

AGREEMENT BETWEEN THE SECRETARY OF STATE AND THE HEALTH AND SAFETY COMMISSION ON INSPECTION AND ENFORCEMENT RELATING TO THE ENVIRONMENTAL ASPECTS OF CONTAINED USES OF LARGER GMOs, AND DELIBERATE RELEASES INTO THE ENVIRONMENT OF GMOs USED IN CLINICAL APPLICATIONS

1. The Secretary of State hereby invites the Health and Safety Commission (“the Commission”), subject to paragraph 3, to perform the functions referred to in paragraph 2 (“the relevant functions”), being functions which in the opinion of the Secretary of State can appropriately be performed by the Commission.
2. The relevant functions are the functions specified in paragraph 1 of Annex A, being the Secretary of State’s enforcement functions under Part VI of the Environmental Protection Act 1990 (“the 1990 Act”).
3. The functions are to be exercised in relation to the release and marketing of genetically modified organisms under the 1990 Act and the Genetically Modified Organisms (Deliberate Release) Regulations 2002 and the GMO (Deliberate Release and Risk Assessment)(Amendment) Regulations 1996. In relation to the import and acquisition of genetically modified organisms, functions are to be exercised under the 1990 Act and the Genetically Modified Organisms (Contained Use) Regulations 2000.
4. Subject to the terms and conditions set out in Annex A and the initial programme of work set out in Annex B, acceptance of this invitation shall:
 - (a) constitute an agreement between the Secretary of State and the Commission under section 125(1) of the 1990 Act and section 13(1)(b) of the Health and Safety at Work, etc Act 1974 (“the 1974 Act”); and
 - (b) activate for the purposes and duration of the agreement the delegation by the Secretary of State to the Commission of the relevant functions.
5. References in this agreement to any Act or subordinate legislation are references to that Act or subordinate legislation as amended, extended or applied

Signed
On behalf of the Secretary of State
Department for Environment, Food and Rural Affairs

Date

The agreement comprised in the terms of the above invitation is hereby accepted:

Signed.....
By authority of the Health and Safety Commission

Date

Annex A

TERMS AND CONDITIONS

Functions

1. The relevant functions are those specified in section 125(2) of the 1990 Act:
 - (i) the service and withdrawal of prohibition notices (section 110);
 - (ii) the appointment of inspectors (section 114(1));
 - (iii) the authorisation of inspectors to prosecute before a magistrates' court (section 114(4))
 - (iv) the service of notices requiring persons to furnish information (section 116);
 - (v) the institution of proceedings (section 118(10));
 - (vi) the power to arrange for the remedying for harm (section 121).
2. The Commission shall direct the Health and Safety Executive ("the Executive") under section 11(4)(a) of the 1974 Act to exercise the relevant functions on behalf of the Commission in accordance with the following undertakings.

Appointment of inspectors

3. The Executive shall:
 - (a) inform the Secretary of State on the relevant qualifications, experience, training, instruction, tasks and instruments of appointment of inspectors under section 114 of the 1990 Act for the purposes of the agreement;
 - (b) appoint under section 114 of the 1990 Act such numbers of inspectors as appear sufficient for the purpose of carrying the agreement into effect and inform the Secretary of State of the arrangements for their deployment; and
 - (c) inform the Secretary of State of any proposed changes to the deployment of the inspectors appointed for the purpose of the agreement.
4. Inspectors appointed under the arrangements shall have the powers set out in sections 115 and 117 of the 1990 Act.

Programme of work

5. The Executive shall perform the relevant functions in accordance with a costed three-year programme of work and the Secretary of State's requirements for environmental protection. The agreed programme of work is at Annex B. The programme may be updated and

revised to cover changed requirements in line with the arrangements described in paragraph 6, in addition to which the strategy for deliberate release inspections of clinical trials will be reviewed after one year. In consultation and agreement with Defra, both the Scottish Executive and the National Assembly for Wales, as devolved administrations, are content for HSE to continue to with the inspection and enforcement arrangements detailed in this Agreement. Separate Agreements, to include an agreed programme of work, will be put in place with the devolved administrations.

