

# **Scientific Review of NIBSC**

**Report of an Independent Panel Chaired by Professor Sir Patrick Sissons**

**Submitted to the MHRA Board and CMO**

**January 2014**

## **Executive Summary**

1. This is the report of a scientific review of the National Institute of Biological Standards and Control (NIBSC) conducted by an independent panel convened in November 2013. The Panel was asked by the Chief Medical Officer (CMO) to consider, and make recommendations about, the current position and future direction of the scientific work of the Institute, and its geographic location, and report by the end of January 2014. Whilst the time allowed for the review did not permit an in depth assessment of the complete range of science at NIBSC, with the detailed documentation available and the information presented during a visit to the Institute, the Panel was nonetheless in a position to draw definitive conclusions.
2. Overall, the Panel concluded that NIBSC was achieving its mission in a commendable fashion. The Institute continues to fulfil its statutory functions, playing a vital role both nationally and internationally in biological standardisation and control and in support of key national interests including: the UK life sciences sector; major public health programmes; and the response to public health emergencies or medicines safety incidents. It continues to operate consistently at a very high level and its national and international standing and credibility has not diminished, but if anything has increased, in recent years. It remains a very highly regarded and trusted centre of scientific expertise in the regulatory field and performs its functions with a high degree of scientific rigor, with a highly skilled, motivated, productive and well organised workforce. The Institute's large programme of collaborative research continues to be productive and underpins its statutory functions and supports the development of its capabilities. All this is despite a context of significant and multiple organisational changes in recent years.
3. The Institute has been adept at keeping pace with scientific developments, scanning the horizon to identify the future challenges and developing its capabilities to respond to new challenges. However, with the proliferation and diversity of new biological medicines and the challenges of establishing their quality, efficacy and safety, the importance and value of the work at NIBSC cannot be underestimated and the scientific challenges it is likely to face may be greater than ever before. The Institute must continue to adapt to meet these emergent challenges. With this in mind, the Panel has made a number of recommendations for consideration by NIBSC, the MHRA Board and the DH to guide and support their decision making about the future development, position and location of the Institute. The Panel recognises that there may be resource implications to many of the recommendations and those will need to be taken into account when the recommendations are considered. These recommendations are set out below under headings which reflect the Review Panel's terms of reference:

*On future direction*

- Given the speed of scientific development and the need to find solutions to the increasingly complex problems in biological standardisation and control, continual evaluation of the Institute's science strategy and capabilities is vital and should be encouraged;
- NIBSC should, as a matter of urgency, re-establish a Scientific Advisory Committee to review the Institute's science strategy and oversee a rolling programme of reviews of NIBSC divisions;
- The membership of the Scientific Advisory Committee should be such that it can provide independent expert advice to the Director on, and scrutiny and oversight across, the increasingly broad range of scientific work at NIBSC and its science strategy, and thus provide assurance to the MHRA Board and to DH about the Institute's activities;
- The Scientific Advisory Committee should review the resource implications of the NIBSC science strategy and advise the Director on possible prioritisation;
- The Scientific Advisory Committee should, with the Director, reinstate the rolling programme of regular reviews of NIBSC divisions, as soon as practicable;
- The Scientific Advisory Committee should oversee a strategic assessment of the Institute's research collaborations to: identify gaps or areas of redundancy; assess the balance between basic and applied research; and monitor the divisional distribution, impact and value of externally generated research funding so that the implications of funding trends can be assessed;
- The Scientific Advisory Committee should examine the process for prioritising and assigning responsibility for development or replacement of international standards and advise the Director on future standards work within the NIBSC science strategy;

*On academic isolation and attracting and retaining staff*

- NIBSC should continue its efforts to establish collaborative research programmes with academic units, its post-graduate research programme, plans for a Masters programme on regulatory science and a post-doctoral fellowship programme and seek other potential avenues for closer working with academic institutions, including further joint appointments for NIBSC scientists with Universities;
- NIBSC should continue to use these schemes to help to ensure a flow of new high calibre and well trained scientists to the organisation, and to identify amongst them some who might later fill senior roles when they arise;
- the MHRA Board should, with the Director, ensure there is succession planning for possible future vacancies arising in the NIBSC senior leadership team (including the Directorship);

*On adapting to future business and scientific challenges*

- The Review Panel firmly believes that the continued pursuit of relevant high quality research within NIBSC is crucial to ensuring it is best placed to fulfil its regulatory role, respond to future challenges, and attract staff of the scientific calibre needed for this. NIBSC should thus at the very least maintain its research activities, and there is a case for expanding these;
- The future funding of NIBSC needs to be considered very carefully by the MHRA Board and DH: development of income generating standardisation and control activities should be encouraged and further reductions in central government funding should be avoided. Consideration should be given as to how the Institute might be financially supported in the event it was called to respond to a sustained crisis (e.g. an influenza pandemic) giving rise to resource pressures. An element of long-term funding for research should be ensured, as well as ensuring the Institute remains well placed to obtain external research funding in competition;
- NIBSC should consider how it can better highlight and communicate the true impact of its work to its sponsor bodies, key stakeholders and the wider scientific community. The NIBSC website should be reviewed with a view to highlighting the work at the Institute and increasing its profile with the scientific, clinical and pharmaceutical/biotechnology communities; an inspection of websites of other regulatory laboratories could be informative;
- NIBSC should consider how it could increase awareness of its capabilities amongst the wider scientific/clinical communities and pharmaceutical/biotechnology industry, including establishing itself as a “scientific lighthouse” – an internationally leading centre of expertise in a particular cutting edge area of science;
- NIBSC should continue to acquire and maintain an increasingly broad range and depth of relevant scientific knowledge and skills as well as new capabilities, including investment in platform technologies and staff skilled in their application to enable the development of new innovative analytical methods that can be applied across a range of areas;
- NIBSC should continue working cooperatively with other regulatory laboratories around the world. These relationships may become particularly important to help to establish principles and evidence requirements for the assessment of the quality, efficacy and safety of, for example, biosimilars and advanced therapies where there is little clarity presently. In this regard, collaborative working with the pharmaceutical and biotechnology industries should also be considered. Whilst collaboration with industry would need to be managed carefully to avoid conflicts of interest, the potential for conflicts of interest could be considered on a case by case basis using the procedures developed within the MHRA;

- NIBSC should consider working more closely with the clinical community involved in clinical trials of new therapeutics to support the identification and development of new potential biomarkers and the analytical methodologies to measure them;
- The MHRA Board and NIBSC should consider very carefully what can be realistically expected of the Institute in regulating individual new Biological and Cellular Therapies, given the expanding number and increasingly complex nature of biological medicines and emerging cell therapies, the resources it has available and its statutory obligations. These expectations should be clarified and clearly communicated;

*On location*

- The Review Panel could see no compelling case for relocating the Institute, and believes the work of NIBSC will be best served by its remaining at South Mimms for the foreseeable future (circa. next 10-15 years).

