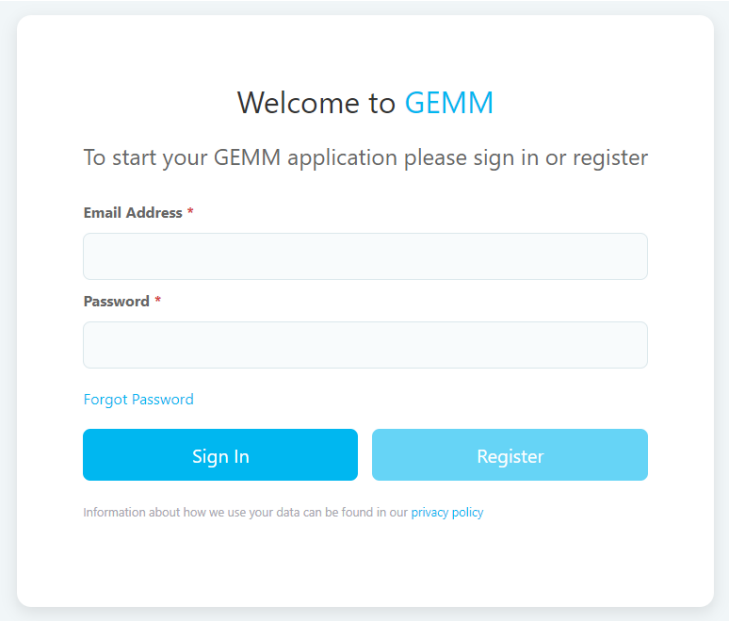
Using the GEMM Applications System

Contents

Signing in

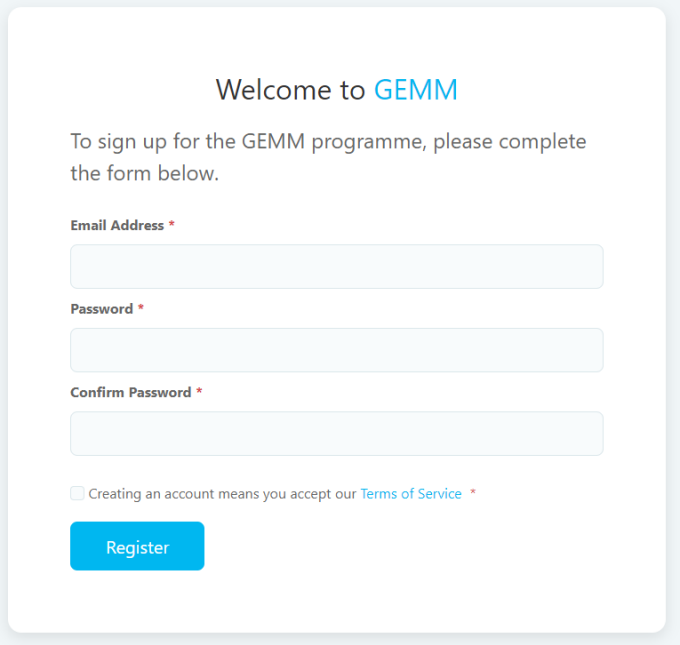
When you first access the GEMM portal, you will be presented with this login screen.



- If this is your first time accessing the GEMM portal, then click the registration link.
- If you already have a username and password, enter these to access your account.
- If you've forgotten your details, click the "reset password" link.

Registration

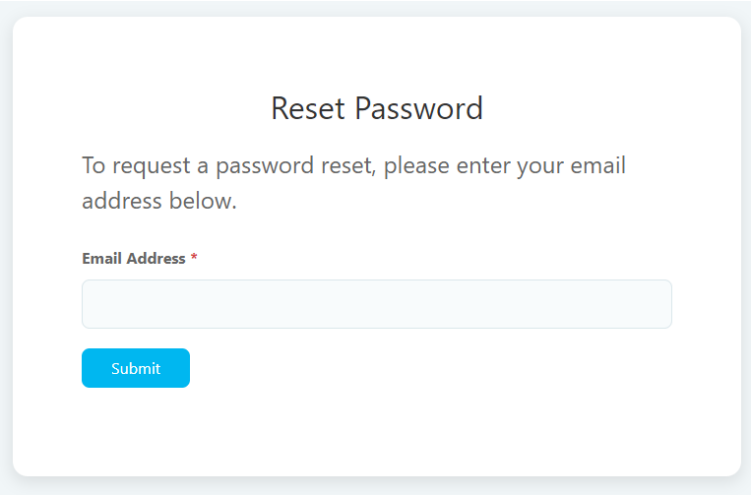
To register, simply fill out the form and submit it.



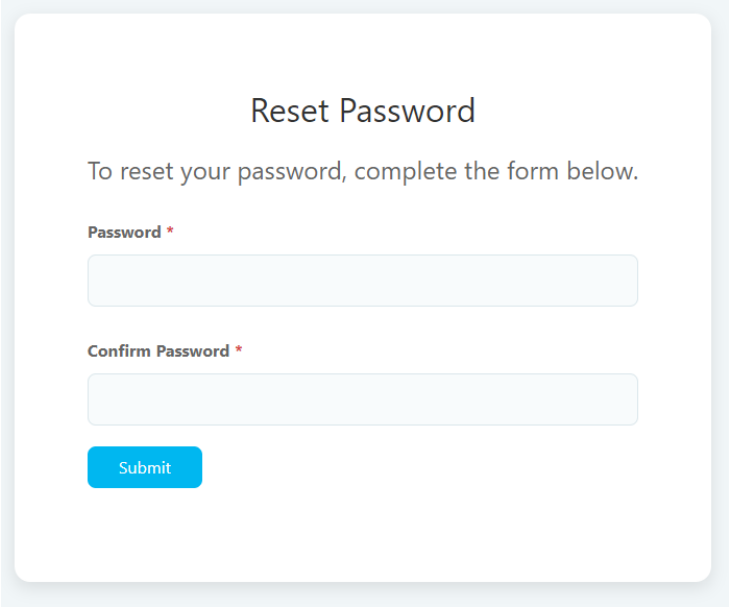
You will be returned to the login screen and should shortly receive an email containing a confirmation link. Click the link to confirm your registration.

Forgotten password

Following the 'forgotten password' link from the login page will take you to this simple form. Please enter your email address and if we have a record of it on our system, we will then email you a link.



Click the link in the email to be taken to the below form, where you will need to enter and confirm your new password:



