Non-Interventional Studies: Europe (Part 2)

Considerations when Managing and Conducting Non-Interventional Studies in Europe

Countries covered include: Austria, Bulgaria, Cyprus, Denmark, Estonia, Finland, Hungary, Ireland, Italy, Latvia, Lithuania, Malta, Norway, Romania, Slovakia, Slovenia and the UK
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Disclaimer

Although this Compilation contains information of a legal nature, it has been developed for informational purposes only and does not constitute legal advice or opinions as to the current operative laws, regulations, or guidelines of any jurisdiction. In addition, because new standards are issued on a continuing basis, this Compilation is not an exhaustive source of all current applicable laws, regulations, and guidelines relating to market health research. While reasonable efforts have been made to assure the accuracy and completeness of the information provided, researchers and other individuals should check with local authorities and/or research ethics committees before starting research activities.
NIS Definitions

European NIS Definitions

Non-interventional Study (NIS)

A non-interventional study is a study fulfilling cumulatively the following requirements:

- The medicinal product is prescribed in the usual manner in accordance with the terms of the marketing authorisation;

- The assignment of the patient to a particular therapeutic strategy is not decided in advance by a trial protocol but falls within current practice and the prescription of the medicine is clearly separated from the decision to include the patient in the study; and

- No additional diagnostic or monitoring procedures are applied to the patients and epidemiological methods are used for the analysis of collected data.

Non-interventional studies are defined by the methodological approach used and not by the scientific objectives. Non-interventional studies include database research or review of records where all the events of interest have already happened (e.g. case-control, cross-sectional and cohort studies). Non-interventional studies also include those involving primary data collection (e.g. prospective observational studies and registries in which the data collected derive from routine clinical care), provided that the conditions set out above are met.

In this context, interviews, questionnaires and blood samples may be performed as normal clinical practice.

(as per Annex I of the EMA Guideline on good pharmacovigilance practices (GVP), Rev 2, 2014)
Post-authorisation Safety Study (PASS)

Any study relating to an authorised medicinal product conducted with the aim of identifying, characterising or quantifying a safety hazard, confirming the safety profile of the medicinal product, or of measuring the effectiveness of risk management measures (Article 1(c)(15) as 2001/83/EC as amended by Directive 2010/84/EU)

Post-authorisation Efficacy Studies (PAES)

Any study conducted where concerns relating to some aspects of the efficacy of the medicinal product are identified and can only be resolved after the medicinal product has been marketed (Article 21(a) as 2001/83/EC as amended by Directive 2010/84/EU)
Common NIS Terminology

Commonly Used NIS Terms

### Common NIS Terminology

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<td>Adverse Event</td>
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<td>AR</td>
<td>Adverse Reaction</td>
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<td>CA</td>
<td>Competent Authority (e.g., MHRA)</td>
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<td>CI</td>
<td>Chief Investigator</td>
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<tr>
<td>CRA</td>
<td>Clinical Research Associate</td>
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<tr>
<td>CRF</td>
<td>Case Report Form</td>
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<td>CRO</td>
<td>Contract Research Organisation</td>
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<td>CSR</td>
<td>Clinical Study Report</td>
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<td>CTD</td>
<td>Clinical Trials Directive (2001/20/EC)</td>
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<td>DPA</td>
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<td>European Federation of Pharmaceutical Industries and Associations</td>
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<td>GCP</td>
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<td>Good Pharmacoepidemiology Practice</td>
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<td>GVP</td>
<td>Good Pharmacovigilance Practice</td>
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<td>ICF</td>
<td>Informed Consent Form</td>
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<td>Acronym</td>
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<td>ICH</td>
<td>The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use</td>
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Introduction

NIS REGULATIONS & GUIDELINES

Europe - General Considerations

It is recognised that at the time of authorisation, there is only a limited amount of information available on both the safety and efficacy of a medicinal product. Non-interventional post-authorisation studies are therefore aimed to complement the information obtained during clinical development of the medicinal products prior to authorisation.

NIS studies should not be planned and conducted for the purpose of promoting medicines, but rather should be conducted for a scientific purpose i.e., to gather ‘real-life’ information on the drugs practices etc (As per Article 15 of the EFPIA Code of Practice as implemented nationally).

For a study to be ethically justifiable it must be well designed and meet the basic ethical principles contained in the Declaration of Helsinki of the World Medical Association on ethical principles for medical research on humans, and its subsequent revisions.

In Europe, the regulatory requirements for non-interventional studies have not been harmonised. As a result, all 28 countries have differing regulations that govern the conduct of non-interventional studies. This report provides a high level overview of those requirements and is only intended as an introduction to the these country-specific requirements.

If you are intending to conduct non-interventional studies, re recommend that you refer to our country-specific reports (CHC UK Country-Specific NIS Reports), which provide detailed guidance on the operational considerations when conducting non-interventional studies in each country.
EU Pharmacovigilance Legislation

In December 2010, a new pharmacovigilance regulation (EU/1235/2010) was published which heralded the beginning of significant changes to the European pharmacovigilance (PV) legislation. These legislative changes have had a direct impact on the safety reporting requirements non-interventional studies:

- Previously, safety reports from prospective non-interventional studies were generally managed as ‘spontaneous’ reports from health care professionals i.e., the sponsors did not actively record safety events during such studies. Now however, non-interventional studies with primary data collection (e.g. prospective observational studies and registries in which the data collected derive from routine clinical care), directly from patients and healthcare professionals should be considered as organised data collection systems where adverse events are actively sought.

- There is now a requirement to expedite non-serious suspected adverse reactions (related to the medical product being studied), as well as serious suspected adverse reactions.

- Mandated multi-country post-authorisation safety studies (PASS) need to be endorsed by the newly appointed Pharmacovigilance Risk Assessment Committee (PRAC) or the national competent authority (NCA) if a single country study. Mandated PASS must also be registered on the EMA PAS Register and adopt the EMA PASS protocol and report templates.

- All non-interventional studies which involve primary data collection can now be inspected by the Pharmacovigilance Inspectorates of the National Competent Authorities within Europe. Previously, only mandated PASS (and NIS in Spain) were subject to such inspections.
NOTE - This report does not address the requirements for mandated post-authorisation safety studies (PASS). Rather, the detailed requirements and considerations for PASS are covered in the CHCUK country-specific e-learning modules and comprehensive country-specific ‘Tools and Resources’ reports.

ETHICAL CONSIDERATIONS


Consideration of ethical issues, data ownership and privacy is an important part of the International Society for Pharmacoepidemiology (ISPE) guideline for Good Pharmacoepidemiology Practices (GPP), section IV. It includes a sub-section (IV.A) on protection of human subjects and a reference to the
ISPE guidelines on Data Privacy, Medical Record Confidentiality, and Research in the Interest of Public Health. The GPP also recommends a stand-alone section within the protocol containing a description of plans for protecting human subjects that includes consideration of the need for submitting the protocol to an Institutional Review Board/Independent Ethics Committee and the requirement of informed consent in accordance with local law (ENCePP Guide on Methodological Standards in Pharmacoepidemiology, EMA/95098/2010).

