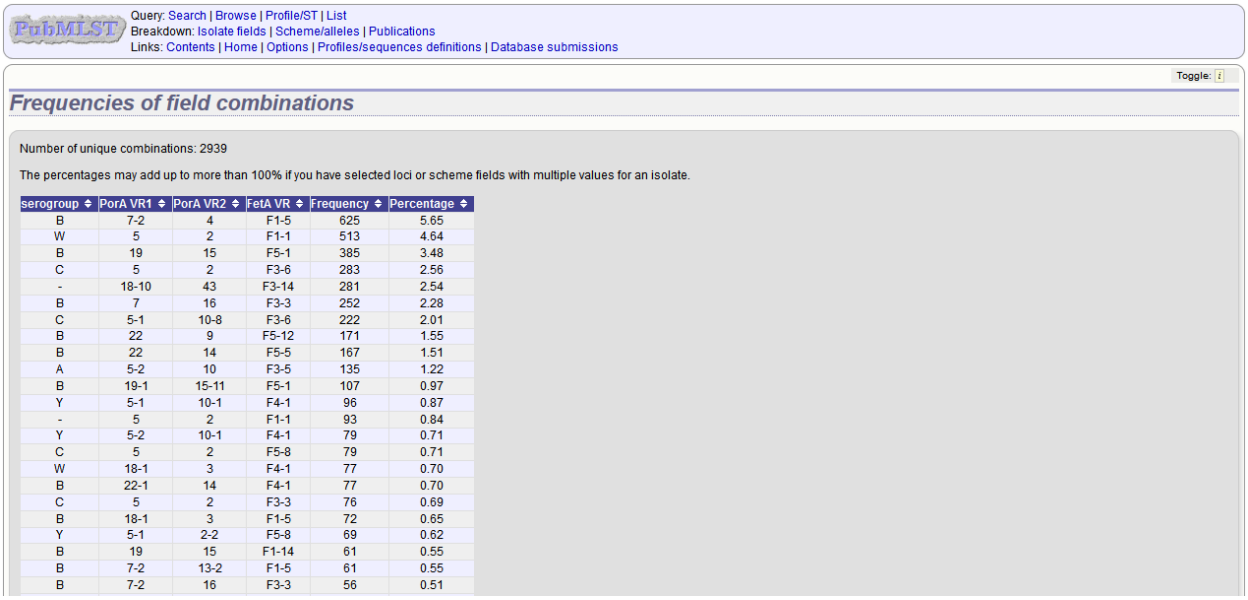
Alternatively, it can be accessed following a query by clicking the 'Combinations' button in the Breakdown list at the bottom of the results table. This will run the analysis on the dataset returned from the query. Please note that the list of functions here may vary depending on the setup of the database.



Select the combination of fields to analyse, e.g. serogroup and finetyping antigens.

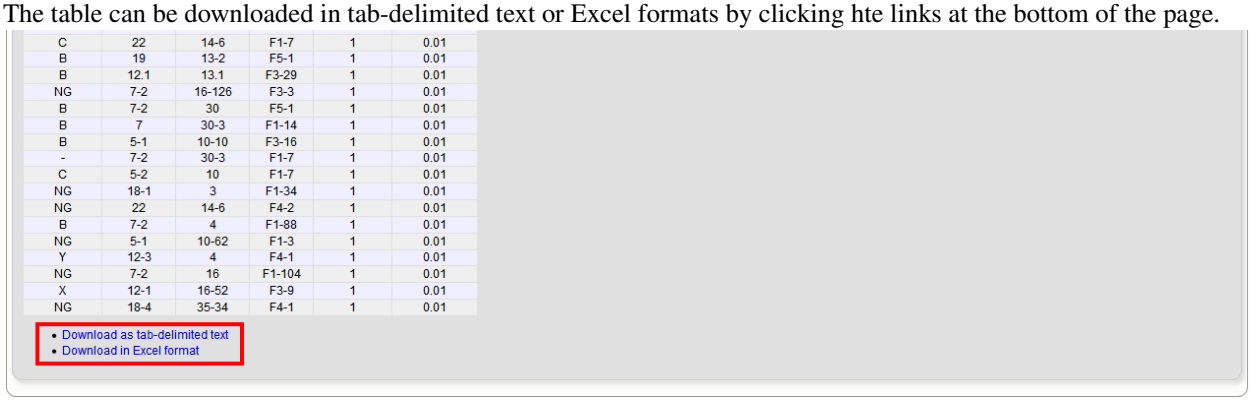


Click submit. When the analysis has completed you will see a table showing the unique combinations of the selected fields along with the frequency and percentage of the combination.



serogroup	PorA VR1	PorA VR2	FetA VR	Frequency	Percentage
B	7-2	4	F1-5	625	5.65
W	5	2	F1-1	513	4.64
B	19	15	F5-1	385	3.48
C	5	2	F3-6	283	2.56
-	18-10	43	F3-14	281	2.54
B	7	16	F3-3	252	2.28
C	5-1	10-8	F3-6	222	2.01
B	22	9	F5-12	171	1.55
B	22	14	F5-5	167	1.51
A	5-2	10	F3-5	135	1.22
B	19-1	15-11	F5-1	107	0.97
Y	5-1	10-1	F4-1	96	0.87
-	5	2	F1-1	93	0.84
Y	5-2	10-1	F4-1	79	0.71
C	5	2	F5-8	79	0.71
W	18-1	3	F4-1	77	0.70
B	22-1	14	F4-1	77	0.70
C	5	2	F3-3	76	0.69
B	18-1	3	F1-5	72	0.65
Y	5-1	2-2	F5-8	69	0.62
B	19	15	F1-14	61	0.55
B	7-2	13-2	F1-5	61	0.55
B	7-2	16	F3-3	56	0.51

The table can be downloaded in tab-delimited text or Excel formats by clicking hte links at the bottom of the page.

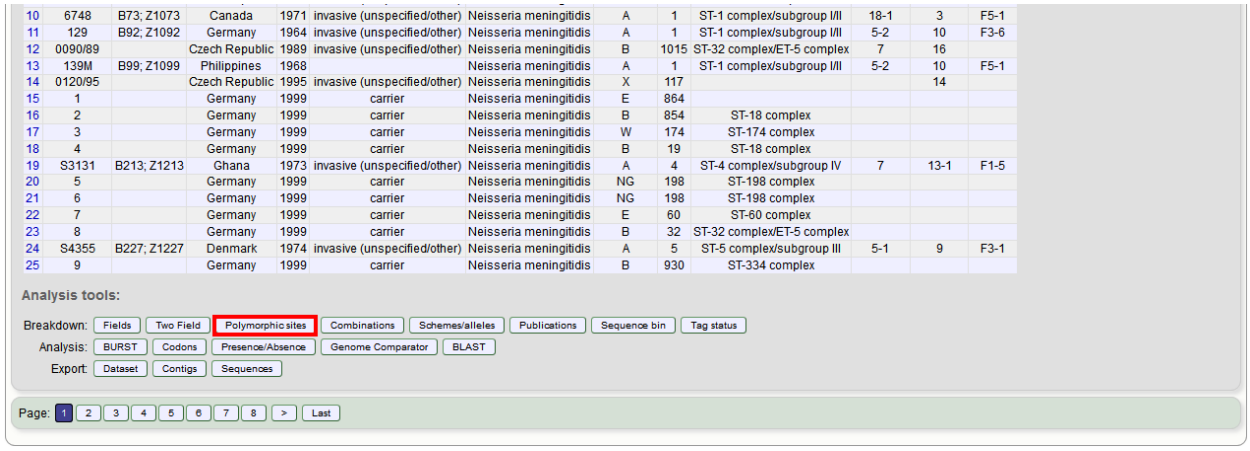


C	22	14-6	F1-7	1	0.01
B	19	13-2	F5-1	1	0.01
B	12.1	13.1	F3-29	1	0.01
NG	7-2	16-126	F3-3	1	0.01
B	7-2	30	F5-1	1	0.01
B	7	30-3	F1-14	1	0.01
B	5-1	10-10	F3-16	1	0.01
-	7-2	30-3	F1-7	1	0.01
C	5-2	10	F1-7	1	0.01
NG	18-1	3	F1-34	1	0.01
NG	22	14-6	F4-2	1	0.01
B	7-2	4	F1-88	1	0.01
NG	5-1	10-62	F1-3	1	0.01
Y	12-3	4	F4-1	1	0.01
NG	7-2	16	F1-104	1	0.01
X	12-1	16-52	F3-9	1	0.01
NG	18-4	35-34	F4-1	1	0.01

11.11 Polymorphisms

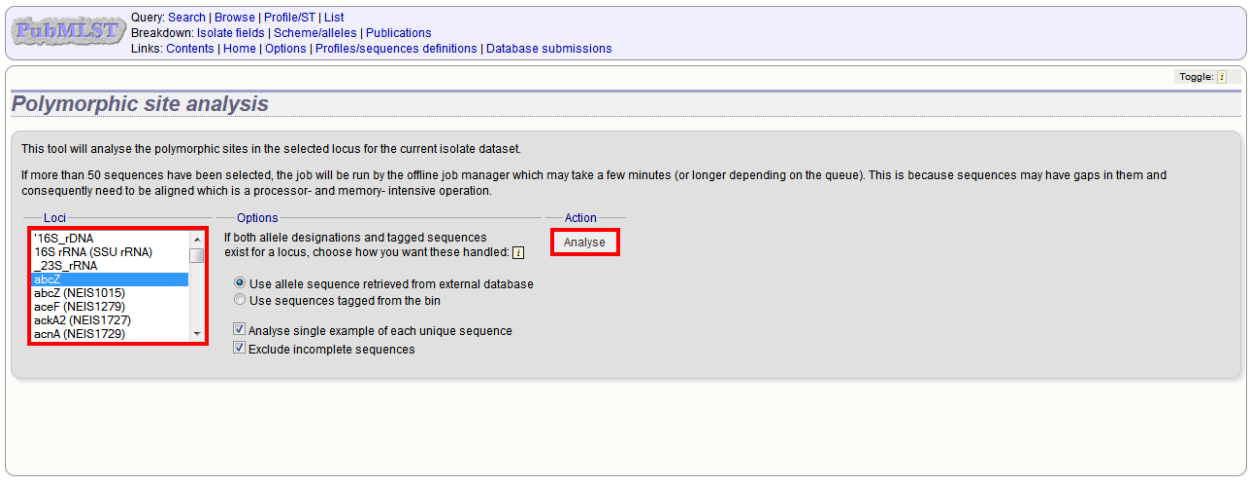
The Polymorphisms plugin generates a *Locus Explorer* polymorphic site analysis on the alleles designated in an isolate dataset following a query.