Data Protection and opting-out

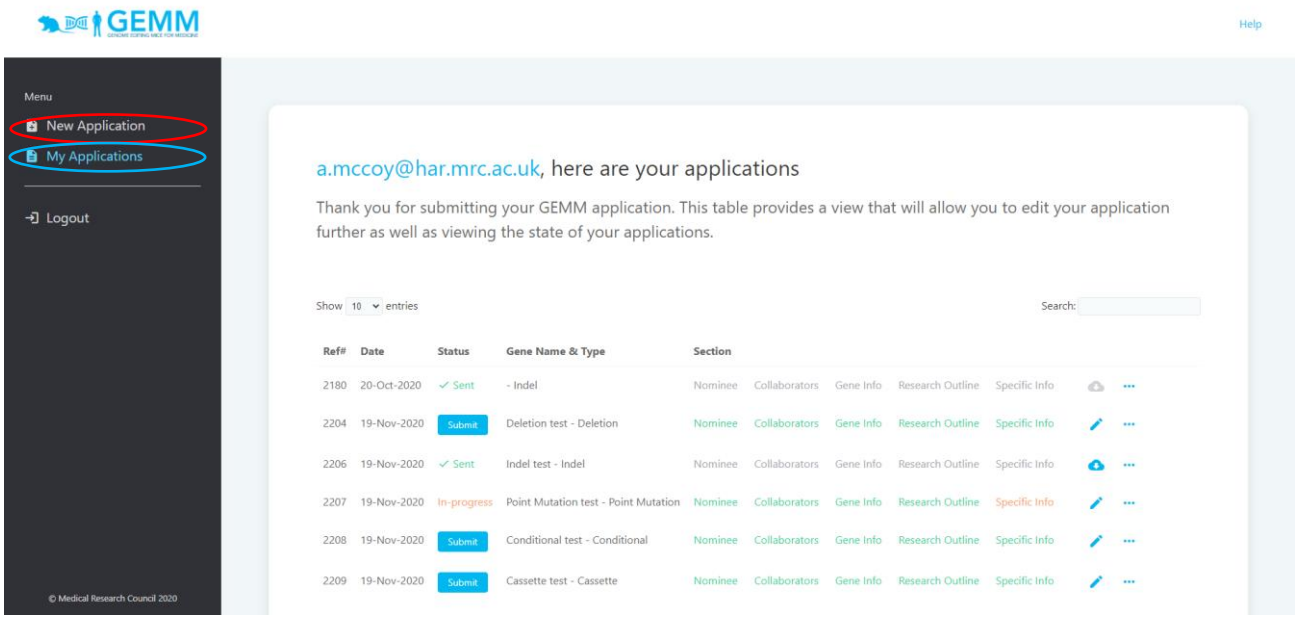
The information provided in this application will be shared with review panel members to enable its evaluation and subsequently with relevant members of staff to enable completion of successful projects. All data is managed in line with the General Data Protection Regulation.

Further information can be found in our privacy policy (https://www.har.mrc.ac.uk/privacy-policy).

However, if you wish to restrict, delete or block the cookies which are set by our website, or indeed any other website, you can do this through your browser settings. The 'Help' function within your browser should tell you how. This may however alter how the site performs. For further information or to request complete deletion of your records, please contact gemm@har.mrc.ac.uk.

Creating a GEMM application

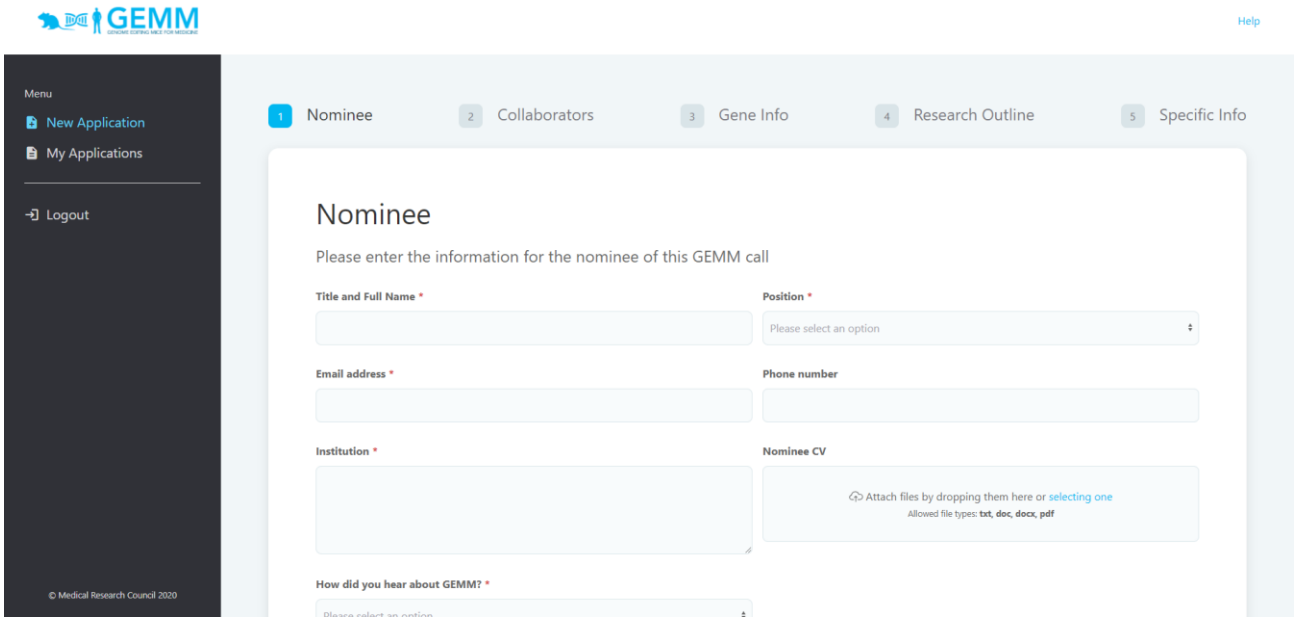
Once logged in, to create a new GEMM application, click the "New GEMM Call" link on the lefthand side (circled in red).



If completing the form in one go, there will be a 'Next section' button at the bottom of each page that will lead you through the application. Once the Nominee information has been filled in, all subsequent sections will allow you to return and edit them before submission. As such, it is possible to maintain a 'work-in-progress' application on the system. If completing the application over a series of occasions, each section will be accessed via the 'My calls' (circled in blue).