## **Introduction**

4. NIBSC is a centre of the UK Medicines and Healthcare products Regulatory Agency (MHRA), which is an executive agency of the Department of Health (DH). It has been in existence since 1972 and since then has built an international reputation as a centre of excellence in the standardisation and control of biological medicines. NIBSC is responsible for developing and producing over 90% of the International Standards in use to assure the quality of biological medicines such as vaccines, monoclonal antibodies, hormones, and blood products. It is also the UK's Official Medicines Control Laboratory (OMCL), responsible for the testing of biological medicines before they are released for use within the European Union. Additionally, it is the leading World Health Organization (WHO) International Laboratory for Standards, is a WHO Essential Regulatory Laboratory for the development, regulation and standardisation of influenza vaccines and is the home of the UK Stem Cell Bank.
5. NIBSC has statutory functions that are set out in section 57 of the Health and Social Care Act 2012. This states that the Institute acts on behalf of the Secretary of State for Health "to:
  - a) *devise standards for the purity and potency of biological substances;*
  - b) *prepare, approve, hold and distribute standard preparations of biological substances;*
  - c) *design appropriate procedures for testing biological substances;*
  - d) *provide or arrange for the provision of laboratory facilities for testing biological substances;*
  - e) *carry out tests on biological substances;*
  - f) *examine records kept in connection with the manufacture and quality control of biological substances;*
  - g) *report on the results of tests or examinations conducted in pursuance of paragraph (e) or (f); and*
  - h) *carry out or arrange for the carrying out of such research, or provide or arrange for the provision of such information or training, as it considers appropriate in connection with the functions mentioned in paragraphs (a) to (g)."*
6. NIBSC performs these functions on a UK-wide basis.
7. NIBSC is located at a single site at South Mimms, Hertfordshire – a few miles from the outskirts of North London – and has been in that location since 1987. It employs around 300 staff, two thirds of whom are scientists.

## **Background to the Review**

8. NIBSC was last reviewed in 2008<sup>1</sup> to inform the final stages of a merger between NIBSC and the Health Protection Agency (HPA) in 2009. This review included a strengths, weaknesses, opportunities and risks (SWOT) analysis. This analysis identified a number of strengths, including: the scientific quality of the work of NIBSC; its high national and international standing; and the Institute's organisational structure and facilities. Concerns raised included: a perception of academic isolation; potential future difficulties in retaining and recruiting staff; succession planning in light of the impending retirement of senior staff; and limitations on resources for research. The 2008 review panel also identified development opportunities for NIBSC, particularly in relation to emerging biological medicines, noting that this might also present challenges to the scientific capacity and capabilities of the Institute.
9. Since the 2008 review, there have been scientific developments with implications for the statutory functions and activities of NIBSC. In addition, there have been further organisational changes. In March 2013 the HPA, of which NIBSC was then a centre, was abolished with its functions, with the exception of NIBSC, subsumed into Public Health England (PHE) – a new executive agency of the Department of Health created in April 2013. NIBSC was merged with the MHRA at the same time.
10. Furthermore, when NIBSC became a centre of the HPA, it was within the scope of the Chrysalis Programme (later to become the Science Hub Programme) exploring the co-location of a number of HPA centres, including NIBSC, at a single location with the laboratories vacated by GSK at Harlow in Essex identified as a potential site. Following the merger with MHRA, the inclusion of NIBSC within the scope of this programme was reconsidered.
11. Thus in September 2013, DH and MHRA agreed that a review of NIBSC was timely in light of developments since the 2008 review and considerations about its future location. The review was commissioned by DH in October 2013. Although NIBSC was subsequently removed from the scope of the Science Hub Programme in November 2013, the location of the Institute either at South Mimms or elsewhere remained under consideration.

## **Terms of Reference**

12. DH and MHRA agreed the following terms of reference for the review in October 2013:

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<sup>1</sup> National Institute for Biological Standards and Control Strategic Review 30-31 October 2008. Panel report to the national Biological Standards Board: December 2008. Issued by Professor Sir Alex Markham in February 2009.

*"To assess the current quality of the science carried out by the National Institute of Biological Standards and Control (NIBSC), and to make recommendations on the future direction of its regulatory science:*

- *to help determine what is required for NIBSC to maintain and improve its business over the next 10 to 20 years, including the need to attract and retain high quality staff;*
- *to help underpin and further the work of NIBSC, to examine and identify how the organisation will need to adapt to effectively respond to the future scientific changes in biological medicines – such as the change from simple vaccines towards complex vaccines, non-communicable disease vaccines, gene therapy, monoclonal antibodies, biosimilars, genomics and regenerative medicine;*
- *to advise whether its scientific future is best served by maintaining its current location at South Mimms, or whether it would be better to co-locate with another research organisation(s) to achieve the above aim.*
  - *Should the Review Panel advise a move to be in the best interests to secure NIBSC future, consider and identify the benefits and the risks of relocation to another site.*

*To help answer these key questions, the Review will consider whether the issue of academic isolation identified in the previous Strategic Review of NIBSC in 2008 has been addressed, and how it will be progressed further in the future.*

*The Review Panel will submit its Review for consideration by the MHRA Board on 16 December and the MHRA Chair will then report to DH, in the person of the CMO."*

13. When the terms of reference were agreed, it was envisaged that the review report would inform considerations about whether or not NIBSC should be in the scope of the Science Hub Programme. Following the decision in November 2013 to remove NIBSC from the programme, it was agreed that the Panel should be given more time to complete the review and a new reporting deadline of the end of January 2014 was set.

### **Review Panel**

14. Professor Sir Patrick Sissons was invited by the CMO to chair the review panel and he agreed to that request in mid-October 2013. A six-member panel was convened by early November 2013 with expertise in the broad range of science at NIBSC, including two overseas experts with substantial experience of regulatory biomedical science, that could conduct an authoritative review and address the terms of reference. Several experts with a background in the pharmaceutical industry were invited to join the Panel but none were available within the timeframe for the review. The Panel was joined by three observers – all non-executive directors of MHRA – with long standing knowledge of NIBSC and including the chair of the 2008 review panel. None of the Panel members

had substantive conflicts of interests in NIBSC, although some had previous experience of working with the Institute. Details of the Panel members and observers and their previous work with NIBSC are set out at Annex A. The Panel was supported by a scientist from DH.

### **Review process**

15. Background papers prepared by NIBSC in consultation with the Panel Chair and DH scientist were provided to the Panel on 11 November 2013 and included:

- an overview of NIBSC functions, structure, facilities and governance;
- summary of NIBSC outputs 2008 to 2013 in four areas of key activity: standardisation, medicines control, research and provision of advice and response to incidents/emergencies;
- organisational developments;
- future strategy and planned developments;
- a summary of activities taken forward by NIBSC in relation to the SWOT analysis in the 2008 NIBSC Review.

16. These papers together with a draft agenda for a site visit of the NIBSC facility were considered by the Panel via teleconference on 25 November 2013. During these discussions the Panel identified further information that it wished to consider which was provided by NIBSC in papers issued to the Panel on 28 November 2013 or was presented at the site visit, including:

- a discussion of the impact of NIBSC research;
- detailed organograms of the staff in each NIBSC division and analyses of staff numbers, grade and age profiles;
- a workforce planning and development strategy;
- a list of external organisations and groups that staff at NIBSC provide professional input to either as chair, members or observers;
- an analysis by the Institute of the impact of relocation of NIBSC;
- the NIBSC risk register.