The analysis is accessed by clicking the 'Polymorphic sites' button in the Breakdown list at the bottom of a results table following a query.



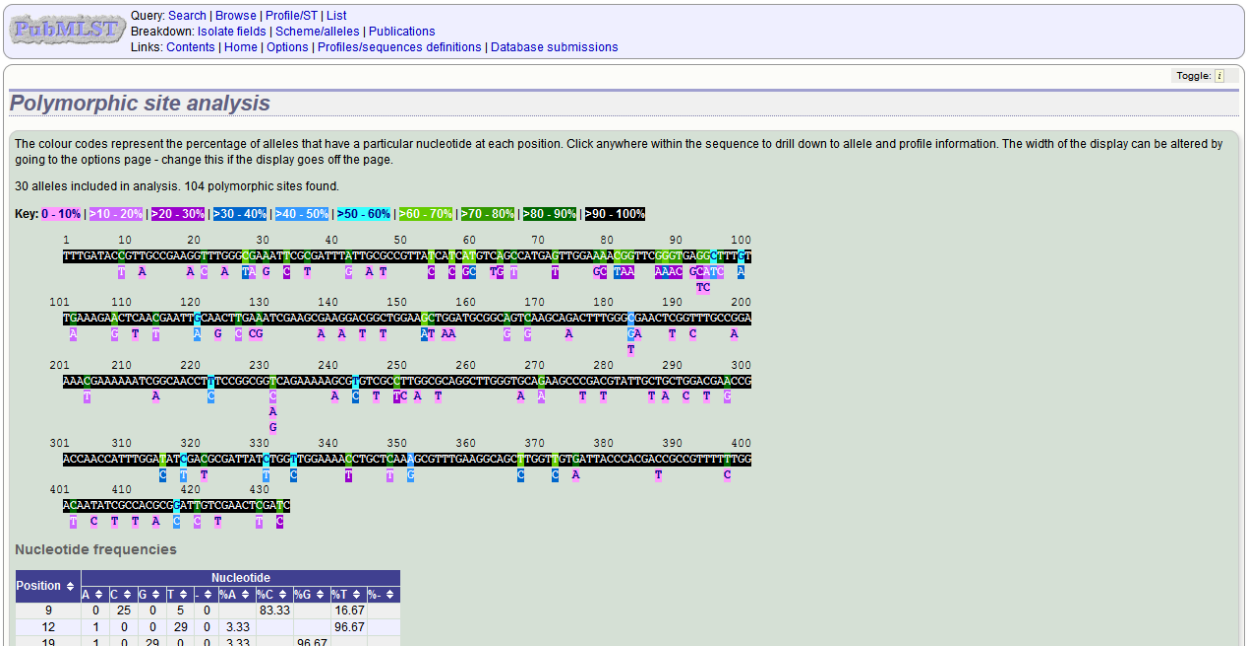
10	6748	B73; Z1073	Canada	1971	invasive (unspecified/other)	Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	18-1	3	F5-1
11	129	B92; Z1092	Germany	1964	invasive (unspecified/other)	Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	5-2	10	F3-6
12	0090/89		Czech Republic	1989	invasive (unspecified/other)	Neisseria meningitidis	B	1015	ST-32 complex/ET-5 complex	7	16	
13	139M	B99; Z1099	Philippines	1968		Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	5-2	10	F5-1
14	0120/95		Czech Republic	1995	invasive (unspecified/other)	Neisseria meningitidis	X	117			14	
15	1		Germany	1999	carrier	Neisseria meningitidis	E	864				
16	2		Germany	1999	carrier	Neisseria meningitidis	B	854	ST-18 complex			
17	3		Germany	1999	carrier	Neisseria meningitidis	W	174	ST-174 complex			
18	4		Germany	1999	carrier	Neisseria meningitidis	B	19	ST-18 complex			
19	S3131	B213; Z1213	Ghana	1973	invasive (unspecified/other)	Neisseria meningitidis	A	4	ST-4 complex/subgroup IV	7	13-1	F1-5
20	5		Germany	1999	carrier	Neisseria meningitidis	NG	198	ST-198 complex			
21	6		Germany	1999	carrier	Neisseria meningitidis	NG	198	ST-198 complex			
22	7		Germany	1999	carrier	Neisseria meningitidis	E	60	ST-60 complex			
23	8		Germany	1999	carrier	Neisseria meningitidis	B	32	ST-32 complex/ET-5 complex			
24	S4355	B227; Z1227	Denmark	1974	invasive (unspecified/other)	Neisseria meningitidis	A	5	ST-5 complex/subgroup III	5-1	9	F3-1
25	9		Germany	1999	carrier	Neisseria meningitidis	B	930	ST-334 complex			

Select the locus that you would like to analyse from the list.



Click 'Analyse'.

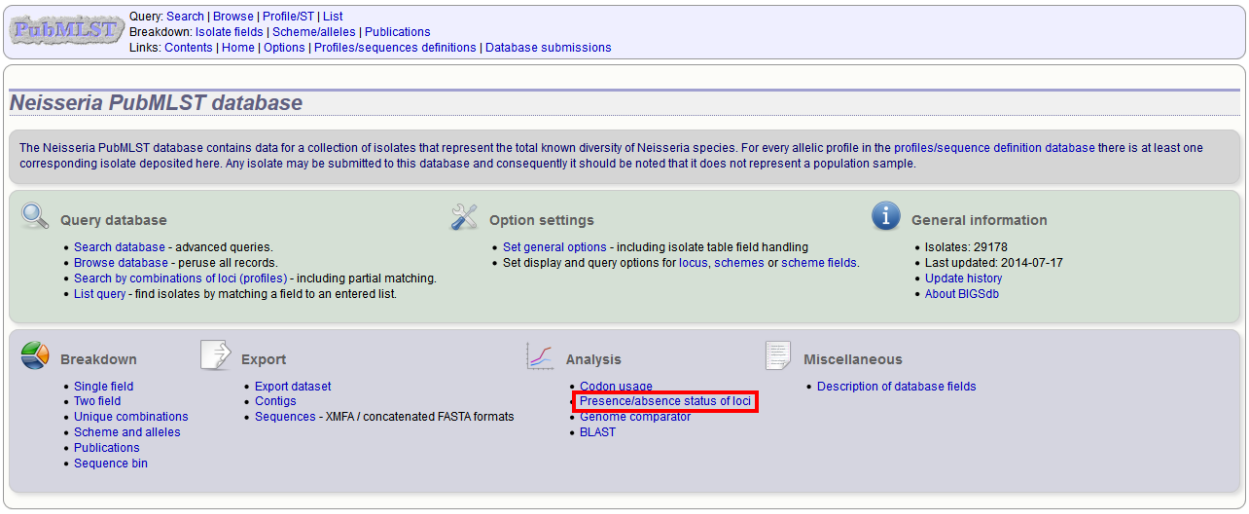
A schematic of the locus is generated showing the polymorphic sites. A full description of this can be found in the *Locus Explorer polymorphic site analysis* section.



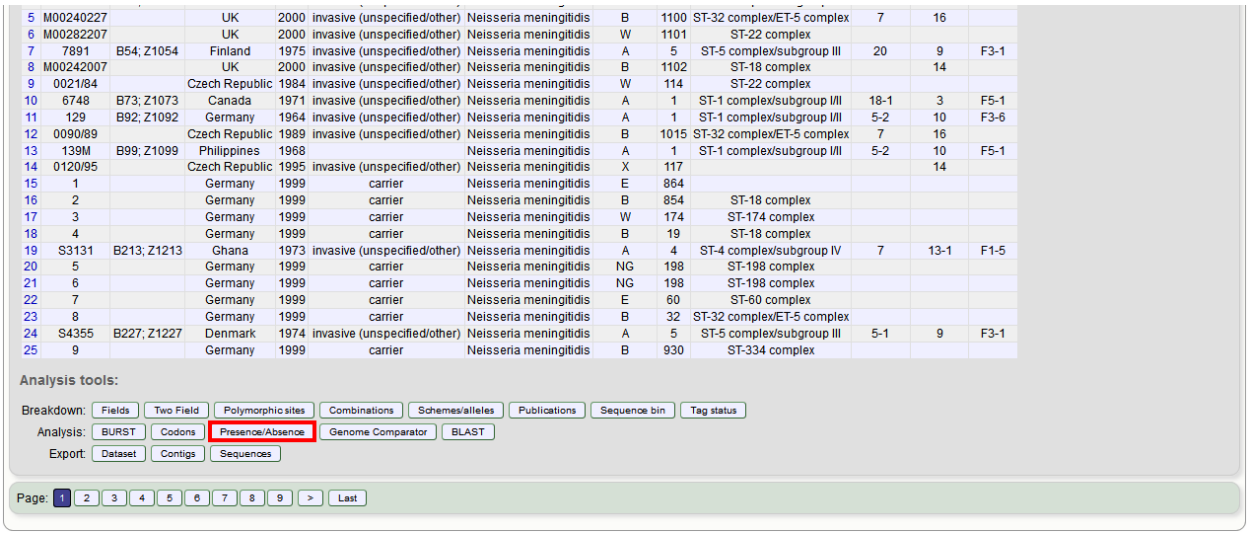
11.12 Presence/absence

This plugin displays the status of loci for isolate records. It will shown whether a locus has been designated with an allele name, has a sequence tag, or both.

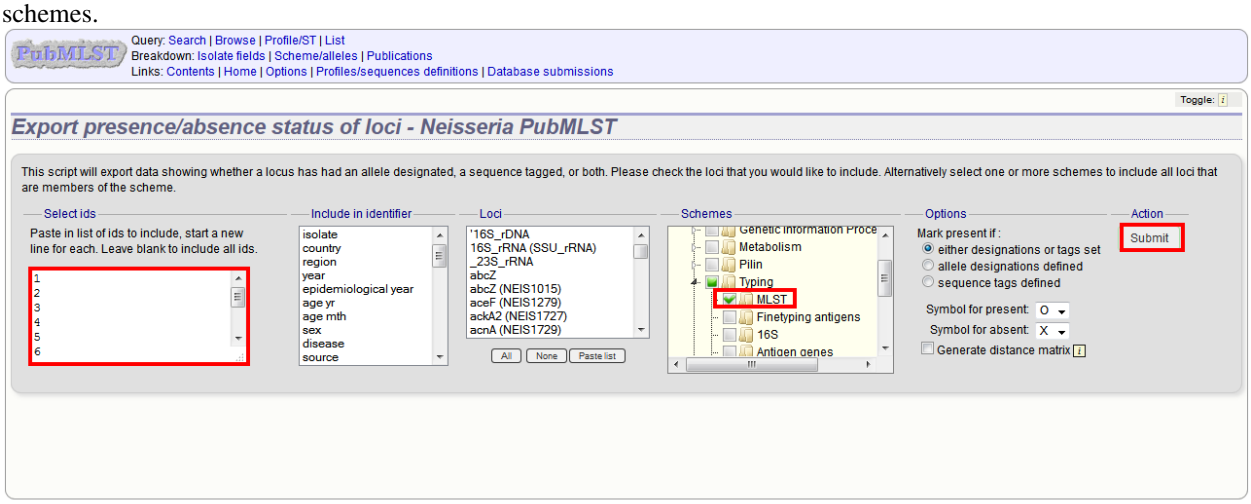
The function can be selected by clicking the 'Presence/absence status of loci' link in the 'Analysis' section of the main contents page.