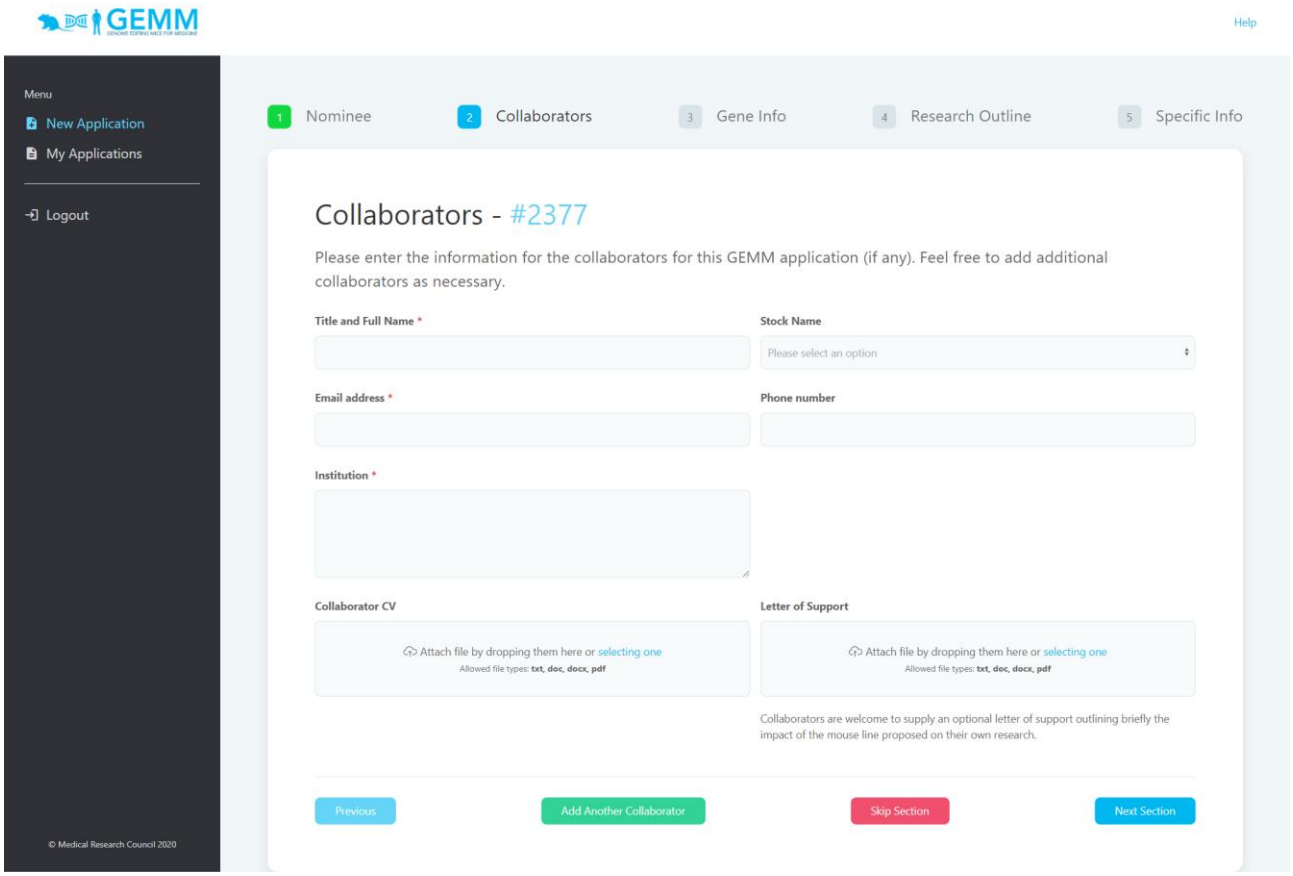
Nominee

Enter the details of the applications' nominee. Name, address and Institution and how you heard about the GEMM call are required fields. Please attach a document detailing the nominee's CV (allowed file types are: txt, doc, docx, pdf). Files are only uploaded once the 'Next' button has been clicked. On returning to this section a green button entitled 'Remove File' will appear indicating file upload is successful. Note that uploading new files will not replace the ones that have already been uploaded.



Collaborators

Similar to the nominee screen, this is where you can enter details of additional collaborators on the application. If there are none, please press the 'Skip this Section'. In addition to the CV upload, collaborators can attach a letter of support outlining the impact of the proposed mouse line on their research (Allowed file types: txt, doc, docx, pdf, rtf). Files are only uploaded once the 'Next Section' button has been clicked. On returning to this section a green button entitled 'Remove File' will appear to the right-hand side of the file name indicating file upload is successful. Note that uploading new files will not replace the ones that have already been uploaded.



To add multiple collaborators, simply click “Add another collaborator” at the bottom of the page.

Gene Info

Complete the fields as indicated.

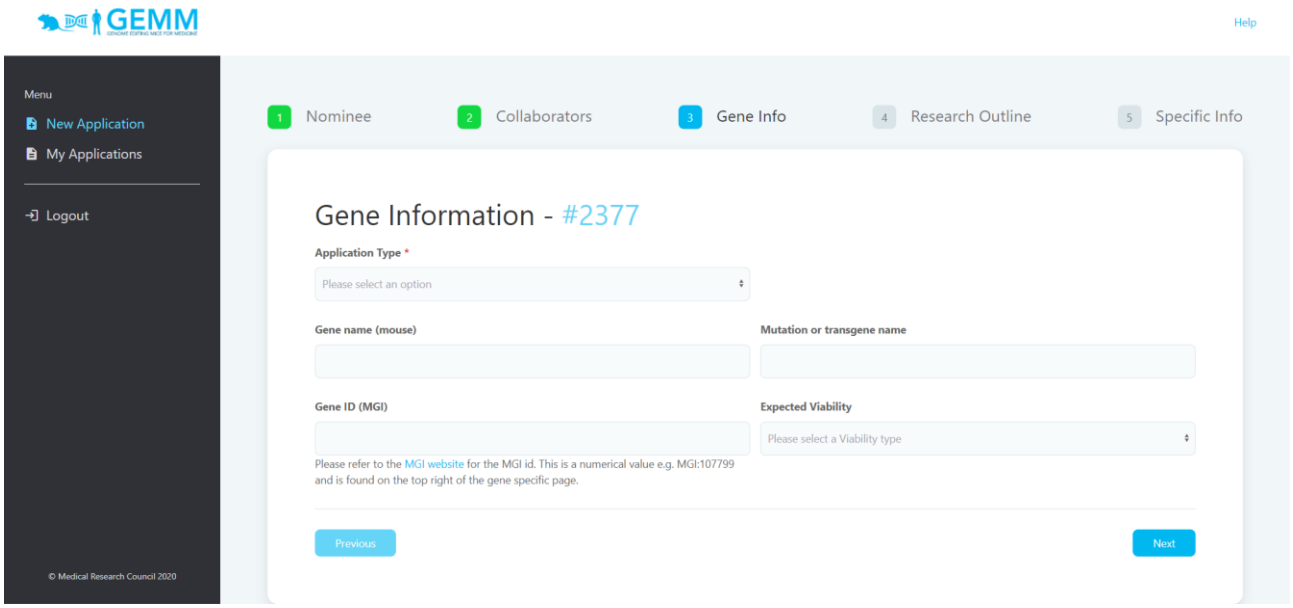
The ‘Specific information’ sections to which you will be directed is dependent upon which type of mutation is selected on this page i.e. the fields for data capture are markedly different between different mutation types.

The five types of mutation/application types available are as follows:

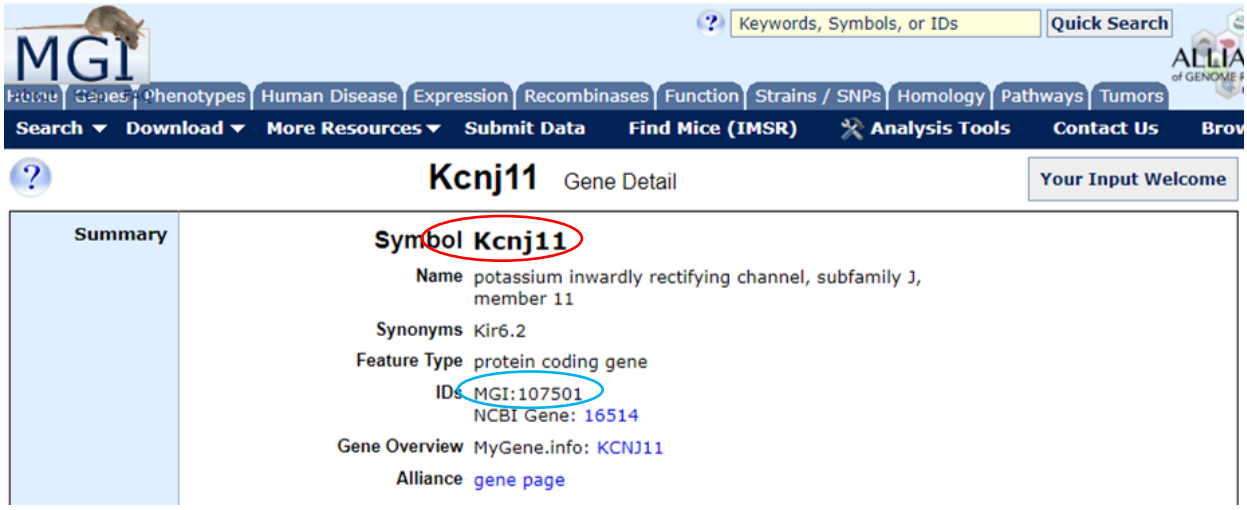
- **Indel** interruption of coding sequence, exact outcome unspecified i.e. if wish to generate a stop codon or frameshift at an exact position then please fill in the Point Mutation form)
- **Deletion** (e.g. removal of exon or segment i.e. regulatory element)
- **Point Mutation** (specified nucleotide change, coding or otherwise)
- **Conditional** (region flanked by LoxP sites for excision upon crossing to Cre expressing line)
- **Cassette** (over-expression, tags, reporters)

Please note that once the application type has been selected (Indel, Deletion, Point mutation, Conditional, Cassette Knock-in) for an application, it cannot be changed. If you make a mistake on

this field, you will need to create a new application with the correct type specified. This can be done by using the grey ‘Copy and add new Gene-Info’ button to the right-hand side of the My GEMM Calls window and deleting the erroneous application.