The main scope of the International Epidemiological Association (IEA) Good Epidemiological Practice (GEP) guideline for proper conduct in epidemiological research is on the ethical principles of pharmacoepidemiological field studies, which could also apply to interventional studies, such as the role of ethics committees, patients’ informed consent, use and storage of personal data and publication of results (ENCePP Guide on Methodological Standards in Pharmacoepidemiology, EMA/95098/2010).

The Council for International Organizations of Medical Sciences (CIOMS) 2009 International Ethical Guidelines for Epidemiological Studies have as their objective the preparation of guidelines to indicate how the ethical principles that should govern the conduct of biomedical research involving human subjects could be effectively applied. The Guidelines set forth ethical guidance on how epidemiologists - as well as those who sponsor, review, or participate in the studies they conduct - should identify and respond to the ethical issues that are raised by the process of producing this information (ENCePP Guide on Methodological Standards in Pharmacoepidemiology, EMA/95098/2010).

The Agency for Healthcare Research and Quality (AHRQ) of the United States has published Registries to Evaluate Patient Outcomes: a User’s guide, Second Edition, which is a reference for establishing, maintaining and evaluating the success of registries created to collect data about patient outcomes. In Section 1: ‘Creating a registry’ is a specific chapter dedicated to ethics, data ownership, and privacy. The concepts are useful although the authors indicate that this section focuses solely on United States (US) law.
The Uniform Requirements for Manuscripts Submitted to Biomedical Journals by the International Committee of Medical Journal Editors (ICJME) includes clear statements on ethical principles related to publication in biomedical journals addressing authorship and contributorship, editorship, peer review, conflicts of interest, privacy and confidentiality and protection of human subjects and animals in research (ENCePP Guide on Methodological Standards in Pharmacoepidemiology, EMA/95098/2010).

From the examples provided above, it may be seen that there is a wide range of documents for protection of human subjects. The applicability of ethical requirements, however, varies based on the nature of the inquiry and the studies to be conducted. Certain human subject protections applicable to clinical studies (e.g. full informed consent) would not apply to other kinds of research (e.g. review of data from de-identified medical records). Furthermore, while protection of privacy is paramount, there may be situations in which the use of data for secondary analyses has public health benefits (ENCePP Guide on Methodological Standards in Pharmacoepidemiology, EMA/95098/2010).

Data Privacy

In Europe, European Union (EU) and national laws are the keys to what may and may not be done with regard to data access, data linkage and consent issues, including such domains as human rights and duty of confidentiality. While differing data custodians currently have differing requirements related to what approvals are needed before data can be released, the requirements will fit within the overall need to meet all applicable EU and national laws and
guidelines for the actual study. This includes situations where multi-country studies are being conducted and there may be transfer of data or information. In addition to meeting legislative requirements, studies also need to adhere to a set of principles that meet with the requirements of scientific and ethical reviews (ENCePP Guide on Methodological Standards in Pharmacoepidemiology, EMA/95098/2010).

**EFPIA Code of Practice**

The guidance provided in Section 15 of the 2013 EFPIA Code of Practice complements that published in Section A of GVP Module VIII, Rev 1 2013. The EFPIA Code of Practice begins by capturing all prospective NIS within the scope of the requirements, thus removing any confusion that may have previously resulted from the guidance provided in Section A of GVP Module VIII, Rev 1 2013. In particular, Section 15 of the EFPIA Code of Practice requires that:

- The study is conducted for a scientific purpose
- There is a written study plan (protocol)
- There are written contracts between the study sponsor and healthcare professionals and/or institutions
- Any remuneration provided is reasonable and reflects fair market value
- The study protocol should be submitted for review in those countries where ethics committees are prepared to review the document
- Local data privacy laws, rules and guidelines must be respected
- The study protocol must be approved by, and the study conduct supervised by, the company’s scientific service
- The study results must be analysed and made available within a reasonable period of time to the company’s scientific service and the healthcare professionals who participated in the study
• If the study shows results that are important for the assessment of the benefit/risk profile of the medicinal product, the summary report should be immediately forwarded to the relevant competent authority

• Medical sales representatives may only be involved in an administrative capacity and such involvement must be under the supervision of the company’s scientific service

• Companies are encouraged publicly disclose the summary details and results of non-interventional studies in a manner consistent with the parallel obligations for clinical trials

• Companies apply the same requirements (to the extent applicable) to all other types of studies, including epidemiological studies, registries and other studies that are retrospective in nature.

The adoption of guidance specific to NIS across Europe is certainly a step in the right direction. However, those individuals and organisations responsible for the management and conduct of NIS across Europe find themselves in a similar situation to those involved in clinical trials before the implementation of the Clinical Trials Directive (2001/20/EC). That is, there is an acknowledged need for these studies and a rudimentary regulatory framework in place, but it is disjointed, driven by individual countries and lacking harmonisation. Although we have certainly taken a step in the right direction, there remains a long and bumpy journey ahead.

**Country-Specific Considerations**

**Country-Specific Considerations for Conducting and Managing NIS**

The rest of this report focuses on summarising the country-specific regulations and guidelines applicable to the conduct and management of non-interventional studies within Europe and is intended as a knowledge management tool.
The report directs the user to the applicable:

- Competent Authority
- Ethics Committee(s)
- Data Protection Agency
- Pharmaceutical Self-Regulatory Body
- Regulations and guidelines
Non-Interventional Studies - Useful Links
<table>
<thead>
<tr>
<th>Useful Links</th>
<th>Accessed From</th>
</tr>
</thead>
<tbody>
<tr>
<td>Association of British Pharmaceutical Industries (ABPI)</td>
<td><a href="http://www.abpi.org.uk/Pages/default.aspx">http://www.abpi.org.uk/Pages/default.aspx</a></td>
</tr>
<tr>
<td>EFPIA Code of Practice on relationships between the pharmaceutical industry and patient organisations (as amended by the Statutory General Assembly on 24 June 2013 – amending Article 10 (previously Article 9) on Events &amp; Hospitality, Article 17 (previously Article 10) on Gifts, and introducing a new Article 9 on Informational &amp; Educational Materials, and Items of Medical Utility, and requiring implementation in national codes by 31 December 2013)</td>
<td><a href="http://www.efpia.eu/uploads/Modules/Documents/efpia-hcp-code---2013-consolidated-final-%281%29-2.pdf">http://www.efpia.eu/uploads/Modules/Documents/efpia-hcp-code---2013-consolidated-final-%281%29-2.pdf</a></td>
</tr>
<tr>
<td><strong>Useful Links</strong></td>
<td><strong>Accessed From</strong></td>
</tr>
<tr>
<td>---------------------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>European Federation of Pharmaceutical Industries and Associations (EFPIA)</td>
<td><a href="http://www.efpia.eu">http://www.efpia.eu</a></td>
</tr>
<tr>
<td>International Society for Pharmacoepidemiology (ISPE)</td>
<td><a href="http://www.pharmacoepi.org/">http://www.pharmacoepi.org/</a></td>
</tr>
<tr>
<td>ISPE guideline for Good Pharmacoepidemiology Practices (GPP)</td>
<td><a href="http://www.pharmacoepi.org/resources/guidelines_08027.cfm">http://www.pharmacoepi.org/resources/guidelines_08027.cfm</a></td>
</tr>
<tr>
<td>Medicines and Healthcare products Regulatory Agency (MHRA)</td>
<td><a href="http://www.mhra.gov.uk/#page=DynamicListMedicines">http://www.mhra.gov.uk/#page=DynamicListMedicines</a></td>
</tr>
</tbody>
</table>
Study Classification

GENERAL CONSIDERATIONS WHEN PLANNING NIS

What are the regulatory requirements for my NIS?

