CORPORATE CONFLICTS OF INTEREST – ANNUAL COMPLIANCE REPORT 2017

PURPOSE OF THIS REPORT

1. Under the Medicine and Healthcare products Regulatory Agency's ('the Agency') conflicts of interest (COI) policy there is a requirement for an annual compliance report to be prepared by both the National Institute of Biological Standards and Control (NIBSC) and the Clinical Practice Research Datalink (CPRD) and for the report to be signed off by a subgroup of the Agency's Corporate Executive Team (CET). Under the policy, the report would subsequently be considered by the Agency's Risk and Audit Committee (ARAC).

2. This report covers the calendar year 2017.

3. This report was agreed by the CET COI Subgroup and then by ARAC in March 2018.

BACKGROUND

4. A policy was developed to set out the approach to handling potential COIs arising out of the merger of NIBSC with the Agency in April 2013 and the launch of CPRD as a function of the Agency in April 2012.

5. The policy was approved by the CET and the Board in April 2013 and last reviewed in 2016 to assess if it remained fit for purpose. A revised policy that better took account of financial conflicts of interest, current activities carried out by CPRD, and the role of the Chief Executive in the COI process, was agreed by the CET COI sub-group and then by the CET and Board at their May 2016 meetings. The policy was then published and is available on the Agency's website.

PROCESSES THAT APPLY UNDER THE POLICY

6. The key arrangements that apply under the policy are as follows:

- Both NIBSC and CPRD operate within clearly defined parameters in accordance with their operational guidance.
- NIBSC and CPRD consider all new areas of business from the perspective of potential COI.
- NIBSC and CPRD ensure that in taking on any new business appropriate strategies are in place to avoid any COI.
- NIBSC and CPRD identify cases that fall outside the operational parameters but where there may be justification on public health grounds for undertaking those activities.
- In those exceptional cases where NIBSC and CPRD consider there may be justification in undertaking activities that fall outside the

restrictions of operational arrangements, a specific escalation process applies. This involves consideration of the specific case by a sub-group of the Agency's CET which also includes an Agency non-Executive Director.

- In those exceptional cases, where the CET sub-group considers there is justification for undertaking activities that fall outside the parameters of operational arrangements, an arrangement is in place whereby the Agency can call upon another EU regulatory authority to provide any independent regulatory oversight that may be required.
- NIBSC and CPRD are responsible for producing regular reports on the operation of the policy including the annual report.

The escalation arrangements in the policy are as follows:

i. Where possible, potential COIs will be managed within NIBSC and CPRD at an operational level in accordance with the criteria and principles set out in the policy. This is anticipated to address the majority of potential COI cases and this has been the case since the policy came into operation.
ii. NIBSC and CPRD are responsible for ensuring that their activities are carried out in accordance with the requirements laid down in operational guidance.
iii. NIBSC and CPRD are responsible for considering any activities they carry out which may create a perceived or possible financial COI. For example, this includes cases where the Agency provides a service and receives a fee for provision of the service.
iv. NIBSC and CPRD are responsible for considering cases where there might be a public health justification for undertaking activities that fall outside the restrictions of operational guidance.
v. In those cases where NIBSC and CPRD consider there may be merit in undertaking activities that fall outside the restrictions of operational guidance including activities that may create a perceived or possible financial COI, they will escalate to a group comprising representatives from the CET (the Chief Operating Officer; Directors of the regulatory divisions, NIBSC and CPRD; a representative from Legal Services; a non-executive representative from the Board and chaired by the Director of Policy Division) for decision.
vi. In those cases where there is a significant risk of reputational damage to the Agency, or where there is a risk of perceived or possible financial COI, the CET sub-group will provide advice to the Chief Executive, who will take account of that advice in deciding an appropriate course of action. Such cases might include services provided by either NIBSC or CPRD where there is a significant financial fee charged for provision of a service and where there is a possibility that MHRA may be required to undertake a regulatory function in the future.
vii. The Chief Executive, taking into account the advice of the CET sub-group, may decide to escalate the issue to the Chairman or another

member of the Board for decision. To preserve separation and clarity of roles, there will not be overlap between NEDs on the sub-group and those on the Agency's Audit, Risk and Assurance committee (ARAC).

viii. The CET sub-group will also have the option to call upon a person independent to the Agency for independent input.

CONSIDERATION OF POTENTIAL COI CASES AND OTHER MATTERS

7. The CET sub-group met twice in the reporting period (March and September 2017). At these meetings, all cases identified during the year were reviewed. The sub-group considered two cases in correspondence (one in April and one in August as detailed below in paragraphs 9 and 10) and held a virtual meeting in December.

8. Two NIBSC cases, and no CPRD cases, have been added to the tracker document (see Annex A) since the last compliance report.

9. The first case concerned collaboration with a company, funded by Innovate UK, to establish models for evaluating novel vaccines. The results of these studies would be likely to be included in dossiers submitted to regulators to seek a licence for this candidate vaccine in European and other markets. The perceived conflict of interest would be from MHRA regulators evaluating a licence application containing data produced by scientists at NIBSC. It was agreed that there was public health justification for proceeding with this work, (as NIBSC is uniquely equipped to perform the work with the model) and the proposed mitigating measures were agreed; that NIBSC would include a condition in its contract to carry out this work that should the customer include any of NIBSC's data in a Clinical Trials Application submission to the UK, or a Marketing Authorisation application in Europe, it must give the MHRA as much advance notification as possible.