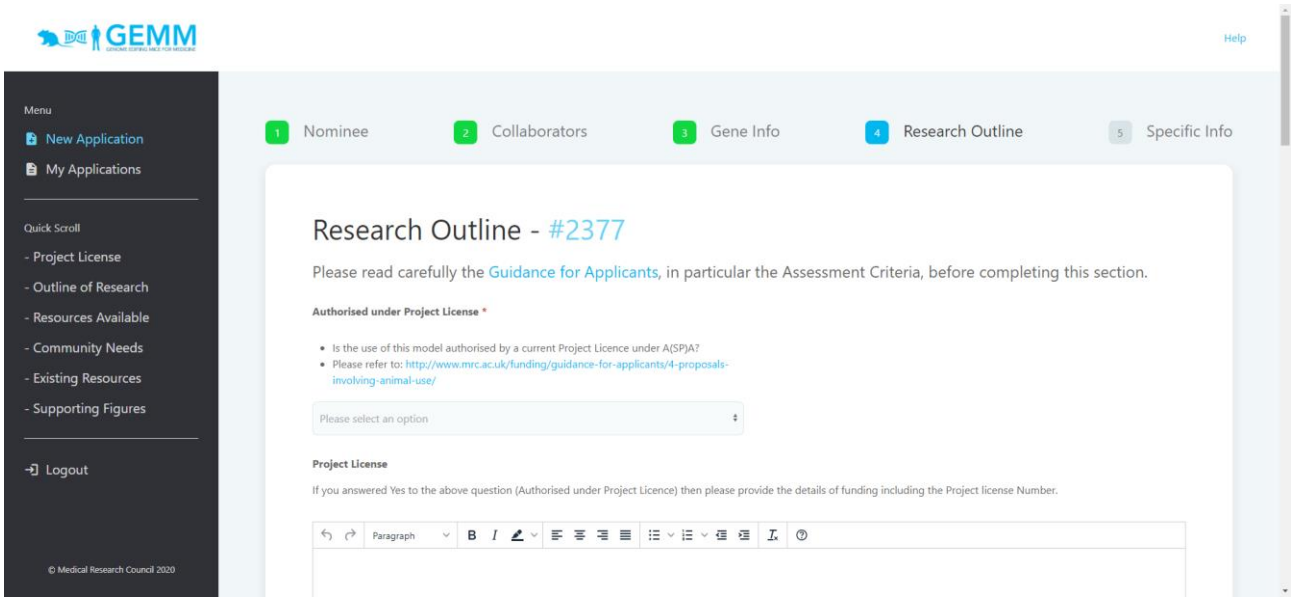


Please visit http://www.informatics.jax.org/ to get up to date mouse gene names (circled in red) and MGI gene ID (circled in blue). This website also has information re the viability of these genes as a note in the Mutations, Alleles and Phenotypes section of the relevant gene page.



Research Outline

This part of the application pertains to the nominee's experimental plans for the mouse line.



Authorised under Project License

Required field, please answer Yes, No or N/A. Is the use of this model authorised by a current Project Licence under Animals (Scientific Procedures) Act?

Please refer to http://www.mrc.ac.uk/funding/guidance-for-applicants/4-proposals-involving-animal-use/

If you answered Yes to the above question (Authorised under Project Licence) then please provide the details of funding including the Project license Number. If you have any questions re this section, please email gemm@har.mrc.ac.uk.

Outline of Research

Required field. Description of research involving proposed mouse line (including the potential to address important gaps in biomedical knowledge or/and answer important scientific questions, and why the mouse represents the best model).

For disease models, include evidence that the variant selected is robustly associated with disease/phenotype e.g. for GWAS studies include sample sizes and p values and/or evidence supporting the role of the gene selected in mediating the impact of the GWAS hit such as cis-eQTLs and/or independent coding variant associations in the same gene for example. (1000 words max)

Resources Available

Description of the expertise, environment and resources in place to support the proposed experimental work. If existing funding is available, please provide details of the award. If it is not, please provide your plans for obtaining funding (approx. 500 words).

Wider scientific community needs

How will this mouse line contribute to the wider scientific community needs (e.g. research or diagnostic tool, preclinical model etc) (approx. 500 words).

Existing models/resources

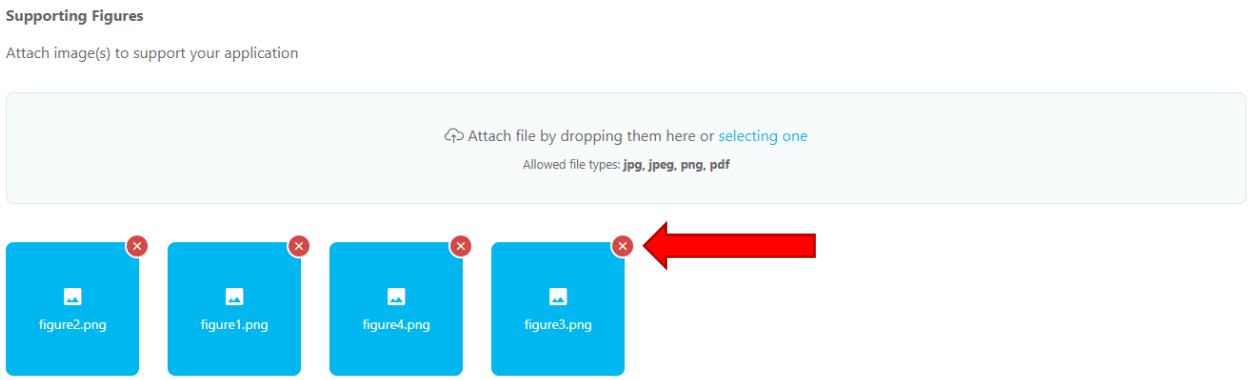
Is this mouse model unique? Are there currently any mouse models which are suitable for the proposed research? (250 words max)

Supporting Figures

Attach image(s) to support your application. Files must be less than 10 MB.

Allowed file types: jpeg png pdf tif tiff. Please provide a description of the attached images.

You can attach multiple files here – specifics on how this is done will vary depending on the web browser you are using. Multiple files can be uploaded in a single action. To upload multiple files on a series of different occasions you must press the 'save' button to ensure the file is captured. Once the file is uploaded, a green button entitled 'Remove File' (indicated by red arrow below) will appear to the right-hand side of the file name indicating file upload is successful. If you return to this page at a later date, you will see a list of the files that you have already uploaded and will be able to remove them if necessary. Note that uploading new files will not replace the ones that have already been uploaded.



Specific Information

This section is to capture the details of the genetic modification you wish to introduce into the mouse genome at the sequence level. This information is used to assess feasibility of each project so please complete as fully as possible. Please direct any queries regarding this section to gemm@har.mrc.ac.uk. The options displayed in this section depends on which application type you selected on the Gene Information screen.