17. A full list of the documents provided to the Panel is at Annex B.

18. The Panel undertook a site visit to the NIBSC facility on 2 December 2013. Ahead of that visit, the Panel Chair and DH scientist visited the facility on 28 November 2013 and discussed with the NIBSC Director the agenda and further information requested by the Panel. A number of Panel members and observers also met on the evening prior to the site visit to discuss aspects of the terms of reference. The site visit, which was attended by all the Panel members and the observers, included a series of presentations covering NIBSC functions, future plans and a wide range of current scientific studies at NIBSC. It

also included a tour of some of the facility with presentations. The Panel was able to discuss the work with the presenters. The agenda for the site visit is at Annex C.

19. At the end of the site visit, the Panel met to discuss what it had seen and heard as well as the evidence provided in the papers in order to form views and address the terms of reference.
20. Following the site visit, a report was drafted, circulated and considered by the Panel at a teleconference on 10 January 2014 along with additional information requested by the Panel on NIBSC publications and research grants. Since it had not been possible for the Panel to include members with an industrial background, two such experts were also consulted on certain aspects: Professor Ian Kimber (formerly Head of Research at Syngenta – Central Toxicology Laboratory and currently Chair of Toxicology and Associate Dean for Business Development in the Faculty of Life Sciences, University of Manchester and Chair of the Board of the UK National Centre for the Replacement, Refinement and Reduction of Animals in Research) and Dr Ian Tomlinson (Senior Vice President of GSK Worldwide Business Development and Biopharmaceuticals R&D and a Board member of the Stevenage Biocatalyst)<sup>2</sup>. The views of these experts were also considered at the teleconference.
21. The report was revised to take into account comments and recirculated for any further final comments. The final draft report was provided to the NIBSC Director for comment in order to identify any factual misunderstandings or inaccuracies. The final report was submitted in January 2014 to the MHRA Board and the CMO.
22. The Panel Chair provided a verbal update to the MHRA Board on 16 December 2013 about the progress of the review. He presented the final report to the MHRA Board at its meeting on 19 February 2014.

### **Observations and Conclusions**

23. In the time allowed for the review, it was not possible for the Panel to conduct an in depth assessment of the complete range of science undertaken by NIBSC. There were some areas of work of NIBSC that were not covered in the documentation and site visit. However, with the detailed documents provided by NIBSC and the opportunity to discuss a very wide range of the Institute's work first-hand with NIBSC scientists, including in key areas, the Panel nonetheless was in a position to draw definite conclusions about the scientific expertise and capabilities of staff at NIBSC as well as the quality of the science produced and the scientific direction of the organisation.

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<sup>2</sup> Both were provided with papers: Professor Kimber's views were given in writing and Dr. Tomlinson's in a 1.5 hour interview with the Chair.

*Current quality of science*

24. The Panel noted that, despite the significant distractions caused by successive organisational changes around the governance of NIBSC and the financial constraints imposed over the last five years, the Institute had substantially expanded its expertise and activities in order to keep pace with scientific developments. Standardisation work had expanded with the production of a large number of new standards, the replacement of existing standards and the establishment of supply arrangements with international Pharmacopoeias. The Institute had also largely maintained its medicines control activities and had substantially diversified its research capability through investment in new technologies and facilities and by establishing a wide range of research collaborations. NIBSC scientists had continued to support a large number of national and international expert advisory committees on standardisation and the regulation and use of biological medicines either as chairs, members or observers.
25. Thus, it was evident to the Panel that the high national and international standing and credibility of NIBSC has not diminished, and may have become enhanced, in recent years. NIBSC clearly continues to be a very highly regarded and trusted centre of scientific expertise in the regulatory field.
26. Although an in depth assessment of individual scientific projects could not be conducted, it was clear to the Panel that NIBSC performs its functions with a high degree of scientific rigor, and has a highly skilled, motivated and well organised workforce. This was evidenced not least by the speed with which the Institute had been able to respond to the short timescale for the review and the quality of the information in the documents provided and also presented at the site visit. Examples of such high quality scientific work would include the Institute's work on the issues surrounding the polio eradication campaign, and the use of disabled polio viruses in vaccination, and its analysis of the possible immunological/immunochemical mechanisms responsible for the TGN1412 incident.
27. The Panel noted that the Institute's divisions between them had consistently been able to attract over £3 million per annum in external grant funding for a number of years, mainly through a large number of collaborations with academia, from a range of sources including research councils, the Wellcome Trust, the Gates Foundation and the European Union. However the Institute had also been able to attract research funding in its own right. A significant proportion of funding for research that had been provided within the grant in aid from the DH until 2012, is now provided through a five-year research contract with the DH policy research programme. There were no indications of any imminent downturn in external research funding.

28. The Panel noted from an inspection of the Institute's publications record that around three quarters of publications in the last five years were produced by NIBSC scientists in collaboration with others with the remainder produced by NIBSC scientists alone. NIBSC scientists were first authors in around one half of all publications and were also last authors in around one half of all publications. Thus, there appears to be a balance between collaborative and solely NIBSC produced publications, and also in the proportion of publications led by NIBSC scientists, which the Panel considered appropriate given the Institute's mission. Furthermore, publications were distributed across the Institute's divisions and showed evidence of collaboration between divisions, in particular with the Technology Development and Infrastructure division.
29. Nevertheless, the Panel noted that the number of peer-reviewed scientific publications produced by NIBSC had fallen significantly over the last two years: this coincided with the merger with HPA, possibly reflecting the 'opportunity cost' of the additional work involved in facilitating that merger and the subsequent merger with MHRA. In the view of the Panel it is imperative that NIBSC scientists continue to be encouraged to publish their work in the peer-reviewed literature in a timely manner. This is important as a measure of the quality of the science and the impact of the Institute, and to maintain the reputation of the Institute and its staff.
30. However, the Panel considers it would be inappropriate to measure the quality and impact of the Institute's science in terms of the number of publications alone. It was very evident that much of the work at NIBSC has, or may go on to have, substantial impact. Examples include the numerous International Standards produced which support biological testing programmes around the world; the new assays developed to assess the safety and quality of vaccines, immunoglobulins and blood anticoagulant therapy prior to their release for use; and work which contributes to the replacement, reduction and refinement of a number of animal tests. Research papers produced by NIBSC, although not necessarily published in high impact journals, have been cited and accessed frequently. Similarly, the contributions of NIBSC scientists to advisory committees to the UK Government, European Medicines Agency, WHO and other international bodies and the technical papers produced for national and international organisations undoubtedly have an impact, although much of this is not apparent to the wider biomedical science community.
31. The Panel recommends that the Institute considers how it can better highlight and communicate the true impact of its work to its sponsor bodies, key stakeholders and the wider scientific community.

