APPENDIX C

Explanation of published tables

Species of animal
All tables, except the online Time Series ones, are classified by species of animal. The full classification is used in Tables 1, 1a, 6, 6a, 9 and 9a, but the other tables use a condensed classification. All the tables except 1a, 6a and 9a give the number of procedures. Tables 1a, 6a, and 9a give the actual number of animals used for the first, and usually only, time in 2009 classified according to their first use. The list of species or categories of animals is selective to avoid undue complications; when collective terms are used it is because previous experience suggests that the category will contain a relatively small number or because further breakdown is of little interest. In several of the tables, rows which are completely zero have been omitted and if a species is not mentioned it is because the row or rows pertaining to that species is blank.

Genetic status of animal
Tables 2 (source), Table 3 (genetic status), and Table 6 (non-toxicological work by field of research) are subdivided to give more information about animals with abnormal genetic constitutions. Table 2 shows procedures using all animals; Table 2.1 shows the number of procedures using animals with harmful (but naturally occurring) genetic defects and table 2.2 shows the number of procedures using genetically modified animals. Table 6 follows the same pattern. Table 3 is subdivided into three supplementary tables (3.1, 3.2 and 3.3) to present in detail the use of normal animals, animals with harmful mutations, and genetically modified animals respectively, in breeding programmes or research.

Primary purpose (Table 1)
The use of animals for regulated procedures is limited by section 5(3) of the Act to one of the following primary purposes:

(i) **fundamental biological research**; carried out with the primary intention of increasing knowledge of the structure, function and malfunction of man and other animals, or plants. Such studies may be aimed solely at an increase in knowledge, application of that knowledge being beyond the scope of the investigation, or with a view to providing a practical solution to a medical or veterinary problem once the issues are more clearly defined and understood. This category includes physiological, pathological, pharmacological, genetic and biochemical studies, including toxicological evaluation.

(ii) **applied studies - human medicine or dentistry, and veterinary medicine**; consisting of research into, development of and quality control of products or devices, including toxicological evaluation and safety or efficacy testing.

(iii) **protection of man, animals or the environment**; by toxicological or other safety or environmental evaluation. This category is intended to cater for toxicological work which is not related either to fundamental research or to the solution of medical and veterinary problems as such (see (i) and (ii) above), but also includes some non-toxicological procedures. This category is further divided into a number of subgroups (listed in Tables 9 and 9a). These are largely self-explanatory but the following notes may be helpful in understanding the figures:

(a) while any one substance may be used in industry or in the home, or may be an environmental pollutant, a herbicide or a pesticide, the project licence holder classifies the procedure in accordance with the particular context of the procedure and the expected primary use of the product;

(b) animal pesticides (distinct from plant pesticides) are not included amongst the types of substances listed, because a substance intended to kill pests which infest or attack animals would be regarded as a veterinary product. These are included in the appropriate body-system group covered by primary purposes described in (ii) above;

(c) many of the procedures recorded under this category are required by UK law or by the laws and regulations of countries in which it is intended to use the substance concerned;

(d) the term 'food additives' covers substances deliberately added to food as preservatives, artificial colourants or flavouring agents but not studies on the nutritive value of food, accidental contamination or infection of food, or medicines administered to animals or humans in food.

(iv) **education and training;** these categories include procedures carried out under project licences for the purposes of education or training under the 1986 Act. They also include killing of animals by methods not included in Schedule 1 to the 1986 Act, if the killing takes place for educational purposes at a designated establishment. Such killing may be authorised to provide, for example, tissues subsequently used for education or training. The use of animals for the acquisition of manual skills is currently permitted only for training in microvascular surgery, and at present this is always carried out under general anaesthesia, without recovery.

(v) **forensic enquiries**; may refer to animal use in human or veterinary enquiries relevant to potential legal proceedings.

(vi) **direct diagnosis;** investigation of disease including investigating suspected poisoning. This caters for procedures carried out under the 1986 Act for the purpose of diagnosing disease in an individual human or animal patient or a group of such patients. There is no research function: these are essentially applied studies, predominantly involving the production of biological reagents, for example antibodies and clotting factors.

(vii) **breeding**; a category for recording the production and breeding of animals with harmful genetic defects, and genetically modified animals. The numbers recorded in this category include those animals which are identified as possessing a harmful mutation or are genetically modified, but not used subsequently on procedures which are recorded elsewhere in the tables. The numbers also include some genetically normal animals which were subjected to regulated procedures such as tissue sampling or hormonal administration for the purpose of regulated breeding programmes (see also Tables 3, 3.1, 3.2, 3.3).