If you are applying to model a human allele/mutation, please provide supporting information/data on the following (or explain why these approaches might not be relevant/possible for your studies)

a. Further human genetic studies (additional families etc)

b. Cell-based assays

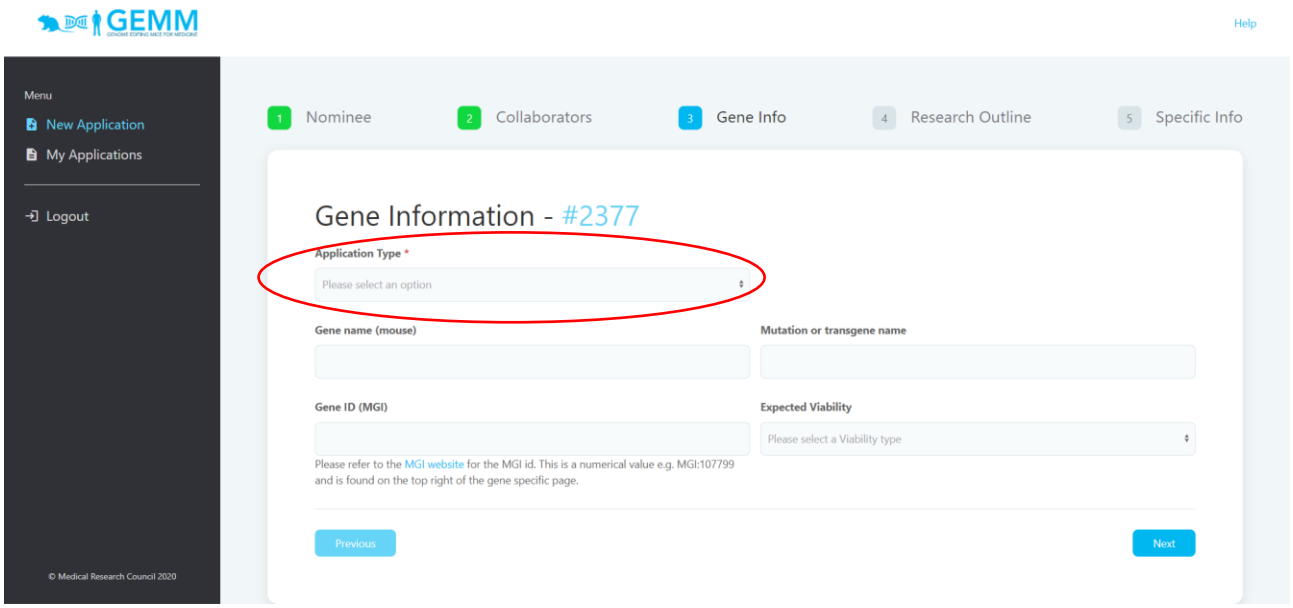
c. Human derived tissue

d. *In-silico* studies

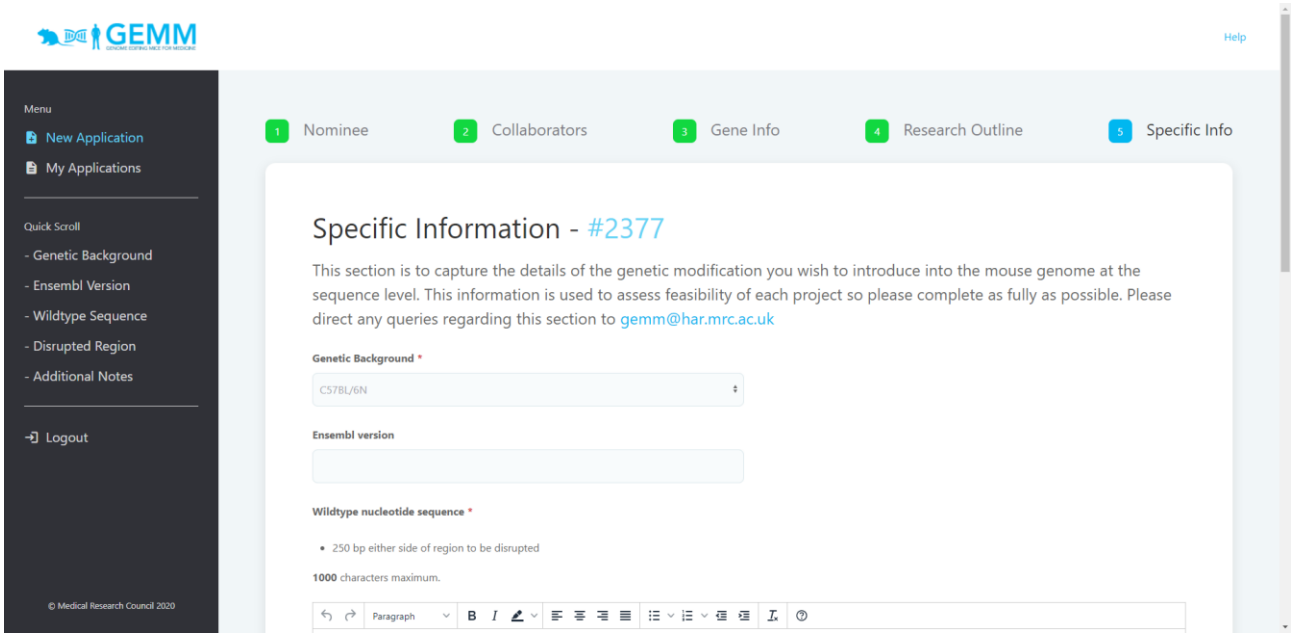
The majority of inputs in these forms are free text boxes, but there is also capacity to upload schematics of the allele you wish to nominate. Example screenshots of each application type are below, but each page will also provide additional information for the five types of modification:

- **Indel** (interruption of coding sequence, exact outcome unspecified i.e. if wish to generate a stop codon at an exact position then please fill in the Point Mutation form)
- **Deletion** (e.g. removal of exon or segment i.e. regulatory element)
- **Point Mutation** (specified nucleotide change, coding or otherwise)
- **Conditional** (region flanked by LoxP sites for excision upon crossing to Cre expressing line)
- **Cassette** (over-expression, tags, reporters)

PLEASE NOTE: Different types of mutation require different data in order for the panel to make a feasibility assessment of the model to be made. As such, please take care to use the appropriate application type for your model, and please email gemm@har.mrc.ac.uk if you require clarification as the form most appropriate for your nomination. Please see 'Creating Further Applications' section if you need to edit the Application type of an ongoing application.



Indel Specific Information



Additional fields in this section include:

Genetic Background

Required Field. Drop down box with following options:

C57BL/6N

C57BL/6J

129S9(/SvEV)

C3H.PDE

Wildtype nucleotide sequence Required Field.

- 250 bp either side of region to be disrupted
- 1000 characters max.