*Assessment of actions arising from the 2008 NIBSC Review*

32. The Panel noted that NIBSC had responded to almost all of the issues raised in the 2008 NIBSC Review, although progress in some areas may have been constrained by the diversion of management resources required by the successive organisational changes.
33. The Panel could find relatively little direct evidence of NIBSC being isolated in an academic sense or having problems in recruiting scientists of appropriate calibre. However the Panel is conscious that it is hard to measure what does not happen, or 'might have been' (were NIBSC, for example, located elsewhere) and these remain issues that will require on-going monitoring and attention.
34. The Panel found that NIBSC had been active in establishing collaborative research programmes with academic units. It has a graduate (PhD) student programme, and had also established a post-graduate research programme with London-based Universities and is in discussions about establishing a Masters programme on regulatory science and a post-doctoral fellowship programme. There is also an active programme of science seminars with both internal and invited external speakers.
35. The Panel strongly encourages NIBSC to continue to actively pursue these and other potential avenues for closer working with academic institutions including joint appointments for NIBSC scientists with universities; currently such joint appointments are very few in number (the Panel were told there were only 3). The Panel were also told of the agreement with University College London, whereby their former Dean of the Faculty of Life Sciences will be seconded (for an initial period of 2 years) to Head the new NIBSC Division of Advanced Therapeutics, which provides further evidence of academic institutional collaboration.
36. The Panel noted that NIBSC had workforce plans in place and, following a series of retirements of senior staff in recent years, vacant positions had been filled with apparently very able scientists. Greater academic links and the establishment of post-graduate and post-doctoral fellowship programmes should help to ensure a flow of new high calibre and well trained scientists to the organisation, some of whom might later fill senior roles when they arise. Nevertheless, the Institute will need to continue to recruit from outside the organisation – and it is appropriate that it does so if this ensures the best appointments are made, particularly to key scientific leadership roles.
37. The Panel welcomed all these developments. However, there was some concern should NIBSC lose the leadership, scientific skills and experience of its Director and senior team. It is clear that the excellent position that NIBSC retains, despite significant organisational upheaval and other challenges, is in large part attributable to the success of the

Director, with his senior team, in maintaining institutional morale through this period of change. The Panel recommends that the MHRA Board considers carefully succession plans to deal with vacancies arising in the NIBSC senior leadership team.

*Factors affecting NIBSC future - funding*

38. The Panel noted that over the last five years NIBSC appears to have been able to withstand the financial constraints imposed by a series of organisational changes and real-terms reductions in central government funding: DH recurrent annual funding has remained flat in actual terms (circa £11.5m) with a proportion of this now provided as a DH research grant (although substantial capital investment has been provided by DH). This had been mitigated by careful and shrewd management, a growth in the income generated, particularly in the sales of standards, and the winning of research grants from a range of sources. Nevertheless, it was noted that NIBSC operates on a budget several-fold smaller than another comparable European regulatory institute. If NIBSC is to meet the future challenges it faces, it is likely to need to maintain and expand its current capacity and capabilities, which will consequently necessitate an increase in the funds available.
39. Whilst the growth of income from sales of standards seems likely to continue with the welcome expansion of the Institute's links with international Pharmacopoeias, other avenues of income generation available to NIBSC, for example from OMCL activities, may be more uncertain as biologics manufacturers generally select the local OMCL and thus OMCL revenue is dependent on company manufacturing strategies. Furthermore, funding for research at NIBSC is now acquired through fixed-term grants. Thus, any loss or reduction in funding streams could place NIBSC capabilities and status at significant risk.
40. The Panel considers that the consequences of any further reductions in central government funding should be considered very carefully, and would be likely to compromise the Institute's function. Furthermore, there may be little room for manoeuvre should NIBSC be called to respond to a sustained crisis (e.g. an influenza pandemic). Consideration should be given as to how the Institute might be financially supported (for example with an in year financial supplement from the DH) in the event it was called upon to respond to a sustained crisis giving rise to resource pressures. Consideration also needs to be given to how best to ensure long-term funding for research, particularly when the current DH Policy Research Programme contract expires, or requires renewal.
41. The Panel was informed that, given the anticipated expansion in biological medicines, there is sufficient space, on an international scale, for existing and emerging regulatory laboratories involved in biological standardisation and control. The global need for

these activities can presently only be met by a few organisations. Whilst there was no indication of complacency on the part of NIBSC, the Panel considered it nonetheless vital that NIBSC retains its international position so that it can continue to attract income generating opportunities. This is essential to help fund the inward investment that will be necessary for NIBSC to keep pace with scientific developments and fulfil its statutory functions. This is not only important for NIBSC itself but also for the key national interests that NIBSC supports including: the UK life sciences sector, major public health programmes (e.g. routine immunisation programmes) and the response to public health emergencies (e.g. an influenza pandemic) or medicines safety incidents (e.g. the TGN1412 clinical trial or vaccine recalls).

42. The Panel recommends that further development of income generating standardisation and control activities should be encouraged. In this respect, the WHO Biological Standardisation Team and the WHO Collaborating Centres on Standards are among the most important collaborators for NIBSC. In the last five years NIBSC has established, through the WHO Expert Committee of Biological Standardization, 40 new standards and 41 replacement standards. Whilst it might be expected that this activity may continue at this level or increase, the process for WHO prioritising and assigning responsibility for development or replacement of standards is unclear. The Panel suggests that the process should be clarified and future standards work considered within the NIBSC science strategy.
43. It may also be possible for NIBSC to generate income through commercialisation by others of its intellectual property, although potential conflicts of interest would need to be managed. The recent transfer to GSK of a novel polio vaccine technology developed by NIBSC for the post-polio eradication era is one such example. The Panel understands that NIBSC, consequent on its merging with the MHRA, has developed a policy on intellectual property rights (IPR) so that the Institute can benefit where commercialisation would not give rise to conflicts of interest. Where conflicts of interest could arise, IPR would be transferred to another government organisation (PHE in the first instance). It would be sensible to keep this policy under review to ensure that the Institute benefits from the IPR it generates as much as possible.

#### *Factors affecting NIBSC future – role of research*

44. Following a discussion of the role of research and whether or not NIBSC should conduct research at all, the Panel was very firmly of the view that research remains a critical activity for the Institute. This is because research completely underpins the Institute's statutory functions, both by developing and supporting the standardisation and control methodologies of the future (indeed research itself is one of the statutory functions), and by ensuring NIBSC remains best placed to respond to unforeseen emergency regulatory situations. Research supports the development of necessary in-house

expertise (for example in the major cutting edge technology platforms) and helps to retain and attract the high calibre scientists needed to work for, or collaborate with, NIBSC. Research also enhances the reputation of the Institute and its scientists ensuring that NIBSC remains highly influential in the development of regulatory science in Europe and globally and can continue to attract income generating opportunities. Thus, in order for NIBSC to maintain and build upon its reputation, to support its current functions and fulfil its science strategy, the Panel recommends that the programme of research at NIBSC is at the very least maintained, if not expanded.