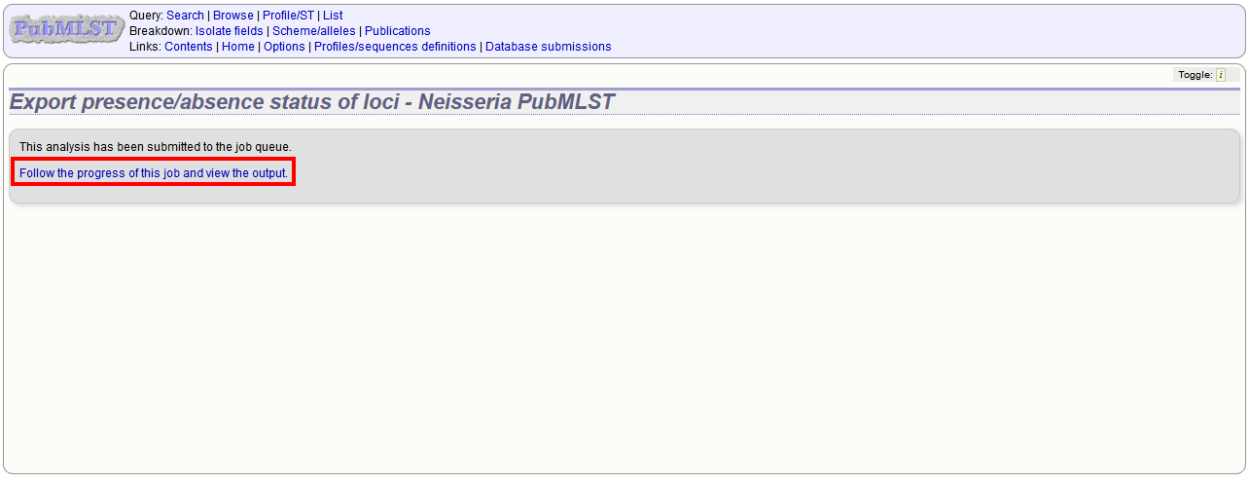
Alternatively, it can be accessed following a query by clicking the 'Presence/Absence' button in the Analysis list at the bottom of the results table. Please note that the list of functions here may vary depending on the setup of the database.



Enter the ids of the isolate records to analyse - these will be already entered if you accessed the plugin following a query. Select the loci you would like to analyse, either from the dropdown loci list, and/or by selecting one or more schemes.



Click submit. The job will be submitted to the queue and will start running shortly. Click the link to follow the job progress and view the output.



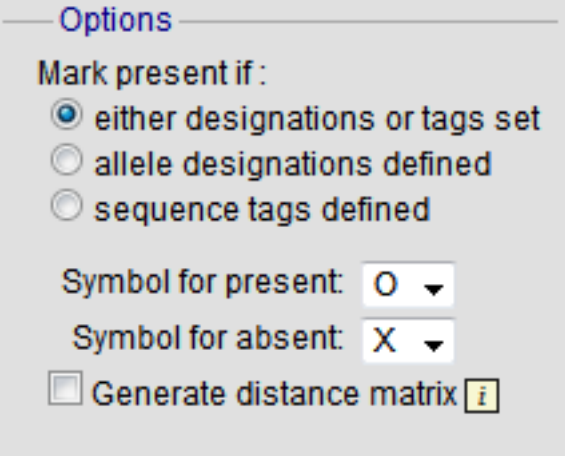
When complete, a single text file will have been generated.

This is a tab-delimited text file that uses 'O' to represent presence and 'X' to represent a missing locus designation or tag.

id	pgm	adk	abcZ	pdhC	gdh	fumC	aroE
1	O	O	O	O	O	O	O
2	O	O	O	O	O	O	O
3	O	O	O	O	O	O	O
4	O	O	O	O	O	O	O
5	O	O	O	O	O	O	O
6	O	O	O	O	O	O	O
7	O	O	O	O	O	O	O
8	O	O	O	O	O	O	O
9	O	O	O	O	O	O	O
10	O	O	O	O	O	O	O

11.12.1 Options

There are a number of options that can be selected to modify the output.

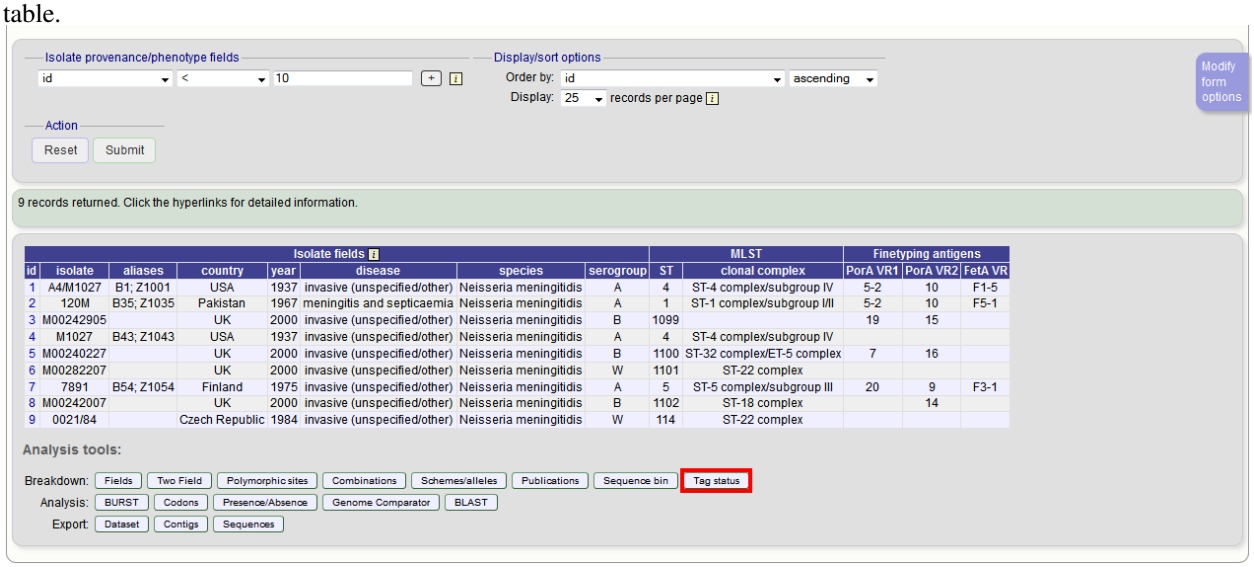


With these you can change the symbols used and whether designations, or tags, or both are counted.

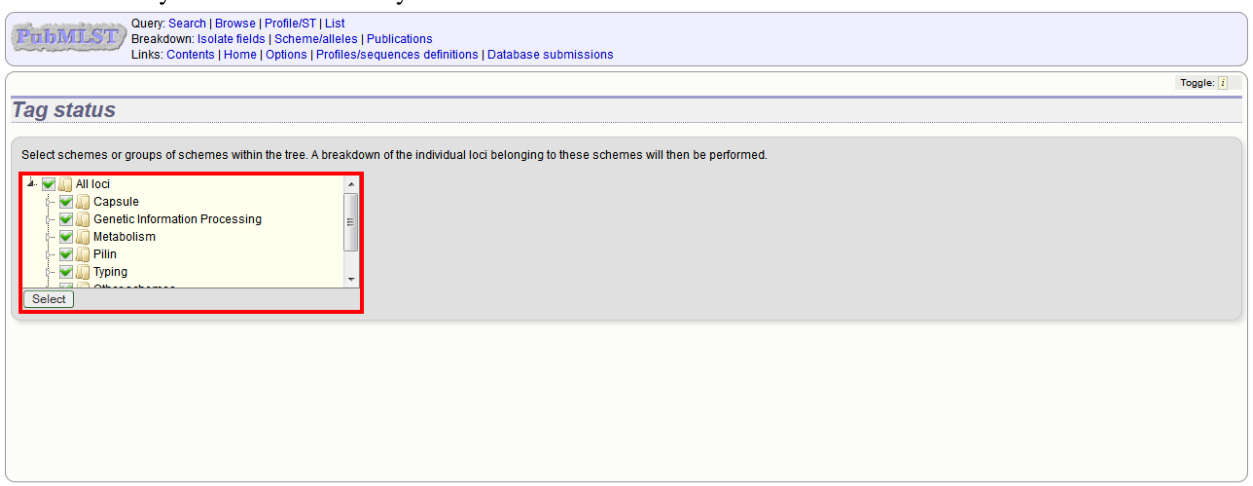
You can also choose to generate a distance matrix based on presence/absence.