It Depends!
Before starting your clinical research it’s important that it is correctly classified as this that dictates what regulations and guidelines are applicable to the conduct of your clinical research.

For example, in Europe the following applies:

Once you’ve classified your clinical research as a non-interventional study it’s important that you then identify and address the country-specific regulatory requirements:

**What?**
- Mandated study?
- Prospective study?
- Retrospective study?
- Is the drug reimbursed?
- Which patient populations?
- Are the patients legally competent?
- Are the patients dead?
- Tissue collection?
- Tissue biobanking?
- Genetic analysis?
- Secondary use of data or tissues?

**Where?**
- Which countries?

**How?**
- Submission procedures
- Notifications
- Approvals
- Registration
- Classification
- Insurance requirements
## Study Classification - Useful Links

<table>
<thead>
<tr>
<th>Useful Links</th>
<th>Accessed From</th>
</tr>
</thead>
</table>
Considerations for Optimising Regulatory Approval of NIS

What can I do to optimise the approval success of my study?

Seek early involvement of NIS regulatory experts in protocol design and review to ensure that language and format is optimal.
We work with many clients and our experience is that there is still a tendency for study sponsors to start with clinical trial protocol templates and try to revise these so that they ‘fit’ non-interventional studies. Please bear in mind that the protocol format and language for non-interventional studies is very different to those for interventional clinical trials.

**EMA PASS Protocol Template**

We always recommend that you use the [EMA PASS Protocol template](#). This is regardless of whether your study is a post-authorisation safety study or whether it is being conducted in Europe.

This [EMA PASS protocol template](#) is the first harmonised template that we’ve had for non-interventional studies. Although it’s still relatively new (January 2012), it is a familiar sight to national competent authorities and ethics committees and anything that helps to make the approval of an NIS more efficient should be accepted and used. Believe me, our experience with submissions since the introduction of this protocol template is that this has definitely helped to improve the approval timeframes and reduce the questions from ethics committees.

**Approval Challenges**

We can summarise the common approval challenges that we’ve seen over the last 12 to 18 months, as follows:

- **Must be very clear that the study is not a ‘seeding’ study**
  - This is one of the first questions that ethics committees will be asking about your study. It’s also a reason why PRAC will reject a study application (multi-country mandated PASS only)

- **Patients should have been prescribed the treatment prior to inclusion in the study**
This is obviously not always a possibility if you have a newly launched drug that isn’t a first line therapy e.g., oncology projects. In these instances, how you word the text for your inclusion criteria and patient population is crucial to the success of gaining approval for your study.

Should be observing routine clinical practice rather than influencing it

That doesn’t necessarily mean that you can’t use patient report outcomes (PROs), or take additional (non-routine) biosamples, but you do need to know what is allowed for the type of study, patient population and specific country where you plan to conduct the study. We’re here to help!

Must address country-specific requirements

Obviously, this is what these NIS Considerations - Europe reports are about. These are intended as an introduction to, and high level overview of, the regulatory requirements and conduct considerations in each of the countries listed.

Please be aware that the information provided is just a high level overview of the requirements. These reports were never intended as an operational ‘bible’. We also provide detailed country-specific elearning modules and comprehensive ‘Tools and Resources’ reports for each country that are intended to be used as operational ‘bibles’

**Approval Solutions**

We always recommend that you involve an NIS submissions expert early on in your protocol development. Their input isn’t intended to impact on the study design but on the language used in the protocol.
Our experience over the years have shown that THE biggest challenge to the gaining ethics committee approval in ensuring that regardless of intent, the study isn’t perceived as a seeding study. For example, we have a client who is conducting a disease registry but the protocol is written in such a way that it reads as if it’s a seeding study. There have been multiple rejections from ethics committees. This is a case where we were handed a finalised protocol and are having to work with the client to amend the protocol in order to facilitate ethics committee approval.

Obviously, this adds unnecessary time and cost to the approval/ start-up phase of the study. Ideally, when we are supporting submissions for our clients we like to be involved as early as possible in order to mitigate for these types of challenges.
# Approval Optimisation - Useful Links

<table>
<thead>
<tr>
<th>Useful Links</th>
<th>Accessed From</th>
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</thead>
</table>
Country-Specific Considerations When Managing and Conducting Non-Interventional Studies in Europe
UK

Country-Specific Considerations
Summary of Changes

Summary of country-specific changes implemented since the publication of the 2nd Edition of Non-Interventional Studies: Europe Part 2 in August 2011
<table>
<thead>
<tr>
<th>Area Impacted</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Legislation</td>
<td>The Medicines Acts and Regulations have been consolidated into a single comprehensive regulation - The Human Medicines Regulations 2012 (SI 2012/1916)</td>
</tr>
</tbody>
</table>

The Medicines Acts and Regulations have been Consolidated into a Single Comprehensive Regulation

The Medicines Acts and Regulations have been consolidated into a single comprehensive regulation - The Human Medicines Regulations 2012 (SI 2012/1916)

Part 11 of [SI 2012/1916](https://www.legislation.gov.uk/si/2012/1916) addresses the new EU PV requirements for post-authorisation safety studies (PASS) and the SAE reporting requirements for all NIS.

The major change for the reporting of suspected ADRs will be the centralised reporting by industry to the Eudravigilance database at the EMA. However this will only come into effect six months after the Eudravigilance functionality has been updated, audited and approved. This is likely to be sometime in 2015 and until then transitional measures will apply (as per the MHRA Guidance on ADR Reporting and Signal Management).

Another major change is the inclusion of reports from patients as valid, reportable ADRs. Also the definition of ADR has been extended to include all reports where harm has occurred to a patient or any reaction that is “noxious and unintended”. This will mean that reports of ADRs that are as a result of error, misuse, abuse and where used off-label should also be reported (as per the MHRA Guidance on ADR Reporting and Signal Management).