45. Whilst the Panel was encouraged by the number and range of collaborative research projects, mostly with academia, it was difficult (given the time available) to assess whether the scope, extent and focus of this research as a whole was most appropriate to meet the Institute's strategic objectives. The Panel recommends that a strategic assessment of the Institute's research collaborations be conducted to: identify gaps or areas of redundancy; assess the balance between basic and applied research; and monitor the divisional distribution, impact and value of externally generated research funding so that the implications of funding trends can be assessed at a more granular level.
46. Whilst the Institute is highly regarded by its immediate stakeholders, the Panel considered that the work at NIBSC and its impact remains insufficiently visible to the wider scientific community, in particular the clinical community. The Institute should consider ways in which it could further promote its scientific work to help ensure that it continues to attract research collaborations and funding. The Panel considered it important that NIBSC should seek to ensure that selected areas of its scientific activity were of the highest international quality: as an example they noted the international profile the Institute currently has for its work on polio. The Panel felt that maintaining such a selected "scientific lighthouse" – an internationally leading centre of expertise in a particular cutting edge area of science relevant to regulation – would both enhance its external profile with the wider scientific community, and set an internal scientific 'benchmark' to which other groups could aspire.
47. The Panel also suggested that, whilst NIBSC may be well known to large pharmaceutical companies, there may be a lack of awareness amongst small and medium enterprise pharmaceutical/biotechnology companies involved in translational medicine. NIBSC could have an important future role for companies developing, for example, cell and gene therapies and diagnostics for stratified medicine. The Technology Strategy Board and some of its Catapult centres, including the Cell Therapy Catapult, the High Value Manufacturing Catapult and its newly created National Biologics Manufacturing Centre and the planned Diagnostics for Stratified Medicine Catapult, could be key collaborators in this regard.

48. The Panel recommends that NIBSC consider ways in which it could increase awareness of its capabilities amongst the wider scientific/clinical communities and the pharmaceutical/biotechnology industry. The Panel found the current NIBSC website to be very uninformative and unhelpful in this regard with no details presented about the scientific staff that work there and very little detail about the impact of the work at NIBSC or about the research conducted and research publications. The Panel recommends that the NIBSC website should be reviewed with a view to highlighting the work at the Institute and increasing its profile with the scientific, clinical and pharmaceutical/biotechnology communities; an inspection of websites of other regulatory laboratories could be informative.

*Future scientific challenges*

49. The 2013-2023 NIBSC science strategy shows that the Institute continues to monitor closely the changing landscape of biomedical science, evaluates the future challenges and how its scientific activities and capabilities might require modification to respond to those challenges. Internal organisational adjustments suggest NIBSC remains flexible and responsive to future challenges. Cross-cutting programmes to deal with, for example, blood-related issues that span a number of scientific divisions, had been established. Divisions had been merged to manage an increase in work related to new viral vaccination programmes. A new Advanced Therapies division had been established to deal with the expected increase in activity related to gene and cell therapies and regenerative medicine with the successful recruitment of a prominent expert from academia to head that division. Given the speed of scientific development and the need to find solutions to the increasingly complex problems in biological standardisation and control, the Panel considers that such continual re-evaluation is vital and should be encouraged.
50. With this in mind, the Panel was surprised to learn that since the 2008 review, the Scientific Advisory Committee, which had previously reviewed the Institute's science strategy on a regular basis, had been disbanded. Furthermore, the rolling programme of quinquennial reviews of NIBSC divisions that was overseen by this committee (with additional co-opted expertise) had also lapsed. Whilst the Panel was reassured to learn that NIBSC plans to convene a new advisory committee during 2014, the Panel recommends that this should be taken forward as a matter of urgency. The membership of the new committee should be such that it can provide independent expert advice to the Director on, and scrutiny and oversight across, the increasingly broad range of scientific work at NIBSC and its science strategy, and provide assurance to the MHRA Board and to DH about the Institute's scientific activities. The rolling programme of regular reviews of NIBSC divisions should be reinstated as soon as practicable.

51. The Panel agreed that the areas identified in the current science strategy were those likely to present the challenges for biological standardisation and control over the next 10 years: regenerative medicines; biosimilars; monoclonal antibody therapies; new vaccines including therapeutic vaccines; gene and cell therapies; and stratified/personalised medicines; although others (for example the future of biological medicines based on nanotechnologies) were as yet unclear. Drug-device hybrid technologies may be one further area that should be considered. However, it was noted that areas of currently intense activity elsewhere could have a major impact on existing areas of NIBSC work within the next 10 years. For example, the successful development of a universal influenza vaccine may obviate the need for much of the work of the Influenza Resource Centre and the eradication of polio would alter the focus of the Institute's work in this area. However, the Panel thought that NIBSC could adapt quickly to reallocate resources should these situations arise, and thus such developments should not put the Institute at fundamental risk.
52. However, the Panel was concerned about the resource implications of the strategy, given its very wide scope, and noted the lack of formal analysis of the resources that would be needed. Should resources be too limited to support the strategy, prioritisation of activities will need to be considered very carefully. The Panel recommends that the new Scientific Advisory Committee should provide advice to the Director about prioritisation decisions, and possible mechanisms for taking these.
53. The Panel noted that to date NIBSC has been successful at expanding its capabilities and developing innovative approaches for standardisation and control. Next generation sequencing, proteomics and bioinformatics capabilities had been established. The Stem Cell Bank had established expertise in the handling and analysis of stem cells. Novel analytical methods are being developed such as: flow cytometry standards from stabilisation of CD4 T helper cells that could be applied to other cell types; and genomic analysis of complex mixtures of pathogens, to identify low level adventitious agents, which could be applied to a range of situations. The Panel considers that the Institute needs to continue to acquire and maintain an increasingly broad range and depth of scientific knowledge and skills as well as new capabilities if it is to address emerging challenges and continue to fulfil its statutory and current national and international roles. Continued investment in platform technologies should be helpful, for example in genomic, transcript microarray, proteomic and metabolomic technologies, and staff skilled in their application could enable the development of new innovative analytical methods that can be applied across a range of areas. In addition, continued development of analytical methods such as the *in vitro* pyrogenicity and influenza vaccine potency assays being established could lead to more effective and less time consuming testing schemes.

54. Understanding the inherent variability in the concentrations of the constituents in biological samples and their clinical significance will be an increasing challenge for biological standardisation and control. Cooperative working with other regulatory laboratories around the world will continue to be important to provide a network for the validation of new standards and assurance about the reproducibility and reliability of new regulatory tests. Furthermore, these relationships may become particularly important to help to establish principles and evidence requirements for the assessment of the quality, efficacy and safety of, for example, biosimilars and advanced therapies where there is little clarity presently. In this regard, collaborative working with the pharmaceutical and biotechnology industries, which is likely to be welcomed by industry, may be helpful and should be considered. Whilst collaborating with industry would need to be considered carefully to avoid conflicts of interest, the potential for conflicts of interest could be considered on a case by case basis using the procedures developed within the MHRA. Development of biomarkers to accurately predict the quality, safety and/or efficacy of biological medicines will also be important. To aid these efforts, the Panel suggests that NIBSC could work more closely with the clinical community involved in clinical trials of new therapeutics to help identify and develop new potential biomarkers and the analytical methodologies to measure them.
55. Given the proliferation and diversity of new biological medicines and the challenges of establishing their quality, efficacy and safety, the importance of the work at NIBSC cannot be underestimated. The Institute's position at the forefront of biological standardisation and control both for the UK and internationally carries huge responsibility. However, it was not clear to the Panel what the extent of future regulatory responsibilities of NIBSC in this area should be. For example, reflecting upon research results presented on the equivalence of innovator and biosimilar products, the Panel questioned whether NIBSC should have an expanded role in the post-market evaluation or surveillance of the quality, safety and efficacy of biosimilars to provide reassurance about the equivalence of products, or identify products failing to meet the specifications in market authorisations. This question (of the full extent of future regulatory responsibilities of NIBSC in this area) appears to be unresolved, and under active debate, in the Institute and MHRA. The evidence the Panel heard from the industry representative consulted indicated that there is considerable uncertainty within the pharmaceutical sector on the regulatory requirements a new 'biosimilar' will have to satisfy to be licenced, and this uncertainty is even greater for the emerging cell based therapies. He indicated that industry would welcome informed guidance on the most appropriate evidence base in these areas (in terms of comparative assays and trials), and that NIBSC, as a research based institution, was both well placed to provide this, and to have its opinion seen as authoritative by the sector. The major pharmaceutical companies in close geographic proximity to NIBSC have large teams working in these areas of biologics and cell based therapies, and it was clear would welcome discussion –