11.13 Tag status

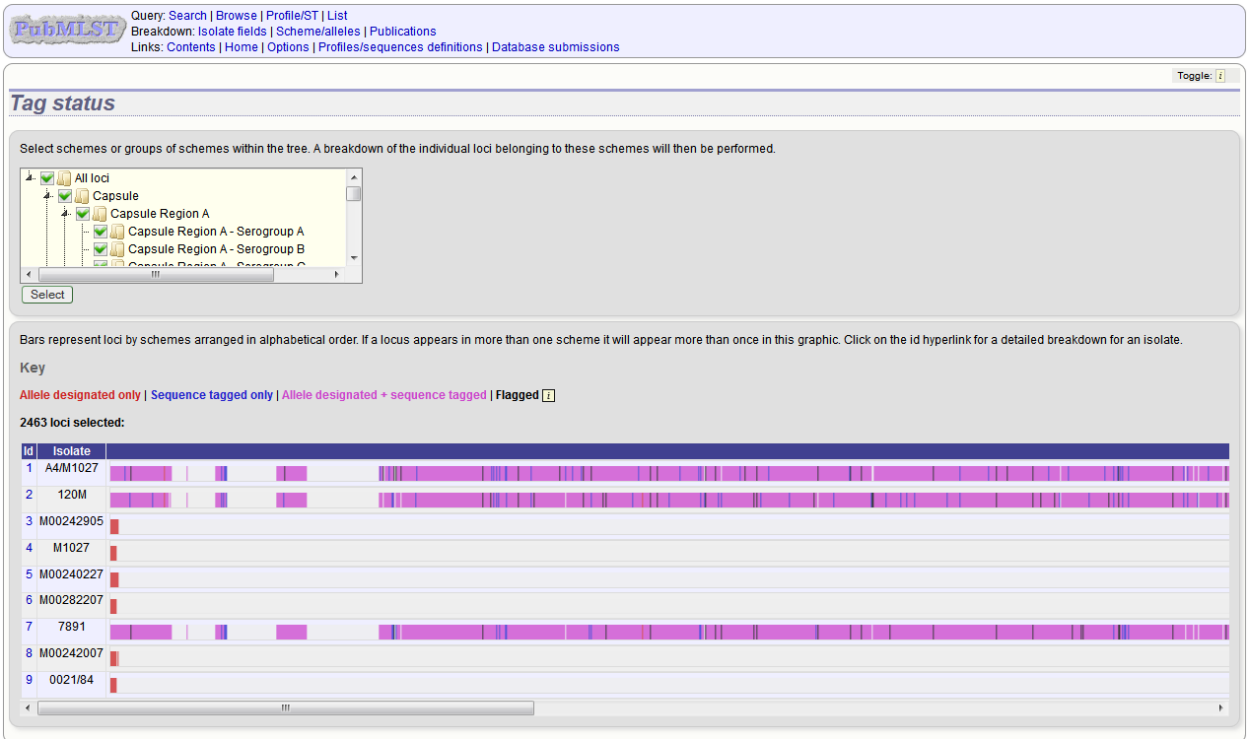
The tag status plugin displays a graphical representation of the status of loci designations or tags for isolate data. It is accessed following a query by clicking the 'Tag status' button in the Breakdown section at the bottom of the results table.



Select the loci you would like to analyse.



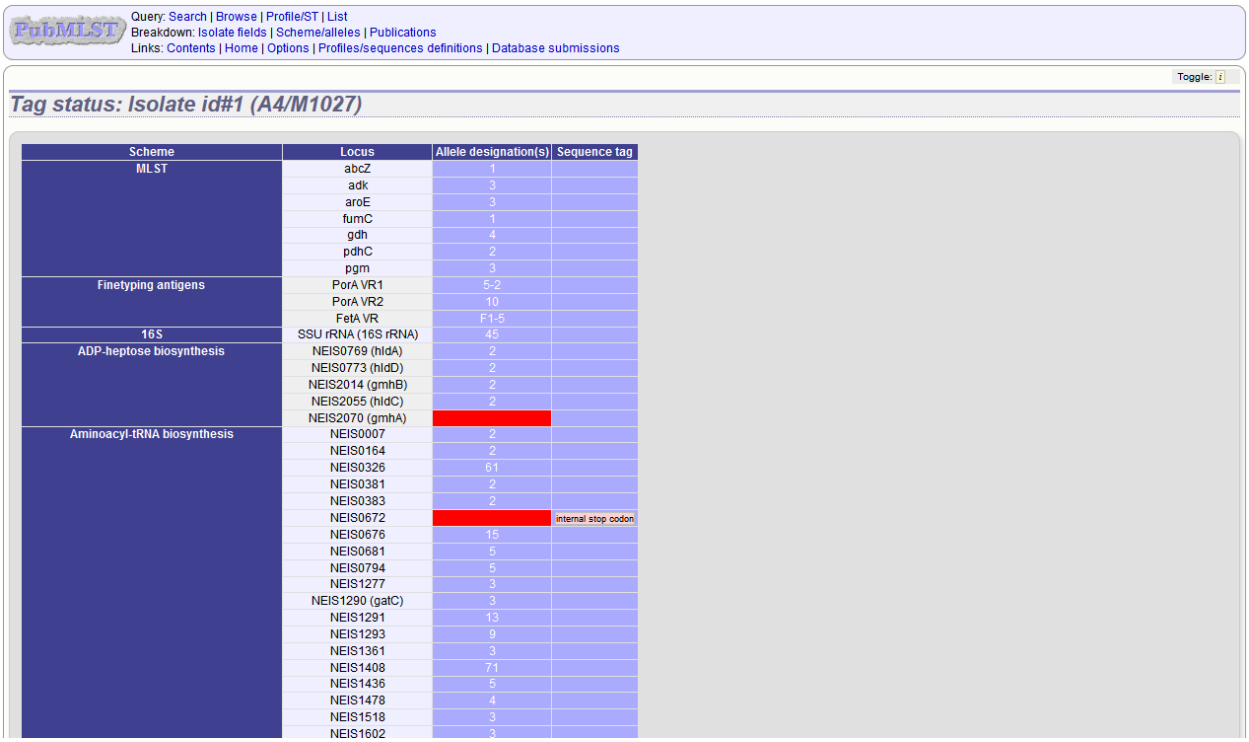
You should see a series of bars representing loci. The colour of these bars designates whether they have an allele designation only, a sequence tag only, both designations or tags, or whether they have flags set.



Hovering the mouse over the bars will indicate the scheme represented.

Note: Loci will be represented more than once if they are members of multiple selected schemes.

Clicking any of the isolate id hyperlinks navigates to a page that breaks down the exacty status for all loci of that isolate.



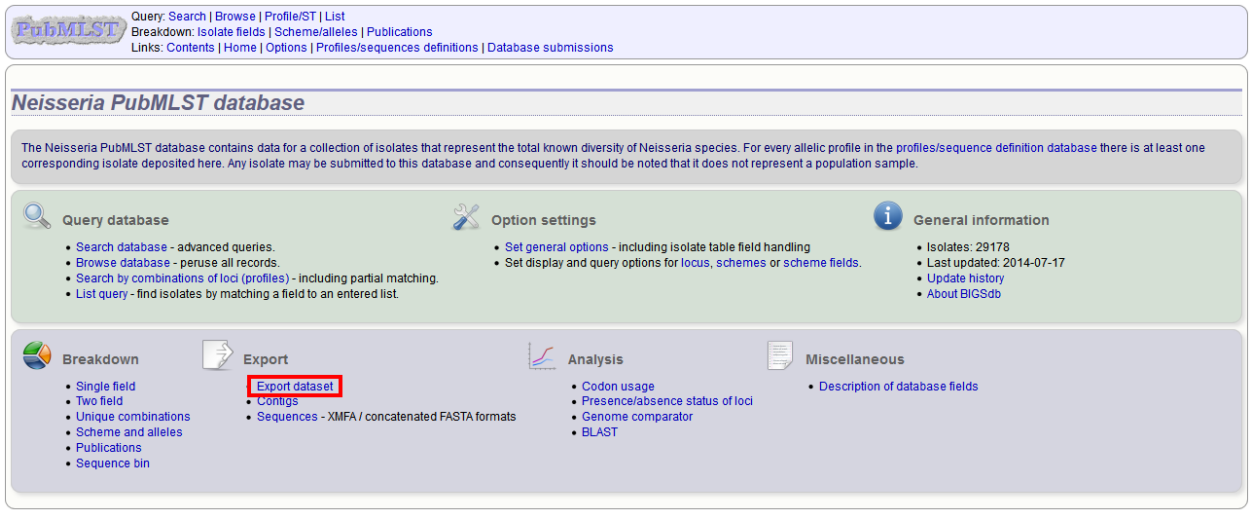
There is a column each for allele designations and sequence tags. If an allele designation is defined, the allele identifier is displayed. Cells shaded in blue show that the designation or tag is present, whereas red indicates thet they are absent.