6. In October 2006 and annually thereafter, the Secretary of State and the Executive shall review the programme of work for the financial year beginning in the following April. Any changes to the proposed programme will reflect the Secretary of State's current requirements for environmental protection and any additional requirements for inspection and enforcement. The programme will also, as appropriate, include details or take account of:

- (a) the expected number of planned inspection visits and the procedure to be used for prioritising them as well as the capacity of inspectors to respond to urgent needs;
- (b) the staff, management and training arrangement for the inspection team, including the grade of each member of it, and the proportion of his or her time allocated to the relevant functions;
- (c) the development of inspection procedures and instructions, including the procedures and warrants necessary for the exercise of rights of entry to and inspection of premises and the taking of samples under section 115 of the 1990 Act;
- (d) proposed arrangements for liaison with and support from other bodies and inspectorates;
- (e) proposed arrangements for liaison with the Secretary of State's officials and for attendance at meetings of the Advisory Committee on Releases to the Environment;
- (f) proposed arrangements for dialogue, nationally and internationally, with scientists, technologists and professional societies and other organisations on matters relating to environmental aspects of inspection and enforcement in connection with the relevant functions; and
- (g) proposals for support and advice to the Secretary of State on the development of standards, technical guidance and publications in connection with environmental aspects of the relevant functions.

Reports to the Secretary of State

7. The Executive shall submit to the Secretary of State at the end of April 2007 and annually thereafter, a report on the work carried out in fulfilment of the agreement during the preceding financial year. It will give an account of the work done under the costed programme of work for that year, and will include in particular the number of inspection visits paid, information on prosecution and other enforcement action taken, and a description of any problems identified which might require action in the future.

8. The Executive shall keep the Secretary of State fully informed on the investigation of any serious incidents or dangerous occurrences which have policy or prosecution implications or which might be widely publicised.

Exchange of information

9. The Secretary of State shall provide to the Commission and Executive such information as either of them may at any time reasonably require for the purpose of performing the functions specified in the agreement, and the Commission and Executive shall provide to the Secretary of State such information as she may at any time reasonably require in connection with the performance of those functions.

Financial arrangements

10. The Secretary of State shall pay the Executive the full amount of the costs incurred in performing the relevant functions, in so far as they are included in the approved programme of work. The Secretary of State's total liability for the three-year programme shall be £115,073 plus a contingency limit of £49,420, divided as follows:

2006-07	£36,883 plus contingency of £16,065
2007-08	£38,634 plus contingency of £16,470
2008-09	£39,556 plus contingency of £16,885

The costs assume that the programme of inspections will be maintained at a constant level over three years and include a 2.5% inflationary element. An allowance has been included for inspections in Scotland and Wales, which Defra shall continue to fund on behalf of the devolved administrations. The work programme is set out in Annex B.

11. The Secretary of State shall be responsible for additional liabilities only where she has consented to that additional expenditure in writing before it was incurred. The Executive shall notify the Secretary of State as soon as possible if the agreed sum for any year in relation to the costed programme of work is likely to be inadequate.

12. The Secretary of State's total liability in the period of 12 months from the commencement of this agreement, and in any subsequent period, shall be limited to the amount, if any, agreed by her in writing in accordance with the arrangements set out in paragraph 6, 10, 11 and with the other terms and conditions of the agreement, except that any costs relating to enforcement action and appeals shall be in addition to the costs specified.

13. The Executive shall produce such accounts, documents, records or explanation as the Secretary of State may reasonably request relating to expenditure in connection with the agreement.

14. The Secretary of State shall make payments to the Executive quarterly in arrears against invoices submitted to Defra's ASD Division. They will be within the limits of the agreed budget or for such higher sums as have been given prior approval.

