Private & confidential: *Please be aware that the contents of this form may be made public resulting from the "Freedom of information Act". Personal details will not be released.*

G: NON-TECHNICAL SUMMARY (NTS)

NOTE: The Secretary of State considers the provision of a non-technical summary (NTS) is an essential step towards greater openness and requires one to be provided as part of the licence application in every case. You should explain your proposed project clearly using non-technical terms which will be understandable to a lay reader. You should avoid confidential material or anything that would identify you, or others, or your place of work. Failure to address all aspects of the non-technical summary may render your application incomplete and lead to it being returned.

This summary will be published (examples of other summaries can be viewed on the Home Office website at http://scienceandresearch.homeoffice.gov.uk/animal-research/).

(WORD LIMIT: 1000 WORDS)

Please complete the following:

<table>
<tr><td>Project Title (max. 50 characters)</td><td>Zebrafish: development, physiology and disease modelling</td></tr>
<tr><td>Key Words (max. 5 words)</td><td>Zebrafish, development, physiology, disease, transgenic</td></tr>
<tr><td>Expected duration of the project (yrs)</td><td>5</td></tr>
<tr><td>Purpose of the project (as in Article 5)[1]</td><td>
<table>
<tr><td>Basic research</td><td>Yes</td></tr>
<tr><td>Translational and applied research</td><td>Yes</td></tr>
<tr><td>Regulatory use and routine production</td><td>No</td></tr>
<tr><td>Protection of the natural environment in the interests of the health or welfare of humans or animals</td><td>No</td></tr>
<tr><td>Preservation of species</td><td>No</td></tr>
<tr><td>Higher education or training</td><td>No</td></tr>
<tr><td>Forensic enquiries</td><td>No</td></tr>
<tr><td>Maintenance of colonies of genetically altered animals[2]</td><td>Yes</td></tr>
</table>
</td></tr>
<tr><td>Describe the objectives of the project (e.g. the scientific unknowns or scientific/clinical needs being addressed)</td><td>To learn more about vital processes that occur during development of vertebrate animals and how these lead to disease in humans when they are defective.</td></tr>
<tr><td>What are the potential benefits likely to derive from this project (how science could be advanced or humans or animals could benefit from the project)?</td><td>1.) To provide an improved understanding of how the kidney functions in healthy animals, and how defects in kidney function lead to disease in humans. This information will inform treatment of patients with kidney disease and can be exploited to develop new drugs for treatment of such disease.

2.) To provide an improved understanding of how the skull and facial skeleton and the heart are formed. The research</td></tr>
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[1] Delete Yes or No as appropriate.
[2] At least one additional purpose must be selected with this option.

	will also reveal how defects in the development of these tissues lead to disease in humans. 3.) To determine the mechanisms and pathways that are required for the formation of new blood vessels. New blood vessel formation is a vital process during development and also for the maintenance of health. A better understanding of how blood vessels are formed will inform better therapy for a number of human diseases including cardiovascular disease and cancer. 4.) To reveal the mechanisms that occur in brain haemorrhage. The work will also lead to design of better screens for testing drugs that may be used to treat or prevent brain haemorrhage.
What species and approximate numbers of animals do you expect to use over what period of time?	168,540 zebrafish over 5 years
In the context of what you propose to do to the animals, what are the expected adverse effects and the likely/expected level of severity? What will happen to the animals at the end?	Zebrafish will be genetically modified. There is the possibility this may lead to developmental abnormality or genetic disease that could incur suffering, but this is unlikely. This will be mitigated by frequent inspection and early intervention. In the rare cases where animals show any abnormality or suffering they will be humanely killed using Schedule 1. In some cases, zebrafish will be injected with molecules that are unlikely to cause any suffering. All animals will be sacrificed at the end of the experiments using humane methods.
Application of the 3Rs	
1. Replacement State why you need to use animals and why you cannot use non-animal alternatives	The processes described in this proposal occur in the context of an entire tissue, and cannot be effectively recapitulated using non-animal models. Invertebrates also cannot be used as the processes under investigation are poorly conserved in such species compared to humans.
2. Reduction Explain how you will assure the use of minimum numbers of animals	Efficient experimental design and statistical techniques such as power analysis will keep the number of protected animals used to a minimum.
3. Refinement Explain the choice of species and why the animal model(s) you will use are the most refined, having regard to the objectives. Explain the general measures you will take to minimise welfare costs (harms) to the animals.	Zebrafish is the vertebrate of lowest neurological complexity that can be genetically modified to study the processes of interest. Any genetic manipulation indicated to interfere with feeding, locomotion, respiration or cardiovascular function, or inducing significant behavioural or other physiological abnormality will result in immediate termination of the organism concerned and other animals sharing the genotype.