[read more...]
<table>
<thead>
<tr>
<th>Area Impacted</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Competent Authority Requirements</td>
<td>New Reporting Requirements for Suspected Adverse Reactions</td>
</tr>
<tr>
<td>- New Reporting Requirements for</td>
<td>The marketing authorisation holder must in relation to marketed products:</td>
</tr>
<tr>
<td>Suspected Adverse Reactions</td>
<td>(a) submit electronically to the Eudravigilance database a report on all serious suspected adverse reactions that occur in the EEA and third countries before the end of the period of 15 days beginning on the day following the day on which the holder gained knowledge of the reaction;</td>
</tr>
<tr>
<td></td>
<td>(b) submit electronically to the Eudravigilance database a report on all non-serious suspected adverse reactions that occur in the EEA before the end of the period of 90 days beginning on the day following the day on which the holder gained knowledge of the reaction;</td>
</tr>
<tr>
<td></td>
<td>(c) establish procedures in order to obtain accurate and verifiable data for the scientific evaluation of suspected adverse reaction reports;</td>
</tr>
<tr>
<td></td>
<td>(d) collect follow-up information on reports submitted under sub-paragraphs (a) or (b) and submit it electronically to the Eudravigilance database by way of an update to the original report within the specified time period; and</td>
</tr>
<tr>
<td></td>
<td>(e) collaborate with the EMA and the competent authorities of the EEA States in the detection of duplicates of suspected adverse reaction reports.</td>
</tr>
</tbody>
</table>

(as per Regulation 188(1) of [SI 2012/1916](#))
<table>
<thead>
<tr>
<th>Area Impacted</th>
<th>Details</th>
</tr>
</thead>
</table>
| Competent Authority Requirements  
- New Reporting Requirements for Suspected Adverse Reactions | **Obligation to Audit the Pharmacovigilance System**                   |
<p>|                                                                              | The marketing authorisation holder must—                                 |
|                                                                              | (a) perform a regular audit of its pharmacovigilance system;            |
|                                                                              | (b) place a note concerning the main findings of each audit on the     |
|                                                                              | pharmacovigilance system master file on completion of each audit; and  |
|                                                                              | (c) ensure that an appropriate corrective action plan is prepared and   |
|                                                                              | implemented as soon as is reasonably practicable after completion of    |
|                                                                              | each audit.                                                             |
|                                                                              | The holder may remove the note placed on the pharmacovigilance system   |
|                                                                              | master file under paragraph (1)(b) when all the measures in the        |
|                                                                              | corrective action plan under paragraph (1)(c) have been fully          |
|                                                                              | implemented.                                                           |
|                                                                              | (as per Regulation 184(1) of SI 2012/1916)                              |
|                                                                              | [read more...](read more...)                                            |</p>
<table>
<thead>
<tr>
<th>Area Impacted</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Competent Authority Requirements - Post-Authorisation Safety Studies (PASS)</td>
<td>New Requirements for Mandated Non-Interventional Post-Authorisation Safety Studies</td>
</tr>
<tr>
<td>Protocol Approval/ Amendments</td>
<td>The marketing authorisation holder of the medicinal product on which the study is to be be conducted must submit the draft protocol to the applicable regulatory body for review and approval before the study can commence</td>
</tr>
<tr>
<td>- Study to be conducted in UK only: MHRA approval</td>
<td>- Study to be conducted in UK only: MHRA approval</td>
</tr>
<tr>
<td>- All other cases: PRAC approval</td>
<td>- All other cases: PRAC approval</td>
</tr>
<tr>
<td>(as per Regulation 199 &amp; 200 of SI 2012/1916)</td>
<td>(as per Regulation 199 &amp; 200 of SI 2012/1916)</td>
</tr>
<tr>
<td>Final Study Report</td>
<td>To be submitted electronically, before the end of the period of 12 months beginning on the day after the day on which data collection for the study ended</td>
</tr>
<tr>
<td>- Study to be conducted in UK only: Submit to MHRA</td>
<td>- Study to be conducted in UK only: Submit to MHRA</td>
</tr>
<tr>
<td>- All other cases: Submit to PRAC</td>
<td>- All other cases: Submit to PRAC</td>
</tr>
<tr>
<td>(as per Regulation 201 of SI 2012/1916) <a href="#">read more...</a></td>
<td>(as per Regulation 201 of SI 2012/1916) <a href="#">read more...</a></td>
</tr>
<tr>
<td>Area Impacted</td>
<td>Details</td>
</tr>
<tr>
<td>---------------------------------------</td>
<td>-------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>REC Requirements</strong> - New UK</td>
<td><strong>New UK Government Authority: The Health Research Authority (HRA)</strong></td>
</tr>
<tr>
<td>Government Authority: The Health</td>
<td>The HRA was established in December 2011 to promote and protect the</td>
</tr>
<tr>
<td>Research Authority (HRA)</td>
<td>interests of patients in health research and to streamline the</td>
</tr>
<tr>
<td></td>
<td>regulation of research.</td>
</tr>
<tr>
<td></td>
<td>The activities of the National Research Ethics Service (NRES) now fall</td>
</tr>
<tr>
<td></td>
<td>under the scope of the Human Research Authority (HRA).</td>
</tr>
</tbody>
</table>

[read more...]
<table>
<thead>
<tr>
<th>Area Impacted</th>
<th>Details</th>
</tr>
</thead>
</table>
| **REC Requirements** - Registration of Clinical Trials (not applicable to non-interventional studies...yet!) | **Registration of Clinical Trials**  
In summer 2013, the HRA consulted upon the expectation that all clinical trials be registered in a publicly accessible register as part of its Transparency agenda.  
What types of research does this apply to?  
This requirement will apply to clinical trials which, for the purposes of registration, are defined as the first four categories on the Integrated Research Application System (IRAS) question 2:  
- Clinical trial of an investigational medicinal product (CTIMP),  
- Clinical investigation or other study of a medical device,  
- Combined trial of an investigational medicinal product and an investigational medical device,  
- Other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice.  
From 30 September 2013, all applications which receive a favourable ethical opinion from a Research Ethics Committee (REC) will, as a condition of that favourable opinion, be required to be registered in a publicly accessible trial register.  
The expectation is that all studies are to be registered before the first participant is recruited. However, research awarded a favourable opinion from a REC after 30 September 2013 will not be considered to be in breach of the favourable ethical opinion if the study is registered within 6 weeks of the first participant having been recruited.  
[read more...]
<table>
<thead>
<tr>
<th>Area Impacted</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data Privacy Requirements</td>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>Pharmaceutical Association Requirements</strong></td>
<td><strong>ABPI Code of Practice for the Pharmaceutical Industry - Updated in Jan 2014</strong></td>
</tr>
<tr>
<td></td>
<td>The ABPI Code of Practice for the Pharmaceutical Industry was updated in Jan 2014</td>
</tr>
<tr>
<td><strong>Pharmaceutical Association Requirements</strong></td>
<td><strong>New Clause - Clause 21: Disclosure of Transfers of Value to Health Professionals and Healthcare Organisations</strong></td>
</tr>
<tr>
<td></td>
<td>The industry recognises that transparency is an important means of building and maintaining confidence. The operation of the Code, including the complaints procedure, is a demonstration of the industry's commitment to transparency as are the requirement to declare pharmaceutical company involvement in activities and materials and the publication of detailed reports of cases considered under the Code. The industry's global agreement to disclose certain clinical trial data is another example of the industry's commitment to transparency. Companies also have to publish the summary details and results of non-interventional studies as well as the monetary value of certain support to patient organisations. Other transparency changes, effective in 2012 and 2013, included disclosure of the total amount of fees paid to consultants for certain services and the total amounts paid to sponsor attendance at meetings organised by third parties. As set out in the 2014 Code, in 2015 and 2016 transparency will be extended in relation to fees and sponsorship provided to health professionals and healthcare organisations, including naming the recipients in many instances.</td>
</tr>
</tbody>
</table>

[read more...]
DEFINITIONS

Chief Investigator (CI)
The investigator with overall responsibility for the research. In a multi-site study, the CI has co-ordinating responsibility for research at all sites. All applications for ethical review should be submitted by the CI (as per the Glossary of NRES SOP, Version 5.1, March 2012).