NIBSC should thus consider whether there are opportunities here for constructive and mutually beneficial engagement with the sector in this important area.

56. Furthermore, the Panel considered that, with a relatively small budget and limited resources, there are risks that NIBSC may not be able to handle effectively the range of regulatory issues that may emerge. The Panel considered whether NIBSC should instead focus on a narrower range of areas. It concluded, however, that it is vital for NIBSC to have the expertise and capabilities to work across a wide range of areas in order to meet its statutory functions and maintain its international position and standing. Nevertheless, there may be an increasing risk that issues might arise relating to the quality, efficacy and safety of biological medicines that may be identified too late with potential public health consequences and reputational damage to NIBSC (and MHRA). The Panel recommends that NIBSC and the MHRA Board consider very carefully what can be realistically expected of the Institute given the expanding and increasingly complex nature of biological medicines, the resources it has available and its statutory obligations. These expectations should be clarified and clearly communicated.

*Location*

57. The Panel noted that there had been very substantial capital investment in the South Mimms site in recent years with the development of unique facilities such as the Influenza Resource Centre and the Stem Cell Bank amongst others. Overall the Facility appears to be in very good order and likely to remain so for quite some time. The location of the entire organisation at one site benefits the activities of the Institute and there appears to be room for possible expansion of the Facility.
58. The current location remains relatively isolated in terms of immediately co-located cognate institutions (with even the adjacent Clare Hall Laboratories being vacated by Cancer Research UK consequent on the opening of the Crick Centre). However this does not appear to the Panel to present a serious obstacle to the work of the Institute, nor to be a major barrier to the recruitment of new staff. The current location should facilitate existing and new potential collaborations with other scientific centres relatively close by including: Imperial College, University College London, University of Cambridge, University of Oxford, the Sanger Centre, pharmaceutical industry sites at Stevenage, and later, the Crick Institute in central London (many of these are situated, with NIBSC, on a geographic and rail ‘corridor’ from North London to Cambridge). Similarly, these opportunities for collaboration would exist, if NIBSC were situated within or close to a Science Hub at Harlow, but the Panel noted that the Harlow option would not obviously place the Institute significantly nearer to University/Academic partners with cognate interests. The Panel was not presented with a specific scientific case for a move to Harlow, but presumed it would be principally the microbiological work under PHE which would synergise with the interests of NIBSC. Importantly, wherever NIBSC is based it will

need to collaborate widely with organisations outside its immediate geographical vicinity, based on wherever the best and most appropriate science relevant to a particular regulatory issue is to be found.

59. The Panel noted the very high financial costs of relocation, involving the construction of new highly specialist and unique facilities. There are also significant risks to relocation. NIBSC has built over decades a world-wide reputation as a trusted and relied upon organisation. Relocation would present major business and reputational risks should key NIBSC activities be interrupted. For example, suspension of standardisation and medicines control work would risk these being transferred to other organisations which NIBSC might not then win back. Should the work of the Influenza Resource Centre be suspended, global manufacture of influenza vaccines would be at risk with potential severe public health consequences. The only effective mitigation of such risks would be by a period of double running of facilities at the existing and new site. For some facilities such as the Influenza Resource Centre and Stem Cell Bank, that are highly complex facilities to build and require lengthy regulatory processes before they can be licensed for operation, double running might be needed for considerable time at potential high cost.
60. The Panel concluded, therefore, that there are no compelling physical, strategic or scientific reasons for NIBSC to relocate to another site at the current time or in the foreseeable future (circa next 10-15 years). Relocation would present very significant risks and costs. The Panel also considered that following the distractions and opportunity costs entailed by successive mergers and demergers, NIBSC would benefit greatly from a sustained period of stability. This would allow it to build upon its excellent position, plan to meet the significant future scientific challenges and take advantage more quickly of the opportunities presented by having merged with the MHRA. Thus, the Panel concludes that the future of NIBSC would be best served by its remaining at South Mimms for the foreseeable future.

## **Recommendations**

61. Based on the evidence reviewed and to address the terms of reference, the Panel made a number of recommendations. The Panel recognises that there may be resource implications to many of the recommendations that will need to be taken into account when they are considered. The recommendations are set out below under headings reflecting the Panel's terms of reference:

### *On future direction*

- Given the speed of scientific development and the need to find solutions to the increasingly complex problems in biological standardisation and control,

continual evaluation of the Institute's science strategy and capabilities is vital and should be encouraged;

- NIBSC should, as a matter of urgency, re-establish a Scientific Advisory Committee to review the Institute's science strategy and oversee a rolling programme of reviews of NIBSC divisions;
- The membership of the Scientific Advisory Committee should be such that it can provide independent expert advice to the Director on, and scrutiny and oversight across, the increasingly broad range of scientific work at NIBSC and its science strategy, and thus provide assurance to the MHRA Board and to DH about the Institute's activities;
- The Scientific Advisory Committee should review the resource implications of the NIBSC science strategy and advise the Director on possible prioritisation;
- The Scientific Advisory Committee should, with the Director, reinstate the rolling programme of regular reviews of NIBSC divisions, as soon as practicable;
- The Scientific Advisory Committee should oversee a strategic assessment of the Institute's research collaborations to: identify gaps or areas of redundancy; assess the balance between basic and applied research; and monitor the divisional distribution, impact and value of externally generated research funding so that the implications of funding trends can be assessed;
- The Scientific Advisory Committee should examine the process for prioritising and assigning responsibility for development or replacement of international standards and advise the Director on future standards work within the NIBSC science strategy;

*On academic isolation and attracting and retaining staff*

- NIBSC should continue its efforts to establish collaborative research programmes with academic units, its post-graduate research programme, plans for a Masters programme on regulatory science and a post-doctoral fellowship programme and seek other potential avenues for closer working with academic institutions, including further joint appointments for NIBSC scientists with Universities;
- NIBSC should continue to use these schemes to help to ensure a flow of new high calibre and well trained scientists to the organisation, and to identify amongst them some who might later fill senior roles when they arise;
- the MHRA Board should, with the Director, ensure there is succession planning for possible future vacancies arising in the NIBSC senior leadership team (including the Directorship);