Region to be disrupted

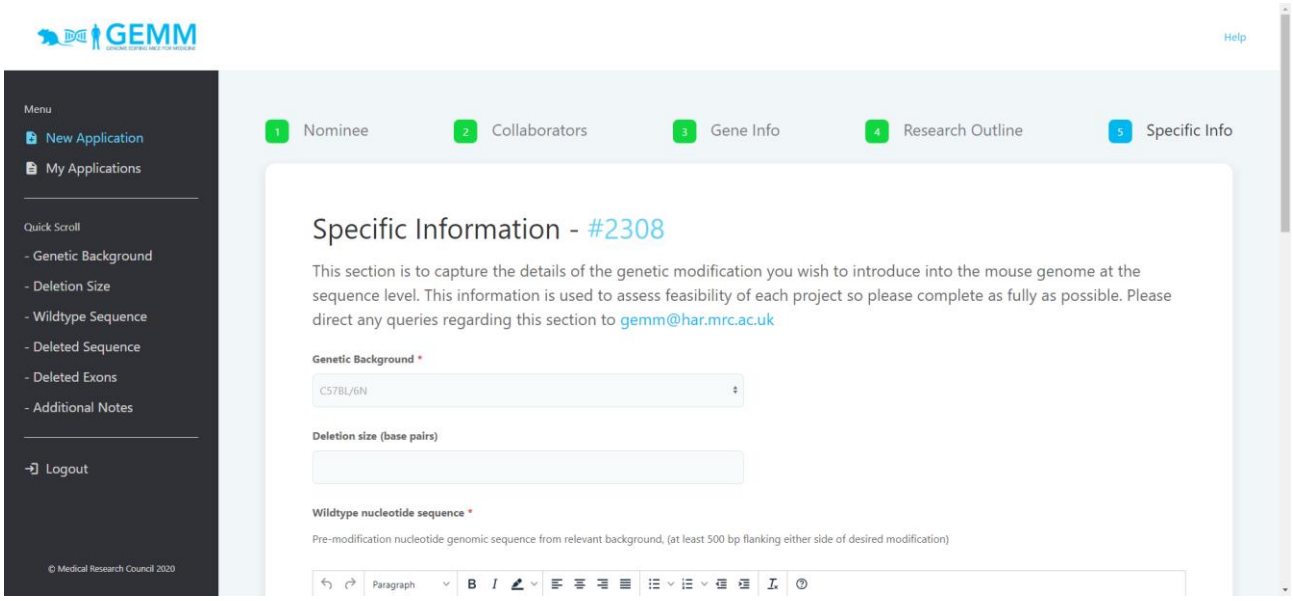
Required Field. This is the region in which we will search for guides which will be used to introduce a double stranded break repaired by non-homologous end joining.

- The region to search for possible guide sequences i.e. the region to target with sgRNAs.
- 1000 characters max.

Additional Notes

Please add any additional information pertaining to the application here e.g. indel to cause frameshift after amino acid 240.

Deletion Specific Information



Nominations for deletions are not restricted to protein coding elements e.g. for deletions of regulatory elements, enhancer regions, silencers etc. are all permitted. Fields in this section include:

Genetic Background

Required Field. Drop down box with following options:

C57BL/6N

C57BL/6J

129S9(/SvEV)

C3H.PDE

Deletion size

Please specify the size of the region you wish to delete e.g. 20 bp.

Wildtype nucleotide sequence

Required Field

Pre-modification nucleotide genomic sequence from relevant background, (at least 500 bp flanking either side of desired modification)

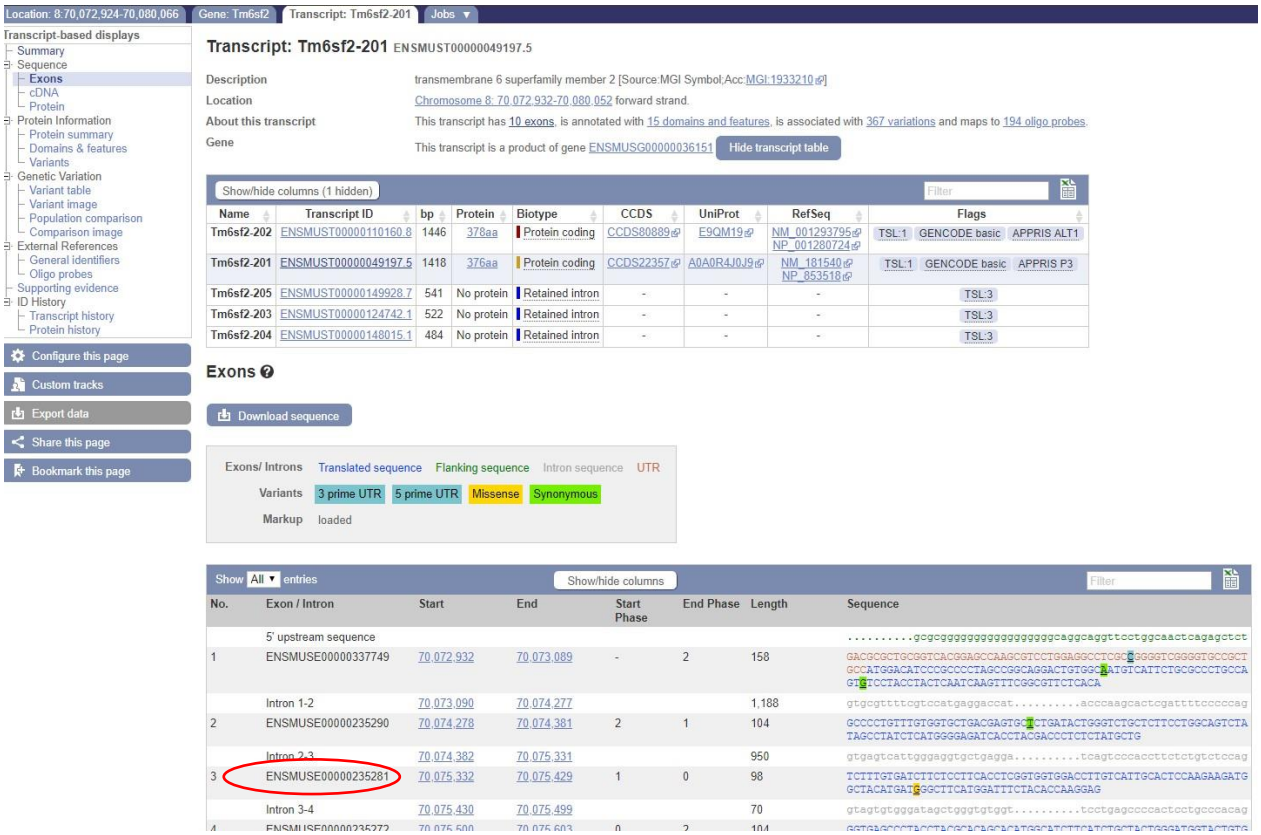
Sequence to be deleted

Required Field

- Please indicate the sequence from the wild type sequence, submitted above, that should be removed.