Source of animals (Tables 2, 2.1, 2.2)
Sections 7 and 10(3) of the Act require, unless a specific exemption is granted, that certain animals, listed in Schedule 2 to the Act, be obtained from designated breeding or supplying establishments certified as such by the Secretary of State. The species so listed during 2007 were: mouse, rat, guinea-pig, hamster, gerbil, rabbit, cat, dog, ferret, primate and quail (*Coturnix coturnix*); also pigs (if genetically modified), and sheep (if genetically modified). Normal pigs and normal sheep remain outside the scope of this schedule. The source of these species is tabulated according to whether it is within the UK, within the remainder of the EU, within certain Council of Europe (but non-EU) countries who are signatories to convention ETS 123, or elsewhere. Animals which originate from non-designated sources, such as overseas breeding centres, but which are acquired by the project licence holder from a designated supplying establishment in the UK, are reported under the heading "Animals acquired from other designated breeding or supplying establishments in the UK."

Table 2 lists numbers of procedures by source of animal, as described above; tables 2.1 and 2.2 list procedures by source for animals with a harmful (but naturally-occurring) genetic defect, and genetically modified animals, respectively. The use of Schedule 2-listed species from non-designated sources in the UK, or from Europe or elsewhere, is subject to prior approval by the Home Office. Such use would be justified on the basis of scientific need or lack of availability of appropriate animals from designated breeding or supplying establishments.

Stage of development, genetic status, and breeding (Tables 3, 3.1, 3.2, 3.3)

Stage of development
Details of procedures on animals in foetal, larval or embryonic form are collected but not shown in any of the published tables because it may be impracticable in some cases to count such procedures, e.g. a foetus resorbed during gestation, or fish fry which are very small and fast-moving.

Genetic status
Only the number of animals in which a harmful genetic defect actually manifested itself has been recorded for spontaneously arising mutants. All genetically modified animals are recorded. Additional information on counting animals in those categories is provided in Annex A at the end of Appendix B.

Table 3.1 shows the use of genetically normal animals in breeding programmes for both animals with harmful mutations and genetically modified animals. The number of procedures is shown for: normal animals used to generate founder genetically modified (GM) animals (which themselves will be further used in breeding programmes), normal animals within GM breeding colonies, and normal animals within breeding colonies of animals with naturally-occurring harmful mutations.

Tables 3.2 and 3.3 show the use of animals with harmful mutations and genetically modified animals respectively in breeding programmes or research. The structure of these two tables is similar. They show, respectively for harmful mutant and GM animals: procedures undertaken for maintenance of the breeding colony; procedures undertaken for research analysis *post mortem*); further regulated procedures, following on from the breeding programme; procedures used for production; and procedures for toxicological (safety evaluation) purposes.

Breeding
The breeding of animals with harmful genetic defects or genetically modified animals is a regulated procedure under a project licence. Animals which are identified as 'harmful mutants' or 'genetically modified' may be used for further breeding or used subsequently in procedures. The numbers also include some genetically normal animals which were subjected to regulated procedures such as tissue sampling or hormonal administration for the purpose of regulated breeding programmes.

The classifications of procedures concerned with breeding distinguish between:

(a) animals used to generate founder genetically modified animals for novel transgenic lines, chimeras or clones;
(b) genetically modified animals generated by recognised husbandry methods for maintenance of a breeding colony;
(c) genetically modified animals used in research programmes not concerned with breeding;
(d) animals with a harmful mutation generated by recognised husbandry methods for maintenance of breeding colonies;
(e) animals with a harmful mutation used in research programmes not concerned with breeding.

Target body system (Table 4)
Some of the headings in the tables are self-explanatory but, for the others, further explanation is given below.

Abbreviated title	Description: studies in which interest centres on:
Nervous	The central or peripheral nervous systems, other than the special senses
Senses	Sight, hearing, smell, or taste
Alimentary	The alimentary (including liver) and excretory systems
Musculo-skeletal	The skeletal or muscle system
Immune and reticulo-endothelial	The understanding and operation of the immune system
Other system	A single body system not separately listed in the table
Multiple systems	More than one system of primary interest
System not relevant	The system or systems affected were not predictable or not relevant

Use of anaesthesia (Table 5)
The codes for anaesthesia distinguish procedures involving one or more stages in which there was anaesthesia with recovery, from procedures in which the only anaesthesia was terminal. They also include the use of local or regional anaesthesia. The categories are:

(a) no anaesthesia used throughout the procedure; this will include procedures without anaesthesia even

where the subject animal may have been killed by use of an anaesthetic overdose at the end of the procedure. It also includes studies of potential anaesthetic agents;
(b) general anaesthesia with recovery;
(c) local or regional anaesthesia;
(d) general anaesthesia without recovery, at the end of the procedure only;
(e) general anaesthesia without recovery, throughout the procedure.

The killing of an animal by the administration of an overdose of an anaesthetic agent (a recognised humane method as cited in Schedule 1 of the Act) is not a regulated procedure and is not recorded as such in the above table.