CTIMP
Clinical trial of an investigational medicinal product. (Any other type of research is known as a non-CTIMP) (as per the Glossary of NRES SOP, Version 5.1, March 2012).

Non-CTIMP
Any research study that is not a CTIMP (as per the Glossary of NRES SOP, Version 5.1, March 2012).

Non-Interventional Study
“non-interventional trial or study” means a study of one or more medicinal products which have a marketing authorization, where the following conditions are met:

- The products are prescribed in the usual manner in accordance with the terms of that authorization,
- The assignment of any patient involved in the study to a particular therapeutic strategy is not decided in advance by a protocol but falls within current practice,
• The decision to prescribe a particular medicinal product is clearly separated from the decision to include the patient in the study,

• No diagnostic or monitoring procedures are applied to the patients included in the study, other than those which are ordinarily applied in the course of the particular therapeutic strategy in question, and

• Epidemiological methods are to be used for the analysis of the data arising from the study;

As per Regulation 2 of The Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031) and Clause 13.2 of the ABPI COP.
## Summary of the Regulatory & Operational Requirements

The following table provides an overview of the approval and notification requirements when planning to conduct non-interventional studies in the UK.

Note: This table is not intended to be exhaustive and does not reflect the requirements for mandated non-interventional post-authorisation safety studies.

<table>
<thead>
<tr>
<th>Study Tasks</th>
<th>NIS Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Competent Authority (MHRA)</td>
<td></td>
</tr>
<tr>
<td>Notification</td>
<td>✗</td>
</tr>
<tr>
<td>Approval</td>
<td>✗</td>
</tr>
<tr>
<td>Research Ethics Committee (REC)</td>
<td></td>
</tr>
<tr>
<td>Approval</td>
<td>✔</td>
</tr>
<tr>
<td>NHS Trust R&amp;D Department</td>
<td></td>
</tr>
<tr>
<td>Approval</td>
<td>✔</td>
</tr>
<tr>
<td>Data Protection Agency (ICO)</td>
<td></td>
</tr>
<tr>
<td>Notification/ Registration</td>
<td>✔</td>
</tr>
<tr>
<td>Approval</td>
<td>✗</td>
</tr>
<tr>
<td>Institutional Approval</td>
<td></td>
</tr>
<tr>
<td>Contractual agreement between study Sponsor and Investigator/ Institution where the study will be conducted</td>
<td>✔</td>
</tr>
<tr>
<td>Pharmaceutical Self-Regulation Body (ABPI)</td>
<td></td>
</tr>
<tr>
<td>Data on payments and transfers of value to Healthcare Professional and Healthcare Organisations shall be made on an annual basis and each reporting period shall cover a full calendar year (the “Reporting Period”). The first Reporting Period shall be the calendar year 2015, whereby the relevant data shall be published in the first half of 2016</td>
<td>✔</td>
</tr>
</tbody>
</table>

* Depends on study type and information to be collected.

\(\times\) = not required; ✔ = required
## Regulatory Bodies

<table>
<thead>
<tr>
<th>Competent Authority</th>
<th>The Medicines and Healthcare products Regulatory Agency (<a href="#">MHRA</a>)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research Ethics Committees</td>
<td>National Research Ethics Service (<a href="#">NRES</a>)</td>
</tr>
<tr>
<td>REC Submissions Portal</td>
<td>Integrated Research Application System (<a href="#">IRAS</a>)</td>
</tr>
<tr>
<td>Data Protection Agency</td>
<td>Information Commissioner's Office (<a href="#">ICO</a>)</td>
</tr>
<tr>
<td>Pharmaceutical Self-Regulation Body</td>
<td>Association of British Pharmaceutical Industries (<a href="#">ABPI</a>)</td>
</tr>
<tr>
<td>Pharmaceutical Code of Practice</td>
<td><a href="#">ABPI Code of Practice for the Pharmaceutical Industry (Jan 2014)</a></td>
</tr>
</tbody>
</table>
Regulatory Framework

Applicable Legislation and Guidance

The laws and guidelines which are applicable to the management and conduct of non-interventional studies in the UK include (but are not limited to):

<table>
<thead>
<tr>
<th>Regulations Applicable to NIS</th>
<th>• The Human Medicines Regulations 2012 (<a href="#">SI 2012/1916</a>)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• The Medicines for Human Use (Clinical Trials) Regulations 2004 (<a href="#">SI 2004/1031</a>, as amended)</td>
</tr>
<tr>
<td></td>
<td>• Research Governance Framework for Health and Social Care</td>
</tr>
<tr>
<td></td>
<td>• HRA/NRES SOPs</td>
</tr>
<tr>
<td></td>
<td>• HRA Resources</td>
</tr>
<tr>
<td>Data Protection Regulations</td>
<td>• Data Protection Act 1998</td>
</tr>
<tr>
<td>Ethical Standards</td>
<td>• Declaration of Helsinki (2013)</td>
</tr>
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Requirements for Mandated Non-Interventional Post-Authorisation Safety Studies

The UK Medicines Acts and Regulations have been consolidated into a single comprehensive regulation - The Human Medicines Regulations 2012 (SI 2012/1916). Regulations 199 to 202 of SI 2012/1916 impose new requirements for mandated non-interventional post-authorisation safety studies (see below).

Note - These requirements are additional to the general requirements for non-interventional studies listed in the sections below.

Protocol Approval/ Amendments

The marketing authorisation holder of the medicinal product on which the study is to be conducted must submit the draft protocol to the applicable regulatory body for review and approval before the study can commence:

- Study to be conducted in UK only: MHRA approval
- All other cases: PRAC approval

(as per Regulation 199 & 200 of SI 2012/1916)

Final Study Report

To be submitted electronically, before the end of the period of 12 months beginning on the day after the day on which data collection for the study ended:

- Study to be conducted in UK only: Submit to MHRA
- All other cases: Submit to PRAC

(as per Regulation 201 of SI 2012/1916)
Requirements for Non-Interventional Studies

According to the applicable UK regulations, guidelines and the ABPI COP, non-interventional studies that are prospective in nature and involve the collection of patient data must comply with the criteria listed below.