*On adapting to future business and scientific challenges*

- The Review Panel firmly believes that the continued pursuit of relevant high quality research within NIBSC is crucial to ensuring it is best placed to fulfil its regulatory role, respond to future challenges, and attract staff of the scientific

calibre needed for this. NIBSC should thus at the very least maintain its research activities, and there is a case for expanding these;

- The future funding of NIBSC needs to be considered very carefully by the MHRA Board and DH: development of income generating standardisation and control activities should be encouraged and further reductions in central government funding should be avoided. Consideration should be given as to how the Institute might be financially supported in the event it was called to respond to a sustained crisis (e.g. an influenza pandemic) giving rise to resource pressures. An element of long-term funding for research should be ensured, as well as ensuring the Institute remains well placed to obtain external research funding in competition;
- NIBSC should consider how it can better highlight and communicate the true impact of its work to its sponsor bodies, key stakeholders and the wider scientific community. The NIBSC website should be reviewed with a view to highlighting the work at the Institute and increasing its profile with the scientific, clinical and pharmaceutical/biotechnology communities; an inspection of websites of other regulatory laboratories could be informative;
- NIBSC should consider how it could increase awareness of its capabilities amongst the wider scientific/clinical communities and pharmaceutical/biotechnology industry, including establishing itself as a “scientific lighthouse” – an internationally leading centre of expertise in a particular cutting edge area of science;
- NIBSC should continue to acquire and maintain an increasingly broad range and depth of scientific knowledge and skills as well as new capabilities, including investment in platform technologies and staff skilled in their application to enable the development of new innovative analytical methods that can be applied across a range of areas;
- NIBSC should continue working cooperatively with other regulatory laboratories around the world. These relationships may become particularly important to help to establish principles and evidence requirements for the assessment of the quality, efficacy and safety of, for example, biosimilars and advanced therapies where there is little clarity presently. In this regard, collaborative working with the pharmaceutical and biotechnology industries should also be considered. Whilst collaborating with industry would need to be considered carefully to avoid conflicts of interest, the potential for conflicts of interest could be considered on a case by case basis using the procedures developed within the MHRA;
- NIBSC should consider working more closely with the clinical community involved in clinical trials of new therapeutics to support the identification and development of new potential biomarkers and the analytical methodologies to measure them;

- The MHRA Board and NIBSC should consider very carefully what can be realistically expected of the Institute in regulating individual new Biological and Cellular Therapies, given the expanding number and increasingly complex nature of biological medicines, the resources it has available and its statutory obligations. These expectations should be clarified and clearly communicated;

*On location*

- The Review Panel could see no compelling case for relocating the Institute, and believes the work of NIBSC will be best served by its remaining at South Mimms for the foreseeable future (circa. next 10-15 years).

**Acknowledgements**

62. The Panel is very grateful to the NIBSC Director and staff for the time and considerable work they devoted at short notice to the site visit and the documentation that facilitated the Panel's review. The Panel is also grateful to Professor Ian Kimber and Dr Ian Tomlinson for their input into the review.

**Annex A – Review Panel members and observers**

<b>Chair</b>		<b>Details of previous work with NIBSC</b>
Professor Sir Patrick Sissons	Emeritus Regius Professor of Physic, University of Cambridge	Member of the Scientific Policy Advisory Committee of NIBSC 1994 - 2005
<b>Members</b>		
Professor Pim van Aken	Emeritus Professor of Medicine University of Twente; former Medical Director Sanquin Blood Supply Foundation; former Chair WHO Expert Committee on Biological Standardization; former Chair of the Netherlands Organisation for Health Research and Development; Current advisory board chair of CARIM Institute, Netherlands	None.
Professor Johannes Lower	Former Director Paul-Ehrlich-Institut; former Chair of the Scientific Committee for Medicinal Products and Medical Devices; member of WHO Expert Panel on Biological Standardization	Paul Ehrlich Institute collaborated with NIBSC on a range of work whilst Director.  Member of the 2008 NIBSC review panel.
Professor Chris Mason	Professor of Regenerative Medicine Bioprocessing, University College London	Collaborative projects with the UK Stem Cell Bank and Division of Cell Biology and Imaging. Shared PhD students (with UK Stem Cell Bank and Division of Cell Biology and Imaging). Senior Editor of the journal 'Regenerative Medicine' for which Glyn Stacey (Head of Division of Cell Biology and Imaging, and Director, UK Stem Cell Bank) is an Associate Editor. Co-published with Glyn Stacey and other members of UK Stem Cell Bank. Member of UK Stem Cell Bank's Income Generation Advisory Board Working Group.

Professor Paul Griffiths	Professor of Virology, University College London	None.
Professor David Goldblatt	Professor of Vaccinology and Immunology, Director NIHR Biomedical Research Centre, Institute of Child Health, University College London	A partner along with NIBSC in the DH funded National Vaccine Evaluation Consortium. Member of a previous review of NIBSC Bacteriology Division.
Professor Sir Stephen Bloom	Head of Division for Diabetes, Endocrinology and Metabolism, Imperial College London	Board member of NIBSC from 1985 to 1999. Member of the NIBSC Scientific Committee from 1981 and chairman from 1993 to 1999. Member of the Finance and General Purpose Committee from 1992 to 1999. Author of a recent report on the NIBSC Immunology Division.
<b>Observers</b>		
Professor Sir Alex Markham	MHRA non-executive director	Chair of 2008 NIBSC review panel
Deborah Oakley	MHRA non-executive director	Former HPA board member and chair of HPA Biological Medicines Committee.
Martin Hindle	MHRA non-executive director	Non-executive director of PHE with involvement in the Science Hub Programme. Member of the former National Biological Standards Board. Former HPA non-executive director and chair of the Finance Committee.
<b>Support</b>		
Dr Tom Barlow	Health Science & Bioethics Division, DH	

## **Annex B – papers and evidence considered by the panel**

### **1. NIBSC Progress Report 2008 – 2013 including:**

- an overview of NIBSC functions, structure, facilities and governance;
- summary of NIBSC outputs 2008 – 2013 on four areas of key activity: standardisation, medicines control, research and provision of advice and response to incidents/emergencies;
- organisational developments;
- future strategy and planned developments;
- an update on activities in relation to the SWOT analysis in the 2008 Markham Review of NIBSC.