General

15. The Executive shall not disclose to a third party information, reports or results relating to work carried out under the agreement, except for the purposes of enforcement action or in compliance with a court order, or in accordance with HSE's policy on open government without the agreement of the Secretary of State.

Period of agreement

18. The agreement shall come into effect as from 1 April 2006 and shall terminate on 31 March 2009, unless it is terminated early on the expiry of six months written notice given at any time by either party to this agreement to the other, or immediately with the consent of both parties.

Annex B

AGREEMENT BETWEEN THE SECRETARY OF STATE AND THE HEALTH AND SAFETY COMMISSION ON INSPECTION AND ENFORCEMENT RELATING TO THE ENVIRONMENTAL ASPECTS OF CONTAINED USES OF LARGER GMOs, AND DELIBERATE RELEASES INTO THE ENVIRONMENT OF GMOs USED IN CLINICAL APPLICATIONS

PROGRAMME OF WORK

1. This document sets out the programme of work from the commencement of the agreement signed by the Secretary of State and the Health and Safety Commission. The period covered by this programme shall terminate on 31 March 2009 but the programme is subject to review and may be amended to meet changed requirements.
2. Responsibility for the day-to-day management of the specified tasks rests with HSE under the supervision of the Head of the Biological Agents Unit . The staff undertaking the specified tasks shall be drawn from the list of staff set out in Appendix 3 hereto.
3. The Department's nominated officer for this agreement shall be Mr David Sherlock, Chemicals and GM Policy Division, Zone 4/E6, Ashdown House, 123 Victoria Street, London SW1E 6DE.
4. The Department shall pay HSE the costs of undertaking the specified tasks in accordance with the programme, subject to a total liability of £115,073 plus a contingency limit of £49,420.

Signed.....

Date.....

DR LINDA SMITH
Department for Environment, Food and Rural Affairs

The offer comprised in the terms of the above invitation is hereby accepted.

Signed.....

Date.....

Mr JOHN NEWBOLD
Health and Safety Executive

WORK PLAN

1. The plan of work is intended to cover that part of the work of HID SI4, Biological Agents Unit concerned with:

- (a) the Genetically Modified Organisms (Deliberate Release) Regulations 2002, in relation to inspection of vaccine or gene therapy trials and
- (b) environmental aspects of the contained use of genetically modified organisms covered by the Environmental Protection Act 1990, and in particular Section 108 (1) (a), as applied by the Genetically Modified Organisms (Risk Assessment) (Records and Exemptions) Regulations 1996

2. Release sites will be inspected in connection with consents for vaccine or gene therapy trials granted by the Secretary of State. All such trials should be inspected, with 5 cases allowed for in the annual budget subject to adjustment in the light of the number of consents actually issued. This element of the programme will be reviewed after one year so that HSE can provide feedback on the workload involved and an assessment can be made as to how effectively this is operating.

3. Planned inspections of sites in relation to the import and acquisition of genetically modified organisms which are larger than micro-organisms (plants and animals) at sites subject to Section 108 (1) (a) of the Environmental Protection Act 1990 and the Genetically Modified Organisms (Risk Assessment) (Records and Exemption) Regulations 1996 will continue. Inspections will be targeted at transgenics centres in the higher risk category, by intelligence gathered during the notification process for the contained use regulations, from published papers, from Defra licences and from any requested by Defra. In relation to the import and acquisition of genetically modified organisms, functions are to be exercised under the 1990 Act and the Genetically Modified Organisms (Contained Use) Regulations 2000, as amended by the Genetically Modified Organisms (Contained Use) Regulations 2005.

4. When HSE inspectors visit premises for their own contained use inspections, they should also carry out any inspections on our behalf of the environmental aspects of contained use of larger GMOs, with the intention of maximising efficiency. The number of inspections proposed is 20 for England, 3 for Scotland and 2 for Wales, with additional visits carried out if required by the competent authorities, to be covered by the contingency fund.