**Purpose**

NIS must be conducted for a scientific purpose (Clause 13.4 of the ABPI COP).

**Prohibition of Promotion**

The study must not constitute an inducement to prescribe, supply, administer, recommend, buy or sell any medicine (Clauses 13.3 and 20.1 of the ABPI COP).

Market research activities, clinical assessments, post-marketing surveillance and experience programmes, post-authorisation studies (including those that are retrospective in nature) and the like must not be disguised promotion. They must be conducted with a primarily scientific or educational purpose (Clause 12.2 of the ABPI COP).

**Scientific Service (Body Responsible for Approval & Supervision of NIS)**

The Company’s Scientific Service must approve the protocol and must supervise the conduct of the study (Clause 13.4 of the ABPI COP).

Companies must have a Scientific Service to deal with the approval and supervision of non-interventional studies. The Scientific Service must include a registered Medical Practitioner or, where appropriate, a pharmacist, who will
be responsible for the oversight of non-interventional studies (including the
review of any responsibilities relating to such studies, particularly those given
to Medical Representatives). That person must state in writing that he or she
has examined the protocol relating to the non-interventional study and that in
his or her belief it is in accordance with the requirement of the ABPI COP (as
per Clauses 13.4 and 22.2 of the ABPI COP).

**Limited Involvement of Sales Reps**

Sales Representatives may only be involved in an administrative capacity and
such involvement must be under the supervision of the Company’s Scientific
Service which will also ensure that the representatives are adequately trained
for the role; such involvement must not be linked to the promotion of any
medicine (Clause 13.4 of the ABPI COP).

**Competent Authority Approval**

Non-interventional trials do not require authorisation by, or notification to, the
MHRA.

**Favourable Ethics Opinion**

In countries where Ethics Committees are prepared to review such studies,
the study protocol must be submitted to the Ethics Committee for review
(Clause 13.4 of the ABPI COP).

In the UK, the favourable opinion from an NHS research ethics committee
(REC) is required before starting a non-interventional study (as per the NRES
SOPs and Section 2.2.2 of the Department of Health Research Governance
Framework).

There are two classification of clinical research acknowledged by NRES,
clinical trials of investigational medicinal products (CTIMPs) and all other
clinical research (Non-CTIMPs). Non-interventional studies fall in to the category of Non-CTIMP.

**Chief Investigator**

The named chief investigator (CI) takes responsibility for the conduct of the proposed research in the UK (as per the [HRA Guidance on Roles and Responsibilities](#)).

The HRA's policy is that the named CI should normally be a researcher who is professionally based in the UK, so that he/she is able to supervise the research effectively in the UK setting and is readily available to communicate with the Research Ethics Committee (REC) and other review bodies during the application process and, where necessary, during the conduct of the research (as per the [HRA Guidance on Roles and Responsibilities](#)).

The appointment of a UK-based CI for the UK arm of the study need not conflict with the overriding responsibility of the coordinating investigator for the study as a whole. The UK-based CI will remain accountable to the coordinating investigator (as per the [HRA Guidance on Roles and Responsibilities](#)).

The REC may allow a person based outside the UK to act as CI in exceptional circumstances; for example, where an overseas researcher is undertaking a clinical or academic placement in the UK, or a UK researcher will be based overseas during part of the study. The REC will require assurances about the arrangements for supervising the research when the CI is out of the UK (as per the [HRA Guidance on Roles and Responsibilities](#)).

**Ethical Review Application to be Submitted by the Chief Investigator**

An application for ethical review of a research study should be made by the Chief Investigator for that study. Applications may not be submitted by the sponsor (s) on behalf of the Chief Investigator. The Chief Investigator should
normally be professionally based in the United Kingdom. For international studies with a co-ordinating investigator outside the UK, a health professional based in the UK should normally be nominated as the Chief Investigator responsible for the conduct of the research in the UK. The REC may agree exceptionally to an application being submitted by a CI based outside the UK but should consider as part of the ethical review whether adequate arrangements are in place for supervision of the study in the UK. (as per Paragraph 1.1 of NRES SOP, Version 5.1, March 2012).

**REC Approval Timeframe**

For all applications subject to a 60 day time limit, both CTIMPs and non-CTIMPs, the aim is for a final opinion to be given within 40 calendar days, allowing for the clock to stop once where a provisional opinion is given (as per Paragraph 3.5 of NRES SOP, Version 5.1, March 2012).

**Proportionate Review**

For applications accepted for proportionate review, the aim is for a final opinion to be given within 14 calendar days, allowing for the clock to stop once where a provisional opinion is given (as per Paragraph 3.6 of NRES SOP, Version 5.1, March 2012).

For more information refer to:

- NHS Research Ethics Committee (REC) - Proportionate Review Service

**Insurance, Indemnity and Compensation**

Before confirming a favourable opinion on any research (including both CTIMPs and non-CTIMPs), the main REC should assure itself that the sponsor and investigators will have appropriate insurance or indemnity cover for the potential legal liability arising from the research, and consider provision
in proportion to the risk for compensation or treatment in the event of injury, disability or death attributable to participation. Detailed guidance is in Annex G (as per Paragraph 3.56 and Annex G of NRES SOP Version 5.1, March 2012).

### On-Line Application Tool (IRAS)

All new applications for ethical review to a Research Ethics Committee (REC) in the UK should be submitted on the standard on-line REC application form in the Integrated Research Application System (IRAS) (http://www.myresearchproject.co.uk) (as per Paragraph 1.4 of NRES SOP Version 5.1, March 2012).

### Non-interventional Trials of Medicinal Products

Trials of medicinal products which are “non-interventional” are not classified as clinical trials of investigational medicinal products (CTIMPs) by the UK RECs and therefore do not require review by a recognised REC. Instead, they should be allocated for REC review in accordance with the normal procedures for non-CTIMPs (as per Paragraph 1.24 of NRES SOP Version 5.1, March 2012).

### Determining whether a study is a CTIMP or a Non-CTIMP

The MHRA has published guidance on the interpretation of the statutory definition of a CTIMP and a non-interventional trial (see algorithm at Annex B). Where there is doubt about the classification of a trial, it is the responsibility of the Chief Investigator or sponsor to seek authoritative advice from the MHRA Clinical Trials Helpline, using the contact details on the MHRA website. (However, the REC may check directly with the MHRA if necessary – see paragraph 13.10.) TheREC should proceed with the ethical review but advise the applicant of the possible consequences if the application has been
wrongly classified. The applicant may be required to provide written evidence from the MHRA as part of the single request for further information (see Section 3). Where the MHRA advises that an application submitted as a non-CTIMP is in fact a CTIMP, the application should be withdrawn and re-submitted with a EudraCT number and the additional information required. Where a study is submitted as a non-CTIMP and given a favourable opinion, and it emerges later that it is in fact a CTIMP, corrective procedures are set out in paragraph 5.3 of Annex D (as per Paragraph 1.25 of NRES SOP, Version 5.1, March 2012).