The use of neuromuscular blocking agents (NMBA) is uncommon and for this reason such use is not shown in the table (except as a footnote).

Type of procedure
The tables are divided into two groups:

A - Fundamental and applied studies other than toxicology (Tables 6–8);
B - Toxicity tests, or other safety or efficacy evaluation (Tables 9–16).

If the purpose was non-toxicological, the licensee was asked to specify the field of research, the nature of the procedure with regard to production and breeding and whether the technique was identified as being of particular interest.

If the purpose of the procedure was toxicological, the licensee was asked to report on the field of safety testing or efficacy evaluation, the type of test or procedure, and the legislative requirements (if any) under which the procedure was performed.

The two strands of reporting are mutually exclusive (as shown in the flowchart and Appendix B) and it is not possible, for instance, to identify procedures using a technique of particular interest if the purpose of the procedure was toxicological.

A Fundamental and applied studies other than toxicology

This group of tables is sub-divided into three main areas of interest:

(i) **Field of research** (Tables 6, 6a, 6.1 and 6.2)

The headings are self-explanatory, but the following should be noted:

(a) pharmaceutical research and development excludes anti-cancer agents, where work is listed separately later in the table under ‘cancer research’;
(b) ecology excludes work done in toxicology and other safety evaluation;
(c) tobacco and alcohol research lists only those procedures done for research on the effects of tobacco or alcohol, and not those where these substances are used as experimental tools or standards; note also that tobacco *safety* procedures would be reported in Table 9.

(ii) **Production of biological materials** (Table 7)

Production:

(a) procedures for production and maintenance of infectious agents (excluding those causing neoplasms);
(b) procedures for production and maintenance of vectors, e.g. parasites;
(c) procedures for production and maintenance of neoplasms;
(d) the ascites model for the production of monoclonal antibodies;
(e) initial immunisation for subsequent *in vitro* or *in vivo* production of monoclonal antibodies;
(f) procedures for production of polyclonal antibodies;
(g) procedures for production of other biological material, e.g. plasma, tissues.

(iii) **Techniques of particular interest** (Table 8)

This table provides a selective list which identifies those procedures in which a technique is of itself of particular interest as, for example, the application of a substance to the eye or exposure to ionising radiation. The procedures recorded in this table do not include those undertaken for toxicology or safety evaluation. However, few of these techniques would be used in routine regulatory toxicology or safety assessments.

B Toxicity tests, or other safety or efficacy evaluation

(i) **Safety and efficacy evaluation** (Tables 9, 9a)

Most of the subdivisions have been described in paragraph 10 (iii) above with regard to general safety of efficacy evaluation but the category also includes work done for pharmaceutical safety and efficacy evaluation, and some other purposes.

(ii) **Legislative requirements** (Table 10)

This identifies medical/dental and veterinary categories which include procedures used in the initial development and selection of such products, those required to satisfy specific legislation (medical and non-medical) such as the Medicines Act 1968 and/or equivalent overseas or international legislation or regulations for purposes such as the intention of registration or the intention of presenting batch quality control data; and those carried out for other reasons. The legislation is divided into seven groups:

(a) United Kingdom legislation only;
(b) legislation specific to one EU country only (excluding the UK);
(c) general EU requirements, including the European Pharmacopoeia;
(d) non-EU member country of Council of Europe legislation;
(e) legislation of other countries;
(f) any combination of (a)–(e);
(g) purposes other than legislative requirements.

The following are examples of specific legislative requirements which may be included:

Medicines Act 1968;
Workplace safety, e.g. Health and Safety at Work Act 1974, COSHH Regulations;
Substances used in agriculture, e.g. Control of Pesticides Regulations 1986; EU Pesticides Directives;
Substances used in foodstuffs, e.g. Food Safety Act 1990.

(iii) **Specific types of toxicity tests** (Table 11)
acute and subacute dose ranging or limit setting lethal toxicity tests;
acute quantitative lethal toxicity tests;
acute and subacute non-lethal clinical sign toxicity tests;
subchronic and chronic toxicity tests;
carcinogen/teratogen/mutagen tests;
other reproductive toxicity tests;
tests for clinical signs in the eye;
tests for clinical signs on the skin, including irritation or sensitisation;
toxicokinetics, pyrogenicity, biocompatibility and other toxicology tests.

(iv) **Tables showing some selected work in greater detail**
There are three further tables which examine some aspects of toxicological work in greater detail (see appendix B for full details of the codes):

Table 12: non-pharmaceuticals (list A, row 10, codes A01–A06);
Table 15: pharmaceuticals (list A, row 10, codes A11–A14);
Table 16: other safety or toxicology (list A, row 10, codes A21–A25).