5. The areas of work covered by this agreement relate to the EPA 1990 as follows:

- scheduled inspections of release or contained use sites or in connection with GMOs, including tests, inspections, information gathering and taking and examination of samples under S. 115 or 116 of the EPA 1990, etc. for the purposes of:

- (a) inspecting and advising on compliance with the conditions attached to consents to release or market GMOs granted in accordance with S. 111 and 112 of EPA 1990;
 - (b) determining the adequacy of environmental risk assessments and associated records made in connection with contained use (i.e. importation or acquisition) of GMOs under S. 108 of the EPA 1990.
- scheduled or unscheduled inspections of release or contained use sites or in connection with approved GMO products for the purposes of investigating or dealing with unforeseen incidents or occurrences, and including:
- (a) the service and withdrawal of prohibition notices under S. 110 in connection with proposals for import, acquisition, release or marketing of GMOs;
 - (b) dealing with any cause of imminent danger of damage to the environment in accordance with S. 117;
 - (c) instituting and pursuing proceedings for offences committed under S. 118;
 - (d) remedying harm in accordance with S. 121 in connection with offences committed under S. 118;
 - (e) any tests, inspections, information gathering and taking and examining of samples required to support activities (a) to (d);
 - (f) investigating public complaints to determine if any offence has occurred.
6. In addition HSE will continue its activities relating to the assessment of applications for release or GMOs considered by the Advisory Committee for Releases to the Environment (ACRE) and its working groups including the development of related guidance.
7. Appropriate staff, training, travel and subsistence costs incurred in carrying out the duties required under this agreement will be met by Defra
8. The details of the programme and the costings are given in Appendix 1. The agreed protocol for the clinical trial inspections has been set out in full at Appendix 2. The staff qualified to undertake inspection, etc. and the contact points for the different aspects of the work are given in Appendix 3. Their qualifications and experience are given in Appendix 4.

APPENDIX 1**PRICE SCHEDULE****FORM OF TENDER AND PRICE SCHEDULE**

Costings are worked out for delivery of the inspection programmes, including management costs, supervision, and travel and subsistence (T&S). Costs are worked out on a daily rate, using Full Economic Costs (FEC) by grade. The T&S component is added to the staff costs, and is on the basis of a *pro rata* split between HSE and DEFRA.

Costs given below are for 2006 –2009. An inflationary element of 2.5% has been added to the 2nd and 3rd years, to give the total price.

Daily FEC costs for:	06/07	07/08	08/09
Band 1 Specialist Inspector	582	597	612
Band 2 Specialist Inspector	496	508	521
Band 3 Specialist Inspector	425	436	447
Band 4 Administrator	325	333	341
Band 5 Administrator (Regulatory Contact Officer)	280	287	294
Band 6 Administrator	241	247	253

Staff days offered for management, training given/received, maintenance of databases:

		06/07	07/08	08/09
Band 1	2 days	1164	1194	1224
Band 2	5 days	2480	2540	2605
Band 4	5 days	1625	1665	1705
Band 6	5 days	1205	1235	1265
Overall costs (including T&S)		6474	6634	6799

Staff days offered for contained use inspections in England - (inc. time for visit preparation, inspection visit, report working and follow-up action):

20 visits to contained use facilities:

		06/07	07/08	08/09
Band 2	2.5 days	1240	1270	1303
Band 3	25 days	10625	10900	11175
Band 5	2.5 days	700	718	735
Band 6	2 days	482	494	506
Overall costs (including T&S)		13047	13382	13719

Staff days offered for contained use inspections in Scotland - (inc. time for visit preparation, inspection visit, report working and follow-up action):

3 visits to contained use facilities:

		06/07	07/08	08/09
Band 2	0.5 days	248	254	261
Band 3	4 days	1700	1744	1788
Band 5	0.5 days	140	144	147
Band 6	0.5 days	121	124	127
Overall costs (including T&S)		2215	2266	2323

Staff days offered for contained use inspections in Wales - (inc. time for visit preparation, inspection visit, report working and follow-up action):

2 visits to contained use facilities:

		06/07	07/08	08/09
Band 2	0.5 days	248	254	261
Band 3	3 days	1275	1308	1341
Band 5	0.5 days	140	144	147
Band 6	0.5 days	121	124	127
Overall costs (including T&S)		1784	1830	1876

The split between England, Wales and Scotland may be adjusted within the overall total to respond to actual inspection requirements.