Non-Interventional Trials Involving Adults Lacking Capacity to Consent

Only one application for ethical review should be submitted in relation to any research protocol to be conducted within the UK (except where two applications are required for non-CTIMPs involving adults lacking capacity in both England/Wales and Scotland – see paragraph 12.57). In the case of studies requiring site-specific assessment as part of the ethical review, the procedures in Section 4 apply. In the case of international studies, an application must be made to an ethics committee in the UK, whether or not the study has a favourable ethical opinion from a committee outside the UK and whether or not it has started outside the UK (as per Paragraph 1.2 of NRES SOP, Version 5.1, March 2012).

Non-Interventional Trial/Research Project or Audit?

Within the NHS and social care services, the responsibility for determining whether a project should be managed as research under the Research Governance Framework lies with the responsible R&D office. Requests for pre-application advice should be referred initially to the R&D office, or a lead R&D office in the case of a project involving multiple organisations. The R&D office may itself seek further advice from a REC or the NRES Queries Line, or recommend that the sponsor or project team seeks such advice, by
submitting a brief outline of the project in writing. Where a REC receives such a request, it should be referred to the Chair, who is encouraged to provide advice but is not obliged to do so. Where the Chair is available and willing to advise, a response should be sent within 5 working days using SL24. Otherwise, the correspondent should be referred to the NRES Queries Line (as per Paragraph 1.94 of NRES SOP, Version 5.1, March 2012).

Where an application is made to a REC, i.e. the project is presented as research, it should be validated and reviewed in the normal way if the research is within the scope of REC review under GAfREC. If the REC considers that the project should not have been presented as research, it may give advice alongside its opinion that the status of the project is reconsidered by the sponsor in consultation with the lead R&D office. If the sponsor or project team subsequently notifies that the REC that the application is no longer considered to be research, the application and opinion letter should be considered to be withdrawn (as per Paragraph 1.95 of NRES SOP, Version 5.1, March 2012).

Further information can be found at:

- Determining Whether Your Study is Research
- Is NHS REC review Required?
- Research Requiring NHS R&D Review but Not Ethical Review
- Ethical Review of Research Using Confidential Patient Information
- Legal Requirements for Research Ethics Review

**Allocation of non-CTIMPs**

Trials of medicinal products which are “non-interventional” (see definition in the Glossary) are not classified as CTIMPs and do not require review by a recognised REC. They should be allocated in accordance with the normal procedures for non-CTIMPs (as per Paragraph 1.24 of NRES SOP, Version 5.1, March 2012).
Management Permission

Management permission is required from the organisation responsible for hosting the research before it commences at any site (as per Paragraph 1.24 of NRES SOP, Version 5.1, March 2012).

All research involving NHS patients, staff or resources must be assessed by a research ethics committee. Furthermore, to comply with the Department of Health’s Research Governance Framework research activities must be formally approved by Trust management before starting.

Studies performed in NHS hospitals will require permission/approval from the relevant R&D Trust before starting the study. Such permission can now be sought using the UK’s integrated research application system (IRAS).

Contract & Protocol

There must be a written protocol and written contracts between the Health Professionals and/or the institutes at which the study will take place and the pharmaceutical company sponsoring the study, which specify the nature of the services to be provided and the payment for those services (as per Clause 13.4 of the ABPI COP).

Health professionals and appropriate administrative staff may be used as consultants and advisors, whether in groups or individually, for services such as speaking at and chairing meetings, involvement in medical/scientific studies, clinical trials or training services, participation at advisory board meetings, and participation in market research where such participation involves remuneration and/or travel. The arrangements which cover these genuine consultancy or other services must, to the extent relevant to the particular arrangement, fulfil all the following criteria (as per Clause 20.1 of the ABPI COP):
• a written contract or agreement must be agreed in advance of the commencement of the services which specifies the nature of the services to be provided and the basis for payment of those services

• a legitimate need for the services must be clearly identified in advance of requesting the services and entering into arrangements with the prospective consultants

• the criteria for selecting consultants must be directly related to the identified need and the persons responsible for selecting the consultants must have the expertise necessary to evaluate whether the particular consultants meet those criteria

• the number of consultants retained must not be greater than the number reasonably necessary to achieve the identified need

• the contracting company must maintain records concerning, and make appropriate use of, the services provided by consultants

• the hiring of the consultant to provide the relevant service must not be an inducement to prescribe, supply, administer, recommend, buy or sell any medicine

• the compensation for the services must be reasonable and reflect the fair market value of the services provided. In this regard, token consultancy arrangements must not be used to justify compensating health professionals and appropriate administrative staff

• in their written contracts or agreements with consultants, companies must include provisions regarding the obligation of the consultant to declare that he/she is a consultant to the company whenever he/she writes or speaks in public about a matter that is the subject of the agreement or any other issue relating to that company. Similarly, companies that employ, on a part-time basis, health professionals that are still practising their profession must ensure that such persons are obliged to declare their employment arrangement with the company whenever they write or speak in public about a matter that is the subject of the employment or any other issue relating to that company.
Model Agreements

Nationally approved standard Agreements help speed up the contracting process for industry-sponsored trials carried out in the NHS by removing the need for site-by-site reviews and local legal agreements to be drawn up. This enables trials to start earlier, improving the speed of industry-sponsored clinical trials and giving NHS patients faster access to innovative treatments (as per the NIHR Guidance on Model Agreements).

The suite of model Agreements are supported by Guidance which sets out the aims and provides details on how the Agreement should be used in the development of contracts for clinical research sponsored by pharmaceutical, biopharmaceutical or medical technology companies (as per the NIHR Guidance on Model Agreements).

2011 versions of the mCTA, CRO mCTA, mCIA and CRO mCIA

The 2011 versions of these agreements, published in December 2011 include two changes from the original versions:

- **Definitions** - In the past, some Universities that are the substantive employers of staff involved in clinical trials and clinical investigations at NHS Trusts were concerned that they might not be covered by the terms of the ABPI or ABHI Form of Indemnity. These Universities often requested the industry sponsors of clinical trials and clinical investigations to issue them with their own Form of Indemnity, separate from that included in the mCTA or mCIA between the NHS body and the sponsor. The new definition of Agent makes it clear that in the context of clinical trials and clinical investigations, Universities are agents of the NHS body that enters into the clinical trial or clinical investigation agreement with the sponsor.

- **Clause 3.5** - The anti-bribery and anti-corruption provisions of earlier versions of the mCTAs and mCIAs, have been revised to take account of the introduction of the Bribery Act 2010, permitting sponsors to comply with their obligations under US as well as UK legislation. In the earlier
versions, Clause 3.5 referred only to corrupt actions that might be committed by Sponsors. The Bribery Act 2010 and similar US legislation makes it necessary for Sponsors to include in agreements with contractors provisions to discourage any corrupt acts on contractors’ parts. The modified Clause 3.5 states that either party to a bipartite agreement (sponsor or NHS body), or any party in the case of CRO-managed trials and investigations, can terminate the agreement in the event that the other party (or any other party in the case of the CRO-managed studies) commits any offence covered by the Bribery Act 2010, in relation to the agreement or the clinical study.