10. The MHRA, at its sole discretion, would have the right to share with other European regulators. If this occurred, MHRA Regulatory proposed to:

    (i) Submit the application for review as appropriate to the
        (a) Clinical Trials Expert Advisory Group and
        (b) Commission on Human Medicines and
    (ii) Seek the opinion of another regulatory agency on
        (a) NIBSC's analytical methodology and test conduct and
        (b) the role of the test data in deciding whether to approve the application.

11. The second case concerned Antitoxin and Antivenom testing that NIBSC carries out for the Department of Health and Social Care (DHSC), via another agency. The DHSC procures a variety of products, including some that are for emergency use for treatment against potentially life-threatening bacterial toxins and bites from venomous animals. Testing for quality and efficacy of the products may be required to provide reassurance that they are safe and effective. NIBSC has the scientific and technical expertise required for testing

these therapeutic products. The test report lists results and pass/fail according to European Pharmacopoeia specifications (where they exist). NIBSC neither gives a recommendation on use nor does it charge a fee for this service. As MHRA review of NIBSC data would not form part of the import/specials licence process, and MHRA do not play a part in assessment of product on retesting it was agreed that there was no conflict of interest.

12. The Group also considered and agreed changes to the NIBSC Operational Guidelines to expand the scope of testing that NIBSC can undertake to include test models and materials. Currently, as worded, this Guidance did not allow for this work to occur and NIBSC gave an example of where they were able to lend their expertise to a relevant project and which did not give rise to any conflict of interest.

13. NIBSC outlined future work it would be carrying out to produce data packages for EU TDC embryonic stem cell lines. They did not think there was likely to be any potential COI but it was agreed that the Group would consider this before the work went live. The stem cell lines would be made available non-exclusively, so the situation could be analogous to NIBSC providing potency data for catalogue reference materials, whereas customised reference materials are not assigned a potency.

14. There were no CPRD cases last year, although the sub-group did receive an update on the DECIDE study.

15. At the meetings in March and September, the Group discussed how potential CPRD COIs are discussed and handled. As a result, COIs was added as a standing agenda item at quarterly CPRD Senior Management Team meetings. The Group felt that further transparency over the process for deciding and logging any potential COIs was required to give them assurance. CPRD therefore submitted a paper to the virtual December meeting outlining how CPRD manages potential COI cases. Comments included requests to make clear:

    - the type of approval processes that applied and which of them were conducted by other bodies,
    - the process for notifying other areas of the Agency, the reasons for doing so and who was responsible for taking action
    - the record keeping process
    - the written procedure for liaising with the COI CET Sub-Group.

    It was agreed that a procedural document would be brought to the following meeting that took account of the comments received.

16. The Group gave consideration to electronic flagging of potential COIs, however no simple automatic solution was apparent using the Agency's current systems. Discussions concluded that a simple system of raising awareness was best using emails and, once fully in place, a Sharepoint teamsite on which relevant documents could be stored and shared.

ONGOING REVIEW OF THE COI POLICY

17. The policy will be kept under review to ensure it continues to fulfil its purpose, including taking account of any new issues that may emerge in the future including innovation and life sciences related work and any complaints from stakeholders about the Agency's COI process. To date, no such complaints have been received.

Annex A

COIs Considered by the COI Sub-Group 1 January 2017 – 31 December 2017

NIBSC

#	Issue	Potential COI	Proposed mitigating action	CET COI subgroup decision (including any required mitigating action)
1	Collaboration with a company, funded by Innovate UK, to establish models for evaluating novel vaccines.	The perceived COI would be from MHRA regulators evaluating a licence application containing data produced by scientists at NIBSC.	NIBSC will include the condition in its contract to carry out this work that should the customer include any of NIBSC's data in a CTA submission to the UK, or a MA application in Europe, it must give the MHRA as much advance notification as possible. The MHRA, at its sole discretion, will have the right to share with other European regulators. If this occurs, MHRA Regulatory propose to: (1) Submit the application for review as appropriate to the (i) Clinical Trials Expert Advisory Group and (ii) Commission on Human Medicines and (2) Seek the opinion of another regulatory agency on (i) NIBSC's analytical methodology and test conduct and (ii) the role of the test data in deciding whether to approve the application	**Agreed** the mitigations.
2	Antitoxin and Antivenom Testing for DHSC via another agency. Since 2005, NIBSC has performed pre-purchase or post-expiry testing on some batches of antitoxin and provided results to enable a decision to be made on procurement and/or issue. No fee has been charged for this.	When procuring a new product (from outside the EEA), a specials licence must be obtained from the MHRA. Any test data generated and provide by NIBSC would not normally be part of this license/import procedure.	Because MHRA review of NIBSC data would not form part of the import/specials licence process, and MHRA do not play a part in assessment of product on retesting, there does not appear to be an actual conflict of interest arising from this activity.	**Agreed** that there is no conflict of interest

CPRD – No cases in this period

#	Issue	Potential COI	Proposed mitigating action	CET COI subgroup decision (including any required mitigating action)