CHAPTER 12

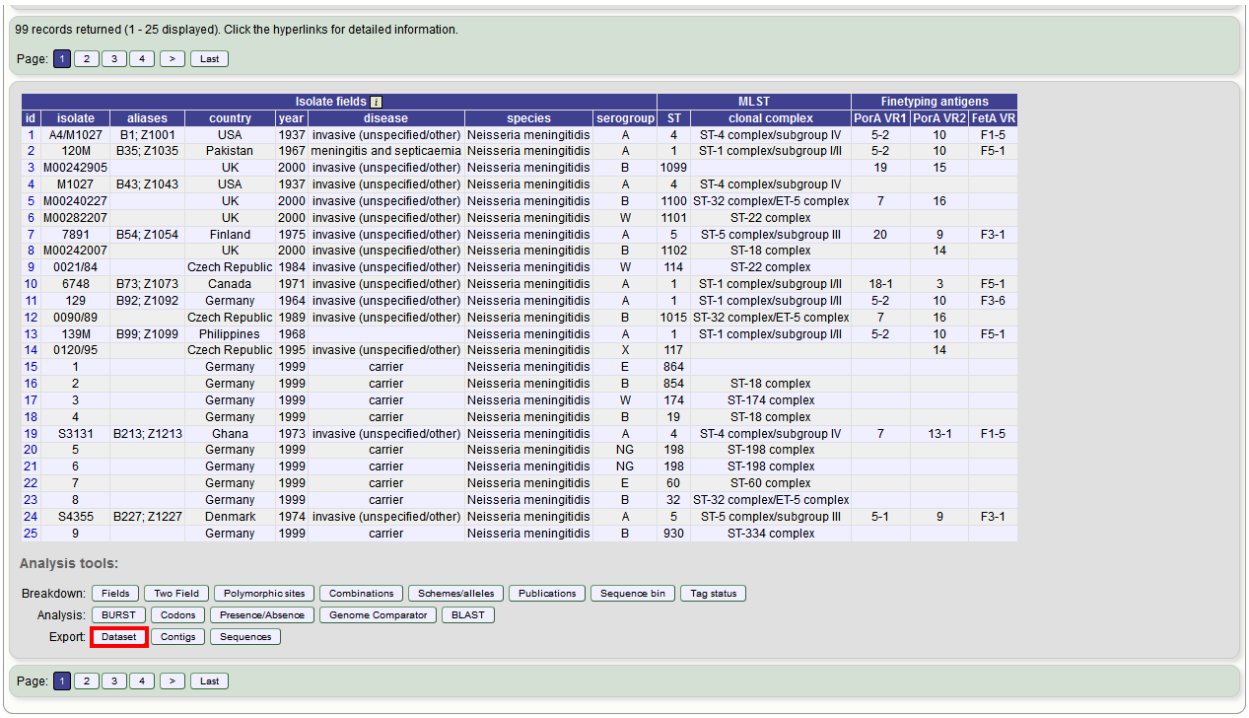
Data export plugins

12.1 Isolate record export

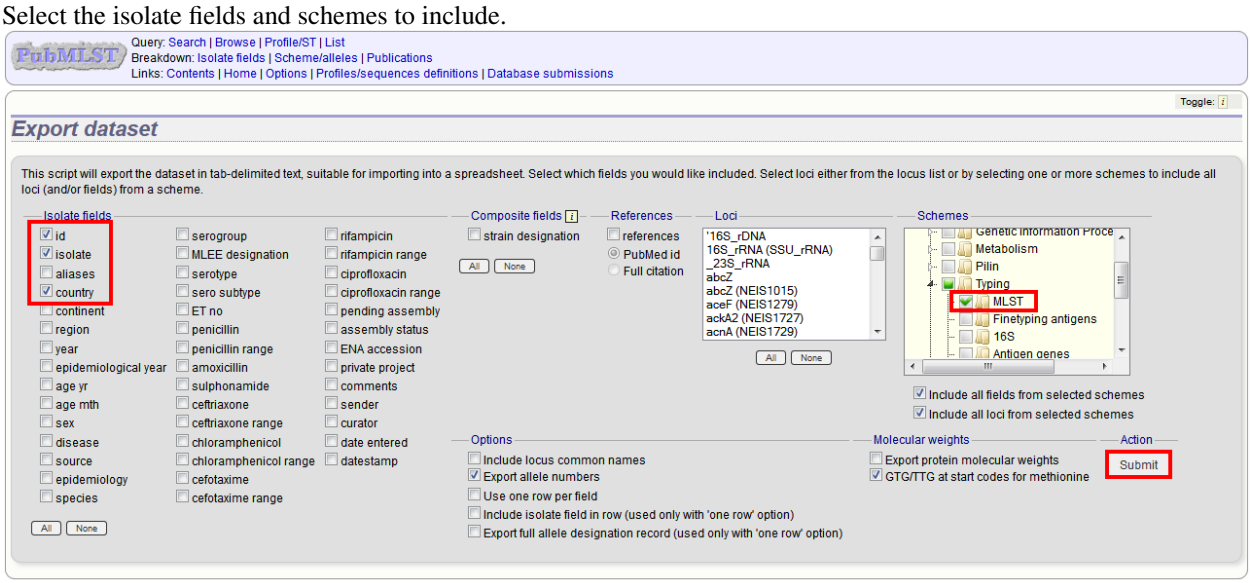
You can export the entire isolate recordset by clicking the 'Export dataset' link in the Export section of the main contents page.



Alternatively, you can export the recordsets of isolates returned from a database query by clicking the 'Dataset' button in the Export list at the bottom of the results table. Please note that the list of functions here may vary depending on the setup of the database.



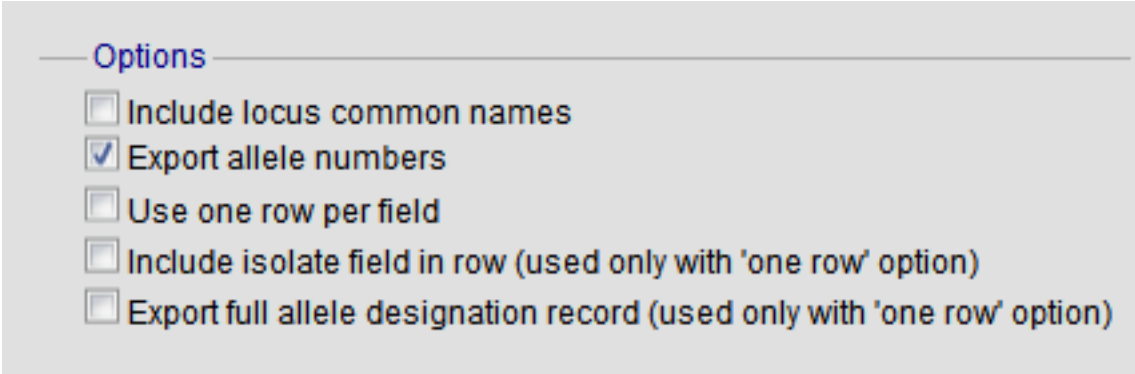
Select the isolate fields and schemes to include.



Click Submit.

You can then download the data in tab-delimited text or Excel formats.

12.1.1 Advanced options

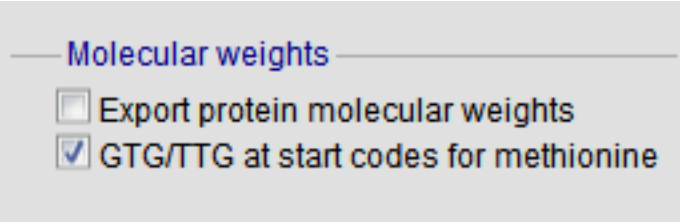


The options fieldset has the following options.

- Include locus common names - any common name for the locus is displayed in parentheses following the primary name.
- Export allele numbers - the allele designation is included for any locus included.
- Use one row per field - this is an alternative output format where instead of each locus and field having a separate column, each field is export on a separate row.
- Include isolate field in row - the name of the isolate is included as a separate column when exporting in 'one row per field' fomrmat.
- Export full allele designation record - export sender, curator and datestamp information as separate rows when exporting allele designation data.

12.1.2 Molecular weight calculation

The plugin can also calculate the predicted molecular weight of the gene product of any allele designated in the dataset.

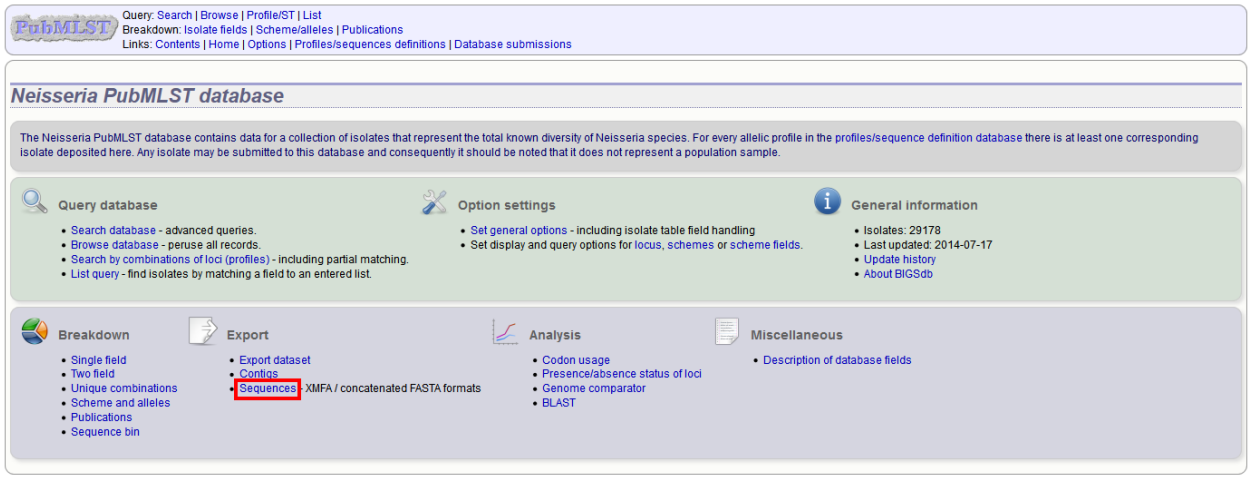


Click the 'Export protein molecular weight' checkbox. Additional columns (or rows depending on the output format) will be created to include the molecular weight data.

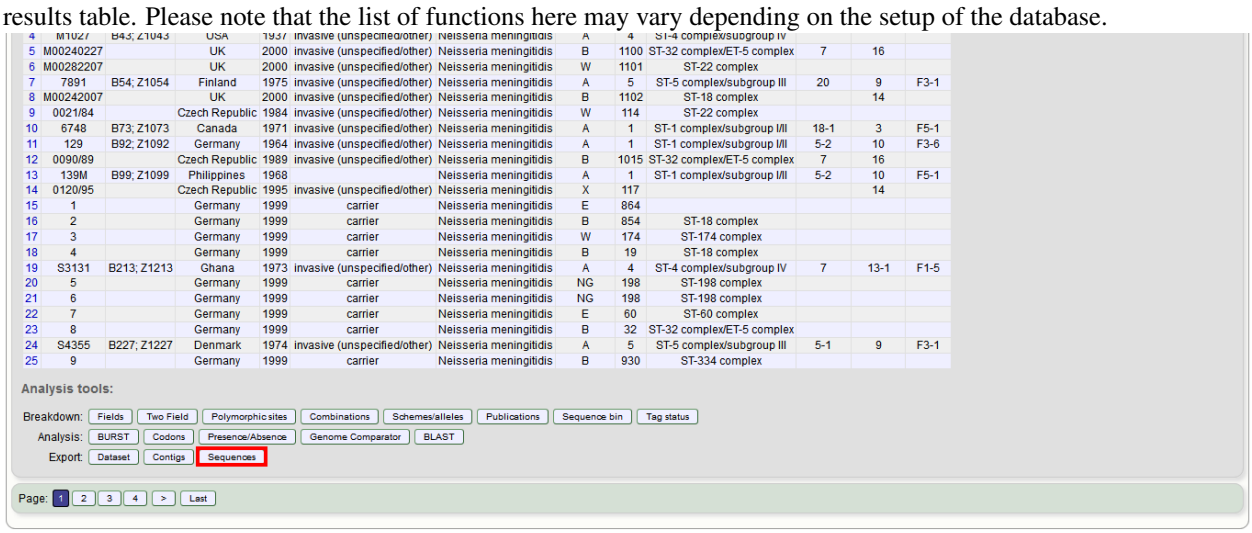
12.2 Sequence export

You can export the sequences for any set of loci designated in isolate records, or belonging to scheme profiles in the sequence definition database.

The sequence export function can be accessed by clicking the 'Sequences' link inthe Export section of the contents page.

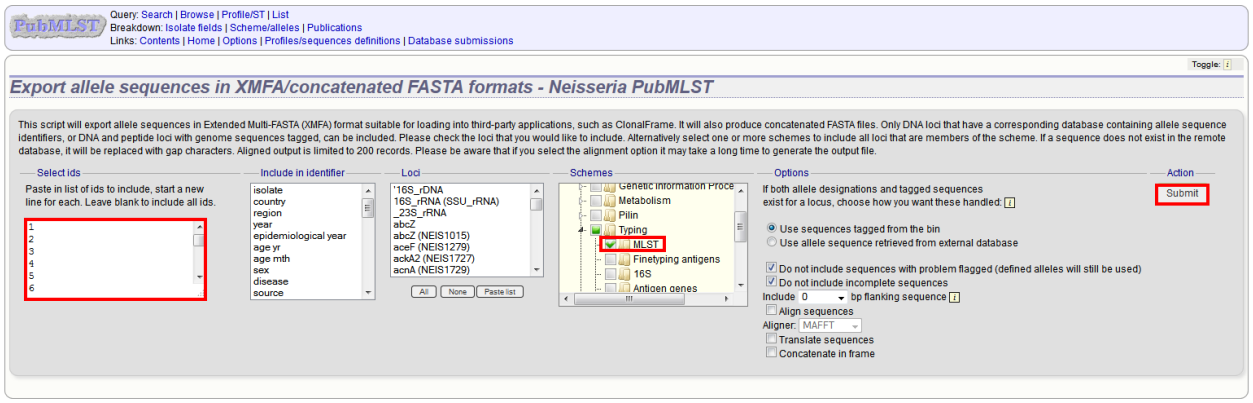


Alternatively, you can access this function by clicking the 'Sequences' button in the Export list at the bottom of the results table. Please note that the list of functions here may vary depending on the setup of the database.