Exon(s) to be deleted

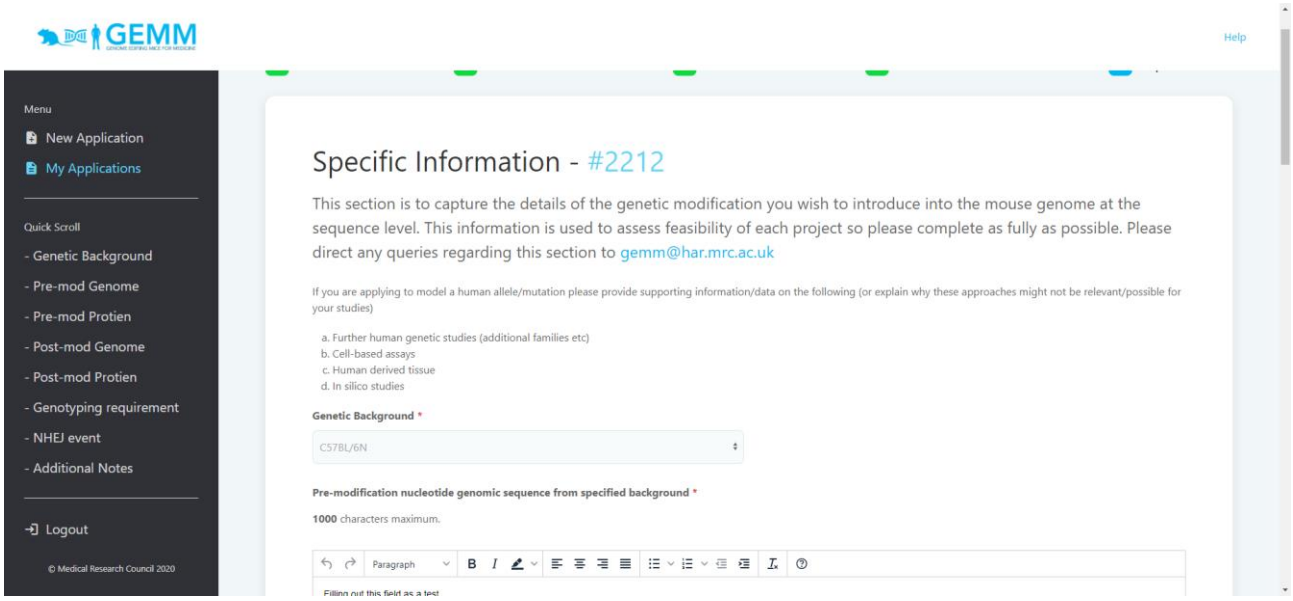
If exon(s) are to be deleted, please enter a comma separated list of Ensembl IDs. Please refer to the Ensembl website for the Ensembl IDs (http://www.ensembl.org/Mus_musculus/Info/Index).



Additional Notes

Please add any additional information pertaining to the application here e.g. ‘Deletions slightly larger or smaller (approx. 10 bp) than the 854 bp deletion proposed would acceptable’.

Point Mutation Specific Information



Fields in this section include:

Genetic Background

Required Field. Drop down box with following options:

C57BL/6N

C57BL/6J

129S9(/SvEV)

C3H.PDE

Pre-modification nucleotide genomic sequence from specified background

- Required Field
- 1000 characters max.

Pre-modification protein sequence from relevant background

(if modification is in coding sequence, 1 letter code)

Post-modification nucleotide genomic sequence

- Required Field
- Post-modification nucleotide genomic sequence from relevant background, (at least 250 bp flanking either side of desired modification)
- 1000 characters max.

Post-modification protein sequence from relevant background

(if modification is in coding sequence, 1 letter code)

Genotyping requirement

Genotyping requirement (i.e. introduction of a restriction site) Please note, the inclusion of further modifications to facilitate genotyping is not always possible to achieve.

NHEJ event

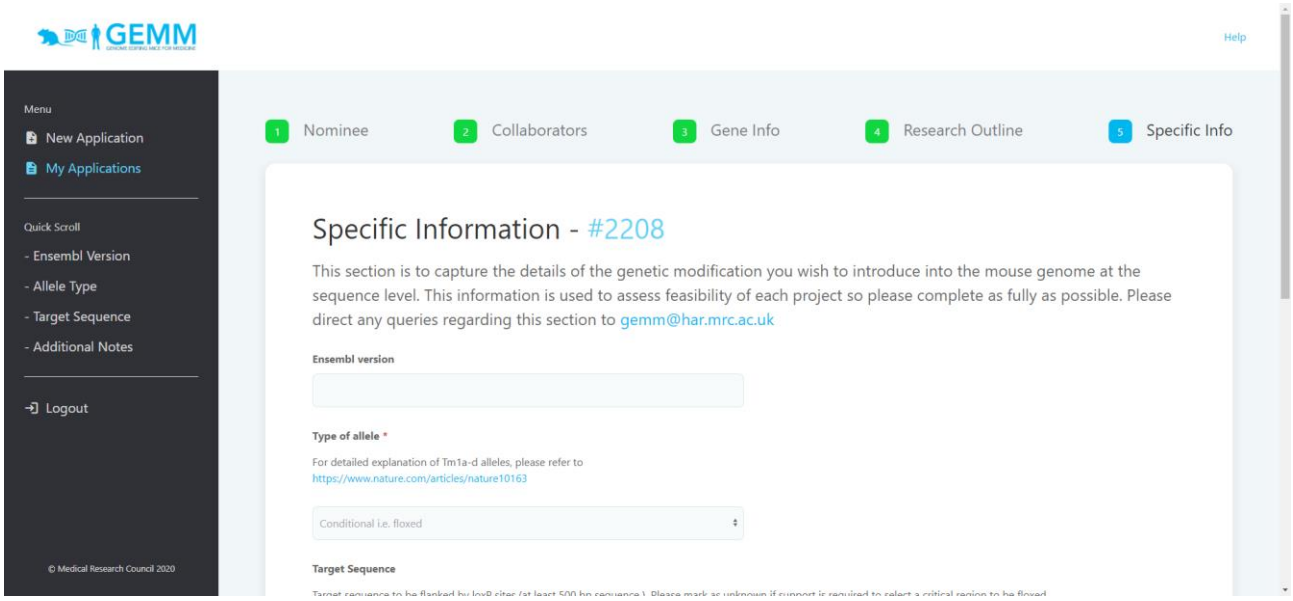
The process of generating point mutations generally also yields other variants e.g. indels. Please specify if these are also of interest to you. Drop down box with following options:

- Yes, please keep the variants
- Only keep frame-shift variants
- No, I am only interested in this point mutation

Additional Notes

Please use this box to input details/data supporting the generation of the mouse i.e. GWAS data.

Conditional Specific Information



Fields in this section include:

Ensembl version

Type of allele

Required Field

Choose from Conditional (i.e. floxed), Tm1a, Tm1b, Tm1c, Tm1d. For detailed explanation of Tm1a-d alleles, please refer to https://www.nature.com/articles/nature10163)