Staff days offered for Deliberate Release inspections in connection with consents to release GMOs in vaccine or gene therapy trials - (inc. time for visit preparation, inspection visit, report working and follow-up action):

10 inspection visits (2 per site):

		06/07	07/08	08/09
Band 2	2 days	992	1016	1042
Band 3	15 days	5525	6540	6705
Band 6	1 day	241	247	253
Overall costs (including T&S)		6758	7803	8000

Staff days offered for work involving liaison with the Competent Authority, dialogue with scientists and professional bodies on matters relating to the inspection and enforcement function, and production of technical guidance supporting the inspection function:

		06/07	07/08	08/09
Band 2	5 days	2480	2540	2605
Band 3	5 days	2125	2180	2235
Overall costs (including T&S)		4605	4720	4840

Conferences and Training

Where specific training is required to fulfil the contract, arising from developments in technology, this will be carried out in the most cost efficient manner. Individual inspectors would attend necessary training, and information would be cascaded within the group.

Attendance at relevant conferences may be required to keep abreast of technical developments.

	06/07	07/08	08/09
Overall costs (including T&S)	2000	2000	2000

Contingency Time and Costs

A contingency element is included to allow for increased inspection demand, for example following an expansion in deliberate releases, or to cover extra time required for formal investigations and enforcement.

These costs will only be incurred in agreement with DEFRA.

		06/07	07/08	08/09
Band 2	10 days	4960	5080	5210
Band 3	20 days	8500	8720	8940
Band 5	5 days	1400	1435	1470
Band 6	5 days	1205	1235	1265
Overall costs (including T&S)		16065	16470	16885

APPENDIX 2

HSE's Intervention Strategy for Premises Undertaking Clinical Trials of GM Vaccines or Gene Therapy Agents Under Deliberate Release Legislation

Aims of Inspections

One of the main aims of inspection of consent holders undertaking clinical trials of GM vaccines or gene therapy agents under deliberate release legislation will be to ensure that the trial is carried out in a way which is compliant with the limitations and the conditions of the consent to release the organism. In particular, the inspections will aim to ensure that the risks to both the environment and human health are those identified in the application and are minimised. However, the issues scrutinised during the inspection will depend on the nature of the trial, the information provided in the application and the conditions of consent for that trial. HSE's approach to undertaking the inspection will be in the manner set out below.

Which Deliberate Releases to Inspect

All consent holders undertaking clinical trials of GM vaccines or gene therapy agents under deliberate release consents will be inspected.

Timing of Inspections

We will carry out initial inspections **before** the trial begins, and a second inspection during the course of a trial. The aim of the initial inspections will be to discuss procedures and protocols, particularly those related to monitoring, and to inspect the facilities. This will be arranged by contacting the consent holder when consent is issued to set up an inspection before work commences or during the trial.

In theory, inspection before the trial begins may not be possible in all cases as the work can begin as soon as consent is issued. In this event, inspection will be carried out during the trial. However, in practice, centres will need to recruit volunteers to take part in trials, and this should provide the opportunity to inspection prior to commencement of the trial. Information obtained during this pre-trial inspection will be reported back to Defra/SE/WA, and may inform the timing and nature of follow-up visits.