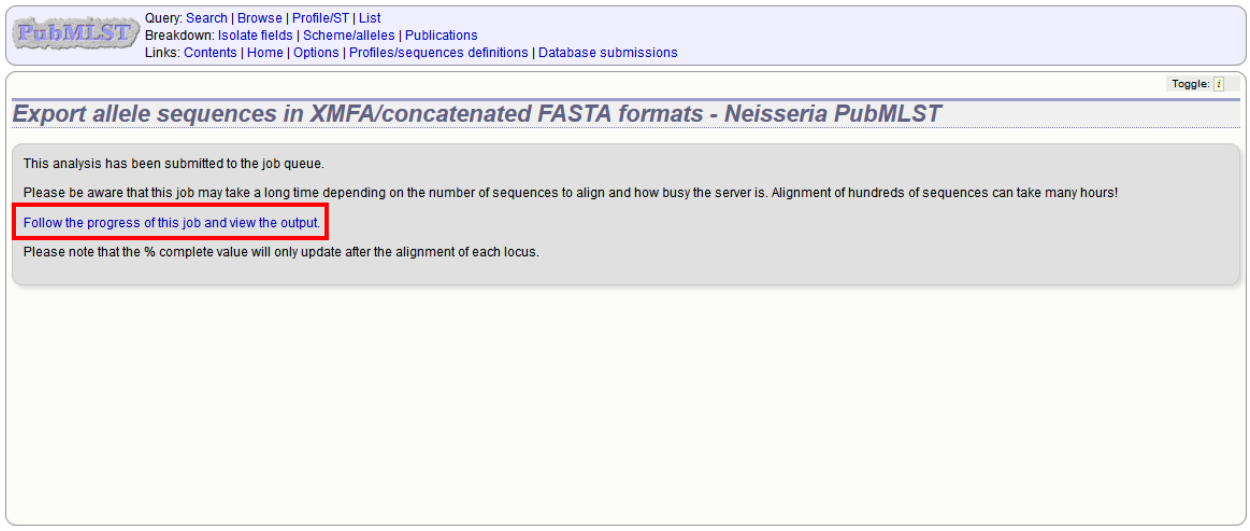


4	M1027	B43; Z1043	USA	1937	invasive (unspecified/other)	Neisseria meningitidis	A	4	ST-4 complex/subgroup IV			
5	M00240227		UK	2000	invasive (unspecified/other)	Neisseria meningitidis	B	1100	ST-32 complex/ET-5 complex	7	16	
6	M00282207		UK	2000	invasive (unspecified/other)	Neisseria meningitidis	W	1101	ST-22 complex			
7	7891	B54; Z1054	Finland	1975	invasive (unspecified/other)	Neisseria meningitidis	A	5	ST-5 complex/subgroup III	20	9	F3-1
8	M00242007		UK	2000	invasive (unspecified/other)	Neisseria meningitidis	B	1102	ST-18 complex		14	
9	0021/84		Czech Republic	1984	invasive (unspecified/other)	Neisseria meningitidis	W	114	ST-22 complex			
10	6748	B73; Z1073	Canada	1971	invasive (unspecified/other)	Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	18-1	3	F5-1
11	129	B92; Z1092	Germany	1964	invasive (unspecified/other)	Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	5-2	10	F3-6
12	0090/89		Czech Republic	1989	invasive (unspecified/other)	Neisseria meningitidis	B	1015	ST-32 complex/ET-5 complex	7	16	
13	139M	B99; Z1099	Philippines	1968		Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	5-2	10	F5-1
14	0120/95		Czech Republic	1995	invasive (unspecified/other)	Neisseria meningitidis	X	117			14	
15	1		Germany	1999	carrier	Neisseria meningitidis	E	864				
16	2		Germany	1999	carrier	Neisseria meningitidis	B	854	ST-18 complex			
17	3		Germany	1999	carrier	Neisseria meningitidis	W	174	ST-174 complex			
18	4		Germany	1999	carrier	Neisseria meningitidis	B	19	ST-18 complex			
19	S3131	B213; Z1213	Ghana	1973	invasive (unspecified/other)	Neisseria meningitidis	A	4	ST-4 complex/subgroup IV	7	13-1	F1-5
20	5		Germany	1999	carrier	Neisseria meningitidis	NG	198	ST-198 complex			
21	6		Germany	1999	carrier	Neisseria meningitidis	NG	198	ST-198 complex			
22	7		Germany	1999	carrier	Neisseria meningitidis	E	60	ST-60 complex			
23	8		Germany	1999	carrier	Neisseria meningitidis	B	32	ST-32 complex/ET-5 complex			
24	S4355	B227; Z1227	Denmark	1974	invasive (unspecified/other)	Neisseria meningitidis	A	5	ST-5 complex/subgroup III	5-1	9	F3-1
25	9		Germany	1999	carrier	Neisseria meningitidis	B	930	ST-334 complex			

Select the isolate or profile records to analyse - these will be pre-selected if you accessed the plugin following a query. Select the loci to include either directly within the loci list and/or using the schemes tree.



Click submit.

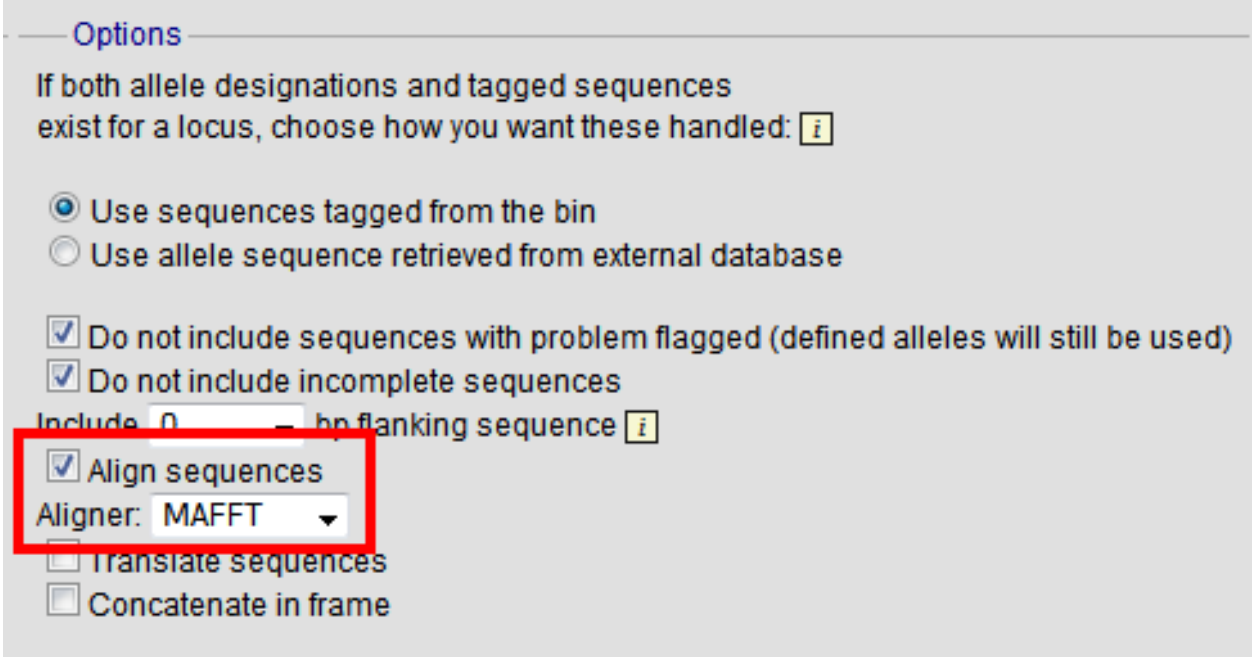


The job will be submitted to the job queue. Click the link to follow the progress and download the resulting files.

Sequences will be export in XMFA and FASTA file formats.

12.2.1 Aligning sequences

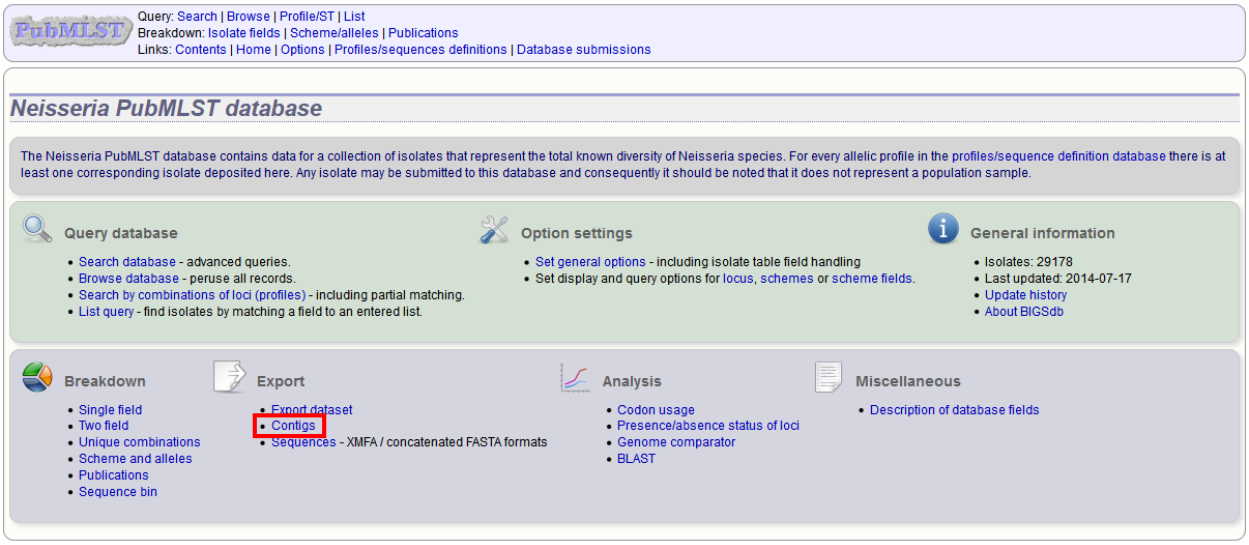
By default, sequences will be exported unaligned - this is very quick since no processing is required. You can choose to align the sequences by checking the 'Align sequences' checkbox.