This report was supplemented by a number of annexes:

Annex A – 2008 Markham Review of NIBSC

Annex B – Outputs 2008 – 2013 for standardisation (list of replacement and new International Standards and Reference Reagents, established CE marked standards and sales and dispatch data)

Annex C – Outputs 2008 – 2013 for medicines control (data OMCL activities)

Annex D1 – list of peer-reviewed scientific publications by NIBSC staff 2009 – 2013

Annex D2 – list and details of research collaborations between NIBSC and external organisations

[There was no Annex E]

Annex F – ‘Realising the benefits’ paper MHRA Board paper on integration of MHRA and NHIBSC following merger including the opportunities and optimising operations

Annex G – MHRA Corporate Plan 2013 – 2018

Annex H1 – Vision statement for NIBSC functions

Annex H2 – NIBSC scientific strategy 2013 – 2023

Annex H3 – Paper on high level principles for establishing partnerships with external organisations

Annex H4 – Paper on establishing a new division with NIBSC focussed on advanced therapies

Annex I – High level NIBSC organogram

Annex J – Glossary

2. Biological Standardization and Control: the scientific basis of standardisation and quality control/safety monitoring of biological substances used in medicine. A scientific review commissioned by the UK national Biological Standards Board (NBSB) chaired by Professor Sir Leslie Turnberg, 1997.
3. Detailed organograms of the staff in each NIBSC division and analyses of staff numbers, grade and age profile.
4. A paper from NIBSC in response to questions arising from the review panel's teleconference on 25 November 2013 on:
  - prioritising and ensuring the financial and skills resources for the science strategy;
  - assessing the impact of NIBSC research and development;
  - details of NIBSC advisory work;
  - the impacts of relocation of NIBSC;
  - revisions to the site visit agenda;
  - questions the panel would look to answer during the site visit.

This paper was supplemented with:

- NIBSC workforce planning and development strategy;
  - A list of organisations and groups that NIBSC staff provide input to either as chair, members or observers;
  - An analysis on the impact of NIBSC relocation – risks and costs;
  - NIBSC risk register.
5. A full list of peer-reviewed scientific publications from 2009 to 2013 by NIBSC staff with the authors and their NIBSC division identified.
  6. Details of recent research grants that NIBSC has been or is involved with and in the pipeline.
  7. Copies of all the presentations made at the site visit (see Annex C).

**Annex C – agenda of the 2 December 2013 site visit**

**Independent Science Review of NIBSC**

**NIBSC site visit agenda**

National Institute for Biological Standards and Control

Blanche Lane, South Mimms, Potters Bar, Hertfordshire EN6 3QG

9am to 6pm

9.00 – 9.15	Panel and observers convene in private to gather thoughts	
<i>Those attending – all Scientific Heads of Division + all presenters (including those from lab tours)</i>		
9.15 – 9.30	<b>Short Introduction to NIBSC</b>	Ian Hudson Stephen Inglis
<i>Additional staff attending for general overviews - all presenters + Dianna Wilkinson, Paul Stickings, Elaine Gray, Mei Mei Ho, Jenny Boyle, Silke Schepelmann, Thea Sesardic, Rory Care)</i>		
9.30 – 11.00	<b>General Overviews</b> <ul style="list-style-type: none"> <li>a) Standardisation (20mins + 5mins questions) (finish by 9.55)</li> <li>b) Control (15mins + 5mins questions) (finish by 10.15)</li> <li>c) Research (15mins + 5mins questions) (finish by 10.35)</li> </ul> <p>General Discussion (25 mins) (including short coffee break) (finish by 11.00)</p>	Adrian Bristow Ian Feavers Neil Almond
11.00– 11.25	Short presentation on forward scientific strategy as platform for subsequent presentations of specific scientific areas (15mins +10 mins discussion)	Stephen Inglis
11.25 – 16.00	<b>Series of scientific presentations highlighting important on-going work flowing from the science strategy.</b> Mix of lecture style presentations and informal poster presentations embedded in the laboratories with chance to meet and talk to a wider group. <i>(Additional staff members related to the topic areas will attend for relevant presentations)</i>	
11.25	<b>Lecture theatre Presentations</b> Brief introduction and orientation (2mins)	Stephen Inglis
11.30	Supporting Safe and effective Biosimilars (15mins +5min)	Meenu Wadhwa
11.50	Stem cell technologies in standardisation and control (15min +5min) <i>(This presentation will focus on Stem cell R and D. The work of UKSCB will be mentioned in outlined, with a visit to the bank later in the day)</i>	Chris Burns
12.10	Immunoglobulin engineering to develop better standardisation and control tools and to inform safe and effective product design	

	<ul style="list-style-type: none"> <li>○ <i>The breadth of cross-subtype neutralisation activity of a camelid single domain antibody to influenza hemagglutinin can be increased by antibody valency (15mins + 5mins) (12.30)</i></li> <li>○ <i>Antibody C region influence on TGN1412-like functional activity in vitro (15mins + 5mins)</i></li> </ul>	Simon Hufton Susan Thorpe
12.50	Fibrinolysis: The interplay between tissue plasminogen activator domains and fibrin structures in the regulation of fibrinolysis: kinetic and microscopic studies. (15mins +5min)	Colin Longstaff
13.15	Break for Buffet Lunch (15 mins)	
13.30	Next generation sequencing for characterisation of biological products <ul style="list-style-type: none"> <li>○ <i>Viral vaccines</i> (10 mins +5mins)</li> <li>○ <i>Cell-based medicines</i> (10 mins +5mins)</li> </ul>	Ed Mee Ross Hawkins
14.00	Polio strains for post eradication (15mins +5 min)	Andrew MacAdam
14.20 – 16.00	<p><b>Laboratory presentations. Two groups setting off at 14.25 sharp to start point of lab talks and following programme in table below.</b>  (Each group with Stephen Inglis, Philip Minor plus Marie Donatantonio and .....as coordinators. Presenters to walk group to next station fielding additional questions.)</p> <ul style="list-style-type: none"> <li>• Proteomics-based quantification of protein antigens (10min)</li> <li>• CBRM – process and formulation development (to include reference to the facilities we have for this work) (15 min)</li> <li>• Influenza Research Centre – development and work of IRC (15 min)</li> <li>• The UKSCB and its work (15min)</li> </ul>	Jun Wheeler/ Chris Jones  Paul Matejtschuk  Othmar Engelhardt  Glyn Stacey

Group 1	Proteomics 10m	Walk	CBRM 15m	Walk	IRC 15m	Walk	UKSCB 15m	Walk
	14.30 - 14.40	5mins	14.45-15.00	5mins	15.05 - 15.20	5mins	15.25 - 15.40	10mins (+ 10 mins spare)
Group 2	IRC 15m	Walk	UKSCB 15m	Walk	CBRM 15m	Walk	Proteomics 10m	Walk
	14.35 - 14.50 (5 mins extra added for distance)	5mins	14.55-15.10	5mins	15.15 - 15.30	5mins	15.35-15.45	5mins (+ 10 mins spare)

16.00- 16.20	Panel and observers convene in private to discuss what they have learned and formulate any further questions for the wrap up session.	
	Coffee served at 16.00	
16.20 – 17.10	<p>Wrap up session (50 mins) - (Present - SCI, AB, PM, IF, NA)</p> <p>Dealing with specific panel questions, for example</p> <ul style="list-style-type: none"> <li>• Science strategy</li> <li>• Collaborative networks</li> <li>• Location</li> <li>• Succession planning</li> </ul>	
17.10 – 18.00	Panel and observers convene in private for discussion on findings (with possibility of calling on NIBSC Director to answer further questions) and agree interim conclusions and next steps (60 minutes)	
18.00	Finish	