A second inspection visit will be carried out during the trial. This will be either during the period when the vaccine is being administered, or during the follow-up work where monitoring for shedding is taking place. The visits will aim to ensure that the procedures for administration and for monitoring of shedding are being carried out in accordance with the consent. Consent holders are required to give details of how all procedures will be carried out, and the inspection will monitor compliance with the stated methods and procedures. Furthermore, where specific conditions are applied to the consent, compliance will be assessed.

Pre Inspection Activities

Prior to the initial inspection being carried out, HSE inspectors will review information provided in the application for consent to release the organisms, as well as any advice from ACRE and conditions attached to the consent to release.

The inspectors will contact the consent holders to arrange the inspection. This will include arranging to discuss protocols and procedures for all aspects of the trial, including follow-up and reporting back. They will also arrange to speak to staff administering the GMO and staff involved in sampling and monitoring, to ensure that there is the appropriate degree of understanding of the issues involved, and that training has been carried out.

Inspection Issues

During the inspection, a range of issues will be looked at. The degree of scrutiny of any particular area will vary between trials and will be based on the judgement of the inspection. The key issues that will be covered will include:

- Supply of GMO, including safe transport.
- Storage of the GMO.
- Preparation of the GMO for administration.
- Compliance with monitoring requirements detailed as part of the application or as a condition of consent. This will include: what samples are taken, timing of sampling, storage and transport of samples, how they are tested, sensitivity of tests used, competence of those carrying out testing and sampling etc. Contingency plans will be discussed, for example, procedures to be followed where unexpected levels of shedding are observed, etc.
- Facilities and areas used in the trial and their suitability. As well as considering the physical nature of the facilities, the location will be considered, for example, in relation to public corridors, waiting rooms etc.
- Cleaning regimes for areas to be used in the trial.
- Treatment of contaminated waste.
- Availability and use of personal protective equipment (where applicable).
- Information on risks to health and environment provided to patients and their families (ideally including speaking to patients).
- Information on risks to health and environment provided to staff, both directly involved in the trial and ancillary staff, such as porters and cleaners.
- Information provided to staff, patients and their families on hygiene measures or use and replacement for dressings.
- Mechanisms in place to ensure effectiveness of staff training and information provided to patients.
- Information on risk provided to staff, patients and their families.
- Contingency plans.
- Monitoring systems in place for general health of patients and any relevant symptoms in staff.

- Copies of monitoring data, specifically methodologies, consistency with application, adverse reactions, and 'daily log'.

Post Inspection

Following the inspection HSE will provide a copy of inspection report and any letter/formal enforcement action sent to trial organisers to Defra/SE/WA. Copies will be forwarded electronically. Copies of any supporting documentation will be held on file by HSE, and copied, as appropriate to Defra/SE/WA. Where issues arise at inspection that require the attention of the Competent Authorities these will be communicated directly by telephone or E-mail, particularly if enforcement action is being considered.

Post Trial

Review any report or monitoring data provided from the trial as a condition of consent.

This inspection protocol will be reviewed after 1 year.

APPENDIX 3

STAFF UNDERTAKING DUTIES UNDER THE AGENCY AGREEMENT

Band 1	Head of Unit
Band 2	Biotechnology Portfolio Holder Intervention Programme Manager
Band 3	Biological Agents Unit Specialist Inspectors (13)
Band 4	Notifications & Consents Administration Manager
Band 5	Regulatory Contact Officer
Band 6	Band 6 Administrators (2)

Any changes to this list will be notified to Defra and the devolved administrations.

APPENDIX 4

QUALIFICATIONS AND TRAINING

All professional staff are required to have a good degree in a relevant discipline. Relevant disciplines include most fields of biology (such as microbiology, biochemistry, ecology or agriculture) and chemical engineering. All inspectors undergo a one-year "in-house" training programme prior to joining the group. Each inspector is required to undertake appropriate further training and professional development through a structure programme set out in the section of the manual for Specialist Inspector Training and Development. This programme includes both internal and external course and meetings. Appropriate training records are maintained.