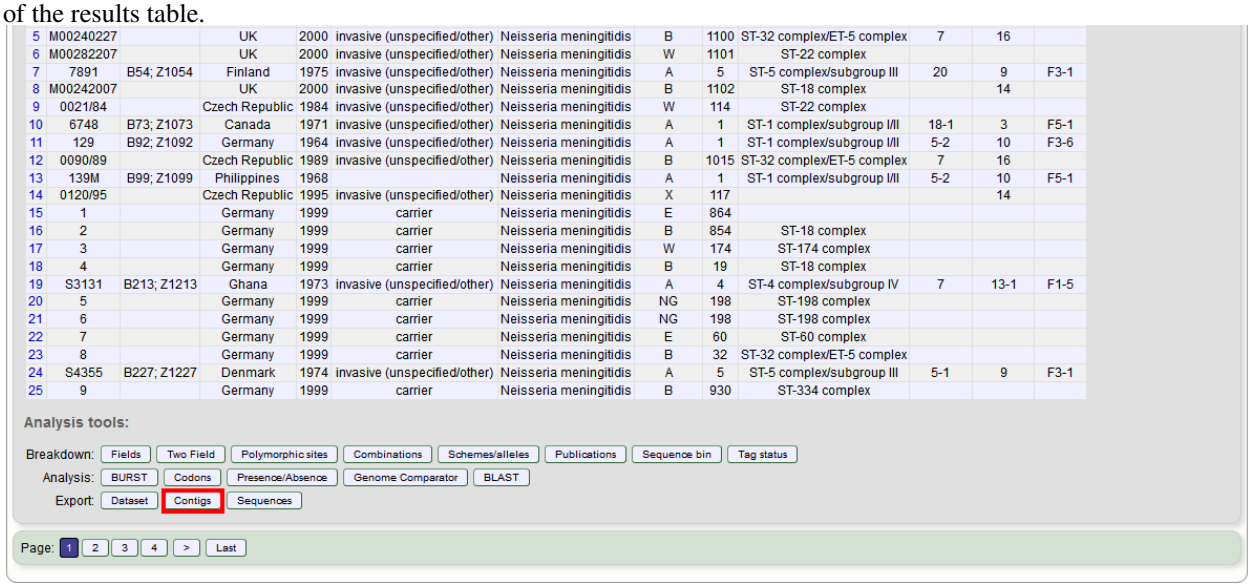
You can also choose to use MUSCLE or MAFFT as the aligner. MAFFT is the default choice and is usually much quicker than MUSCLE. Both produce comparable results.

12.3 Contig export

The contig export plugin can be accessed by clicking the 'Contigs' link in the Export section of the contents page of isolate databases.

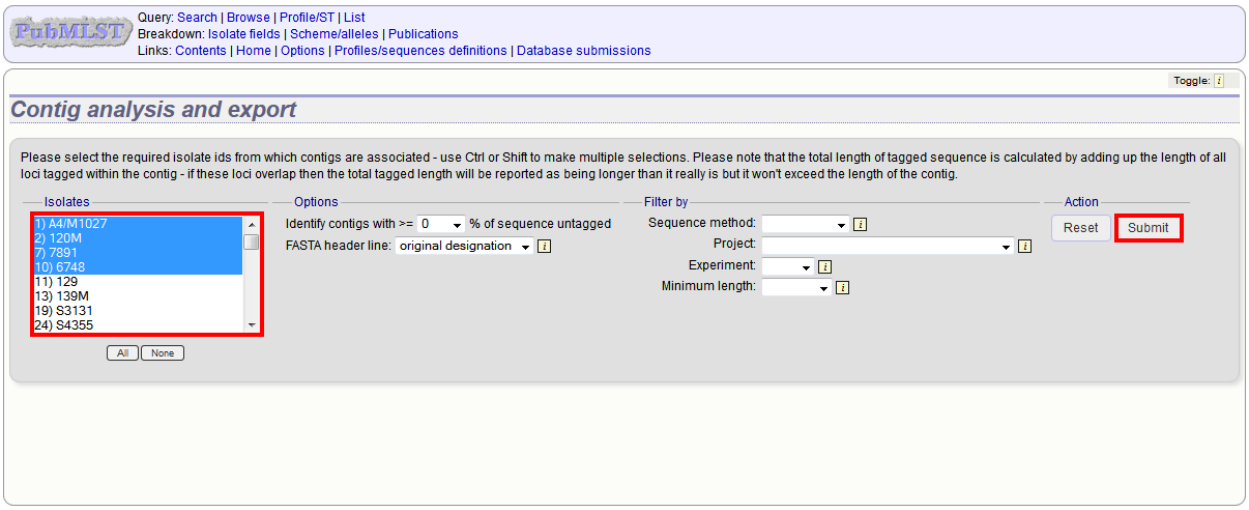


Alternatively, it can be accessed following a query by clicking the 'Contigs' button in the Export section at the bottom of the results table.



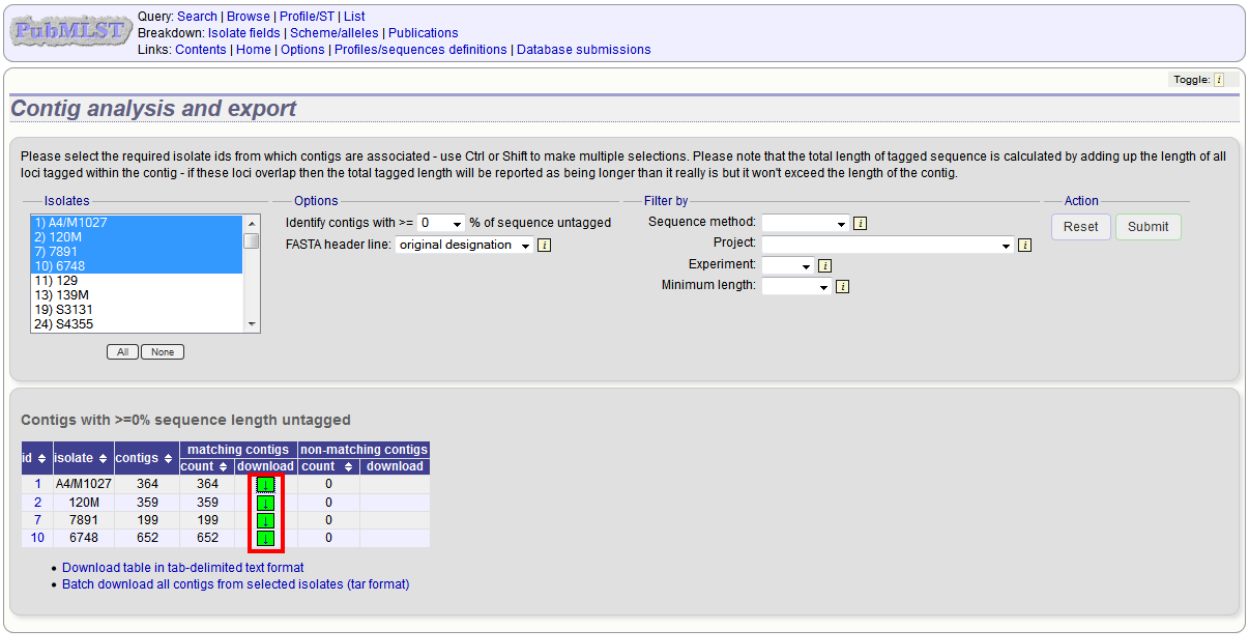
5	M00240227		UK	2000	invasive (unspecified/other)	Neisseria meningitidis	B	1100	ST-32 complex/ET-5 complex	7	16	
6	M00282207		UK	2000	invasive (unspecified/other)	Neisseria meningitidis	W	1101	ST-22 complex			
7	7891	B54; Z1054	Finland	1975	invasive (unspecified/other)	Neisseria meningitidis	A	5	ST-5 complex/subgroup III	20	9	F3-1
8	M00242007		UK	2000	invasive (unspecified/other)	Neisseria meningitidis	B	1102	ST-18 complex		14	
9	0021/84		Czech Republic	1984	invasive (unspecified/other)	Neisseria meningitidis	W	114	ST-22 complex			
10	6748	B73; Z1073	Canada	1971	invasive (unspecified/other)	Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	18-1	3	F5-1
11	129	B92; Z1092	Germany	1964	invasive (unspecified/other)	Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	5-2	10	F3-6
12	0090/89		Czech Republic	1989	invasive (unspecified/other)	Neisseria meningitidis	B	1015	ST-32 complex/ET-5 complex	7	16	
13	139M	B99; Z1099	Philippines	1968		Neisseria meningitidis	A	1	ST-1 complex/subgroup I/II	5-2	10	F5-1
14	0120/95		Czech Republic	1995	invasive (unspecified/other)	Neisseria meningitidis	X	117			14	
15	1		Germany	1999	carrier	Neisseria meningitidis	E	864				
16	2		Germany	1999	carrier	Neisseria meningitidis	B	854	ST-18 complex			
17	3		Germany	1999	carrier	Neisseria meningitidis	W	174	ST-174 complex			
18	4		Germany	1999	carrier	Neisseria meningitidis	B	19	ST-18 complex			
19	S3131	B213; Z1213	Ghana	1973	invasive (unspecified/other)	Neisseria meningitidis	A	4	ST-4 complex/subgroup IV	7	13-1	F1-5
20	5		Germany	1999	carrier	Neisseria meningitidis	NG	198	ST-198 complex			
21	6		Germany	1999	carrier	Neisseria meningitidis	NG	198	ST-198 complex			
22	7		Germany	1999	carrier	Neisseria meningitidis	E	60	ST-60 complex			
23	8		Germany	1999	carrier	Neisseria meningitidis	B	32	ST-32 complex/ET-5 complex			
24	S4355	B227; Z1227	Denmark	1974	invasive (unspecified/other)	Neisseria meningitidis	A	5	ST-5 complex/subgroup III	5-1	9	F3-1
25	9		Germany	1999	carrier	Neisseria meningitidis	B	930	ST-334 complex			

Select the isolates for which you wish to export contig data for. If the export function was accessed following a query, isolates returned in the query will be pre-selected.