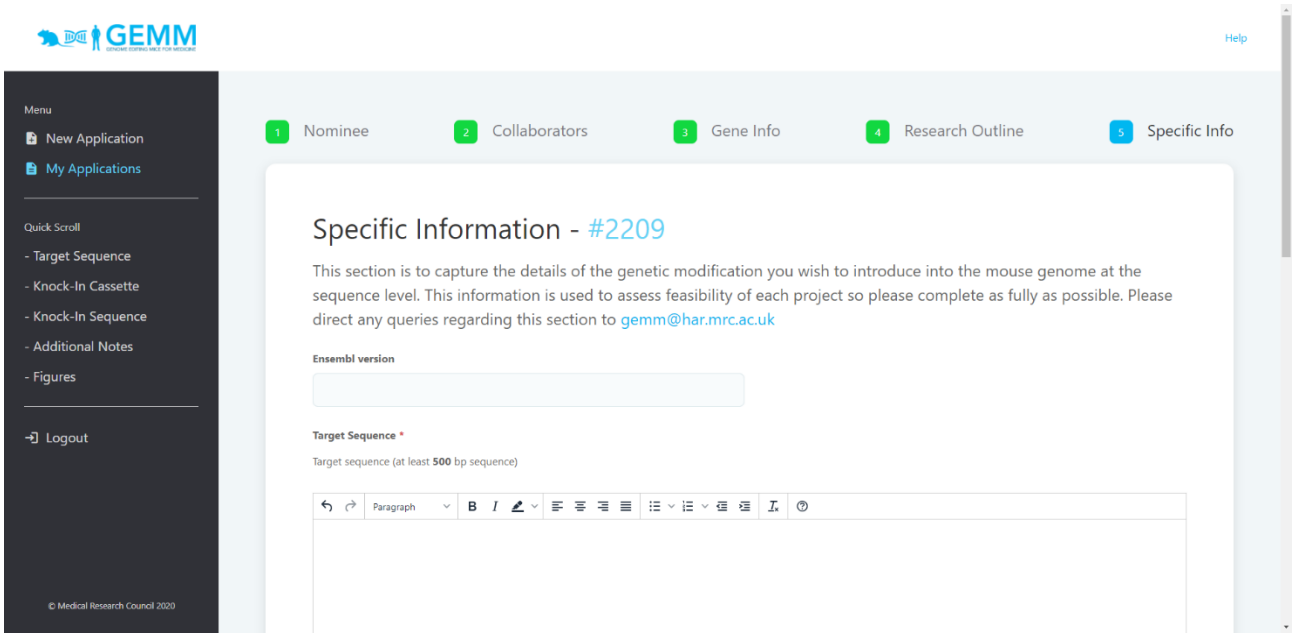
Target Sequence

Target sequence to be flanked by loxP sites (at least 500 bp sequence). Please mark as unknown if support is required to select a critical region to be floxed or email gemm@har.mrc.ac.uk for support.

Additional Notes

Please provide any additional information that pertains to the design of this nominated allele.

Cassette Specific Information



Fields in this section include:

Ensembl Version

Target Sequence

Required Field.

Target sequence (at least 500 bp sequence)

Cassette to knock in

Required Field.

Choose from Cre, Cre-ert2, Flpo, GFP or Other. If selecting Other, please specify further in the Sequence to knock in section below.

Sequence to knock in

Please provide coding sequence or name of standard cassette.

Additional Notes

Figure/Vector Map

Please add a schematic of the genetic modification you would like to achieve.

Files must be less than 10 MB.

Allowed file types: jpeg png pdf tif tiff svg.

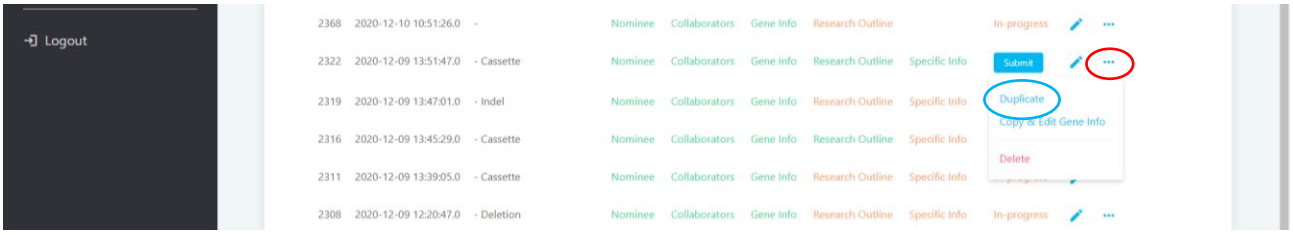
Once the file is uploaded, a green button entitled ‘Remove File’ (indicated by red arrow below) will appear to the right-hand side of the file name indicating file upload is successful. If you return to this page at a later date, you will see the file that you have already uploaded and will be able to

remove them if necessary. Note that uploading new files will not replace the ones that have already been uploaded.

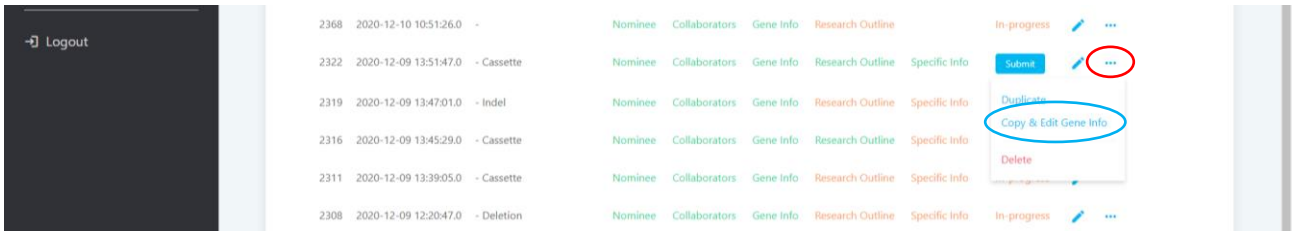
Creating Further Applications

You can, of course, always create another application from scratch by using the New GEMM Call link on the left-hand navigation bar.

However, if you wish to submit multiple applications of the same type i.e. multiple point mutation nominations, you can use the 'Duplicate' button in the Functions column. This will create another copy of a prior application, then use the Edit buttons under the Gene Info, Research Outline and Specific-Info columns to return to those pages and make necessary edits.

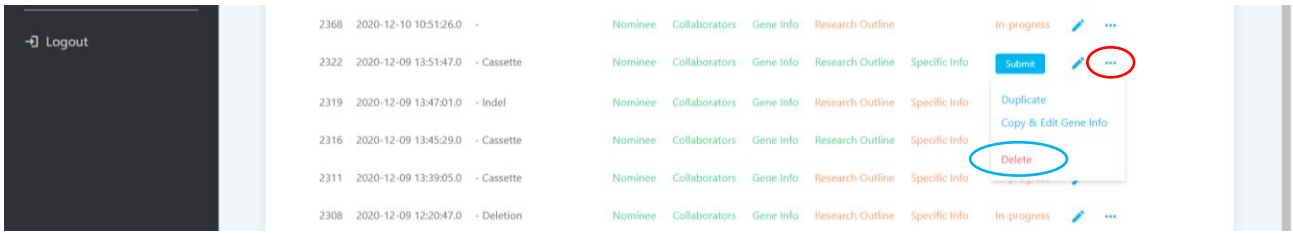


If you want to submit another application of a different type, use the "Copy and add new Gene Info" button – this will allow you to change the type of the duplicated record, but as a result, the Specific Information section will not be copied.



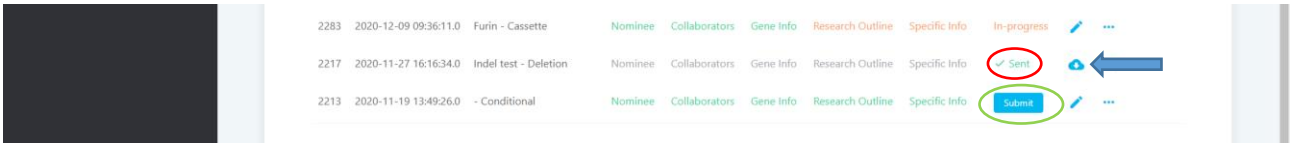
Deleting Applications

If, for any reason, you need to remove your application, just find the application in the "My Calls" page and click the red Delete button. Note that once you do this **IT CANNOT BE RECOVERED**, so if you delete an application in error, you will need to recreate it manually.



Submission, reports and downloading your full application

Once you have completed all the required fields on your application, the "My GEMM Calls" page status column will change from "In-progress" to "Submit" (see red circle). Click this green Submit box to submit your application – note that no further changes will be possible once this is done. Once submitted, your application will be marked as 'Sent' in the status column (see green circle). Nominees will receive and emailed a summary version of the submitted nomination. Whilst the call is live, nominees will also be able to create a PDF report of the submitted application under the 'Functions' column using the 'PDF Report' button (see blue arrow).



PLEASE NOTE: The emailed version does not contain each of the attachments and figures as the PDF building facility requires some time to assemble additional files to the application. To ensure that nominees can check their full submission and keep a record, it is recommended that nominees use the 'PDF Report button' to generate their own PDF after submission.