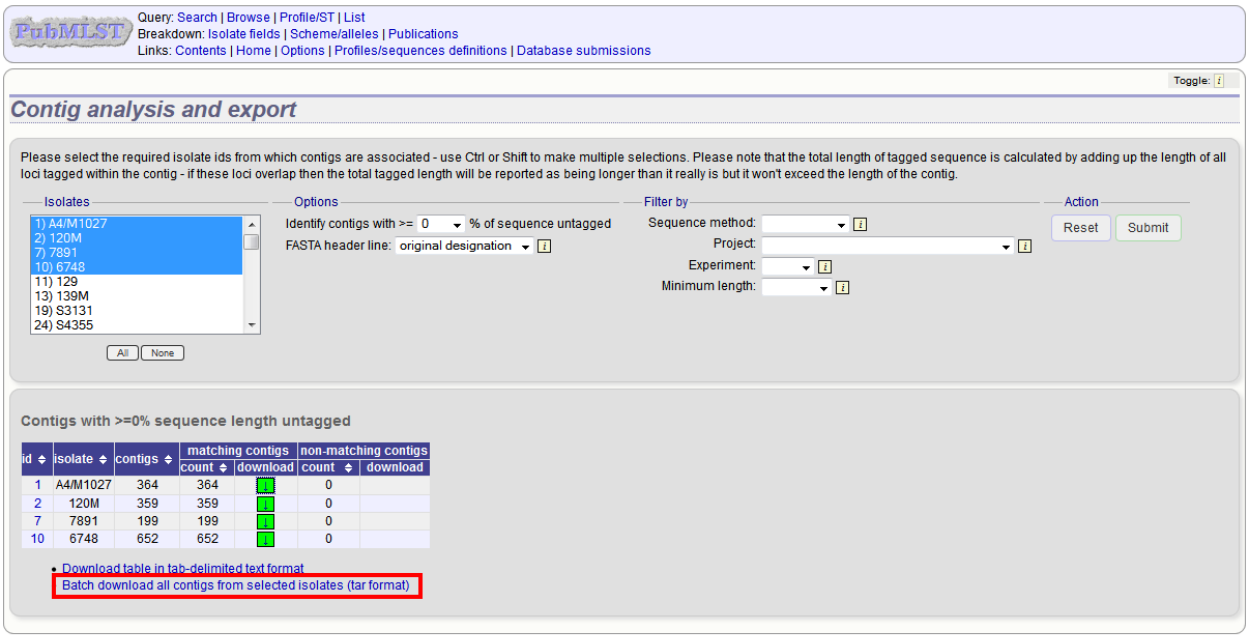


At its simplest, press submit.

A table will be produced with download links. Clicking these will produce the contigs in FASTA format.



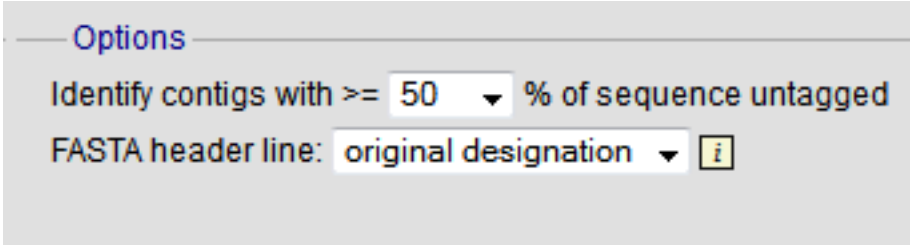
You can also download all the data in a tar file by clicking the 'Batch download' link.



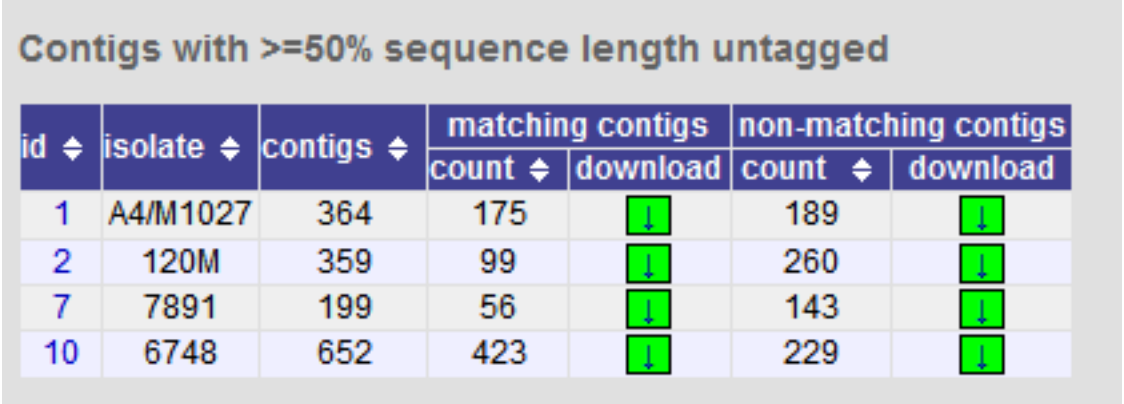
12.3.1 Filtering by tagged status of contigs

You can also export contigs based on the percentage of the sequence that has been tagged. This is useful to find sequences to target for gene discovery.

In order to export contigs where at least half the sequence has been tagged (and also the remaining contigs in a separate file), select '50' in the dropdown box for %untagged.



The resulting table has two download links for each isolate, one for contigs matching the condition, and one for contigs that don't match.



CHAPTER 13

Frequently asked questions (FAQs)

13.1 Installation

1. **BIGSdb is accumulating files in various temp directories - is this normal and how do I clean them out?**

   See: *Periodically delete temporary files*.

2. **BIGSdb is complaining of an invalid script path - what does this mean?**

   In your database config.xml file system tag are two attributes - script_path_includes and curate_path_includes. These contain regexes that the web url to your script (bigsdb.pl and bigscurate.pl respectively) must match. This prevents somebody from accessing a private database using an instance of bigsdb.pl that is not in a protected directory if you're using apache authentication.

   So, if you access the script from http://localhost/cgi-bin/bigsdb/bigsdb.pl then you can set script_path_includes to something like "/bigsdb/" (which is the default), or "/cgi-bin/" or just "/" if you don't care about this check.

13.2 Administration

1. **How can I make some isolates public but not others?**

   The easiest way to do this is to set up two or more separate configuration directories that refer to the database. The URLs to access these will differ by the value of the 'db' attribute, which refers to the name of the configuration directory (in /etc/bigsdb/dbases/). The database view accessed by each of these configurations can be different as can the access restrictions.

   Example:

   We have a database 'bigsdb_test' that contains data, only some of which we wish to make publicly available. The isolates to make public are all members of a project. First we can make a view of the isolates table that contains only isolates within this project.

   For isolates in project id 3, create a database view by logging in to psql as the postgresql user. We will name this view 'public'.:

```
sudo su postgres
psql bigsdb_test

CREATE VIEW public AS SELECT * FROM isolates WHERE id IN (SELECT isolate_id
  FROM project_members WHERE project_id=3);
GRANT SELECT ON public TO apache;
```

Create a private configuration that can access everything in the database in /etc/bigsdb/dbases/test_private. This will be accessible from http://IP_ADDRESS/cgi-bin/bigsdb/bigsdb.pl?db=test_private.

The important attributes to set in the system tag of the config.xml file in this directory are::

```
view="isolates"
read_access="authenticated_users"
```

This means that anyone with an account can log in and view all the isolates (because the view is set to the isolates table).

Now create a public configuration in /etc/bigsdb/dbases/test_public. This will be accessible from http://IP_ADDRESS/cgi-bin/bigsdb/bigsdb.pl?db=test_public. It is better to create a symlink to the private config.xml and then override the attributes that are different. So create a symlink to the private config file:

```
cd /etc/bigsdb/dbases/test_public
sudo ln -s ../test_private/config.xml .
```

You can now override the view and access settings. Within /etc/bigsdb/dbases/test_public, create a file called system.overrides and add the following:

```
view="public"
read_access="public"
```

See also *Restricting particular configurations to specific user accounts*.

CHAPTER 14

Appendix

14.1 Query operators

Various query forms have operators for use with field values. Available operators are:

- =
  - Exact match (case-insensitive).
- contains
  - Match to a partial string (case-insensitive), e.g. searching for clonal complex 'contains' st-11 would return all STs belonging to the ST-11 complex.
- starts with
  - Match to values that start with the search term (case-insensitive).
- ends with
  - Match to values that end with the search term (case-sensitive).
- >
  - Greater than the search term.
- <
  - Less than the search term.
- NOT
  - Match to values that do not equal the search term (case-insensitive).
- NOT contain
  - Match to values that do not contain the search term (case-insensitive).

14.2 Sequence tag flags

Sequences tagged in the sequence bin can have features indicated by specific flags. The presence of these flags can be queried. These are a superset of *flags available for allele sequences*. Available flags are:

- ambiguous read
  - Genome sequence contains ambiguous nucleotides in coding sequence.

- apparent misassembly
  - Sequence has a region of very high identity to existing allele in one region but looks completely different in another.
- atypical
  - Catch-all term for a sequence that is unusual compared to other alleles of locus.
- contains IS element
  - Coding sequence is interrupted by insertion sequence.
- downstream fusion
  - No stop codon present resulting in translation continuing.
- frameshift
  - Frameshift in sequence relative to other alleles, not resulting in internal stop codon.
- internal stop codon
  - Frameshift in sequence relative to other alleles, resulting in internal stop codon.
- no start codon
  - No apparent start codon in immediate vicinity of usual start.
- phase variable: off
  - Coding sequence has a homopolymeric run with a frameshift resulting in a stop codon preventing complete translation.
- truncated
  - Coding sequence is unusually short resulting in a truncated protein (not the same as running off the end of a contig).
- upstream fusion
  - No apparent start codon in immediate vicinity of usual start, likely due to a gene fusion (sequence is transcribed together with upstream coding sequence).

14.3 Allele sequence flags

Sequences can be flagged with specific attributes - these are searchable when doing a sequence attribute query. These are a subset of *flags available for tagged sequences*. These are mainly for use with whole genome MLST type data. Multiple flags can be selected by Ctrl-clicking the list. Available flags are:

- atypical
  - Catch-all term for a sequence that is unusual compared to other alleles of locus.
- contains IS element
  - Coding sequence is interrupted by insertion sequence.
- downstream fusion
  - No stop codon present resulting in translation continuing.
- frameshift
  - Frameshift in sequence relative to other alleles, not resulting in internal stop codon.

- internal stop codon
  - Frameshift in sequence relative to other alleles, resulting in internal stop codon.
- no start codon
  - No apparent start codon in immediate vicinity of usual start.
- phase variable: off
  - Coding sequence has a homopolymeric run with a frameshift resulting in a stop codon preventing complete translation.
- truncated
  - Coding sequence is unusually short resulting in a truncated protein (not the same as running off the end of a contig).
- upstream fusion
  - No apparent start codon in immediate vicinity of usual start, likely due to a gene fusion (sequence is transcribed together with upstream coding sequence).