These changes have been agreed in discussions between the UK Health Departments, the National Institute for Health Research and industry bodies. Versions have been prepared for use in the Devolved Administrations. These are available on the UKCRC website (as per the NIHR Guidance on Model Agreements).

- Refer to the Model Clinical Trials Agreements

Currently, there is no model agreement, which is specific to non-interventional studies. Sponsors may be asked by host institutions to use the model clinical trials agreement (mCTA) and should consider the relevance of such an agreement given that much of the content of the template/agreement will be irrelevant to NIS. A letter of intent or similar contract may be more appropriate for these types of studies.

**Financial Compensation/ Remuneration**

Any remuneration must be reasonable and reflect the fair market value of the work (as per Clause 13.3 of the ABPI COP).
Declaration of Fees Paid to Healthcare Professionals and Healthcare Organisations

Pharmaceutical companies must publicly disclose details of the fees paid to consultants in the UK, or to their employers on their behalf, for certain services rendered by them such as chairing and speaking at meetings, assistance with training and participation in advisory boards etc. It includes payments to consultants in relation to research and development work\(^\text{12}\), including the conduct of clinical trials\(^\text{13}\) (as per Clause 20.2 of the ABPI COP).

In addition to the information required to be made public by Clause 20.2, companies must publicly disclose details of payments made to consultants in relation to market research (unless the company concerned is not aware of the identities of those participating in the market research)\(^\text{14}\) (as per Clause 20.3 of the ABPI COP).

Fees, expenses and the like due to consultants in relation to Clauses 20.2 and 20.3 must be disclosed whether paid directly to them or to their employers or

\(^\text{12}\) For the purpose of disclosure research and development transfers of value are transfers of value to health professionals or healthcare organisations related to the planning or conduct of:

- non-clinical studies (as defined in the OECD Principles of Good Laboratory Practice)
- clinical trials (as defined in Directive 2001/20/EC)
- non-interventional studies that are prospective in nature and involve the collection of data from, or on behalf of, individual or groups of health professionals specifically for the study.

Costs that are subsidiary to these activities can be included in the aggregate amount.

\(^\text{13}\) The information required by Clause 20.2 must be publicly disclosed in respect of the calendar year 2015 and each calendar year thereafter. Disclosure must be carried out in accordance with Clause 21.

The information which must be disclosed is the total amount paid in a calendar year to each consultant who has provided services. Companies may, of course, give greater detail, for example by giving separate figures for different categories of service.

Fees and agreed expenses should be disclosed separately.

The names of the consultants must be disclosed except in relation to payments in relation to research and development work, including clinical trials, as defined below, where disclosure should be on an aggregate basis.

\(^\text{14}\) Clause 20.3 relates only to market research using consultants where the pharmaceutical company knows the identity of the consultants. This is because the focus of the requirements concerning transparency is on areas where there are direct relationships between the parties and that is not so where the company does not know the identity of the participants.
to healthcare organisations or to companies or charities etc (as per Clause 20.4 of the ABPI COP).

Disclosure for Calendar Years 2013 and 2014

For disclosures in relation to the calendar years 2013 and 2014, the requirements and procedures in Clauses 20.2 and 20.3 and their supplementary information in the Second 2012 Edition of the Code still apply.

Transfer of Value to Health Professionals and Healthcare Organisations

Companies must document and publicly disclose certain transfers of value made directly or indirectly to health professionals and healthcare organisations located in Europe15 (as per Clause 21.1 of the ABPI COP).

Consent to Disclosure: Companies are encouraged to include in a contract involving a transfer of value provisions regarding the consent of the recipient to its disclosure. In addition, companies are encouraged to renegotiate existing contracts at their earliest convenience to include such consent to disclosure. Companies must ensure that they have appropriate arrangements in place to lawfully disclose information about transfers of value.

Mode of Disclosure: Disclosure will be on the company’s website but, if a central platform for disclosure in the UK is established, the use of that platform is likely to be obligatory.

The decision as to whether there will be a central platform for disclosure in the UK will be made by the end of 2014.

15 Disclosure is required even if the payments etc are made by overseas affiliates, head offices in the UK or overseas and UK based offices.
A template which can be used is available to download from the Authority’s website (www.pmcpa.org.uk).

**Date of Implementation:** The information required by Clause 21.1 must be disclosed in respect of transfers of value made in 2015 and each calendar year thereafter.

The disclosure of information about certain transfers of value was a requirement of the Second 2012 Edition of the Code and its immediate predecessors. The provisions in the Second 2012 Edition of the Code (Clauses 18.6, 19.4, 20.2 and 20.3) continue to apply in relation to transfers of value made in calendar years prior to 2015.

The transfers of value covered by Clause 21.1 are (as per Clause 21.2\(^{16}\) of the **ABPI COP**):

- joint working in accordance with Clause 18.5
- donations, grants and benefits in kind provided to institutions, organisations and associations in accordance with Clause 18.6
- contracts between companies and institutions, organisations and associations in accordance with Clause 18.7
- sponsorship of attendance by health professionals and appropriate administrative staff at meetings in accordance with Clause 19.5
- fees paid to health professionals and appropriate administrative staff, or to their employers on their behalf, in accordance with Clauses 20.2 and 20.3
- contributions towards the costs of meetings paid to healthcare organisations or to third parties managing events on their behalf, which

\(^{16}\) Further Information: The clauses of the Code noted in Clause 21.2 should be consulted for further information about the requirements. In addition, the requirements of Clauses 19.1 and 19.5 should be borne in mind in relation to sponsorship of meetings.
may include sponsorship of health professionals by way of registration fees and accommodation and travel.

Clause 21.1 does not apply to transfers of value to patient organisations. These transfers of value are covered by Clauses 24.7 and 24.8 (as per Clause 21.3 of the ABPI COP).

Disclosures must be made annually in respect of each calendar year. Disclosure must be in the first six months after the end of the calendar year in which the transfers of value were made (as per Clause 21.4 of the ABPI COP).

The information disclosed must remain in the public domain for at least three years from the time of disclosure (as per Clause 21.5 of the ABPI COP).

Companies must document all disclosures and retain the records for at least five years after the end of the calendar year to which they relate (as per Clause 21.6 of the ABPI COP).

Different categories of transfers of value can be aggregated on a category by category basis, provided that itemised disclosure would be made available upon request to the relevant recipient or the relevant authorities (as per Clause 21.7 of the ABPI COP).

Where a transfer of value is made to a health professional indirectly via a healthcare organisation such a transfer should be disclosed once only, preferably as being a transfer to the health professional (as per Clause 21.8 of the ABPI COP).

Where recipients of transfers of value cannot be identified for legal reasons, the amount attributable to such transfers must be disclosed on an aggregate basis. The number of recipients involved must be stated together with the percentage of all recipients that they represent and the aggregate amount attributable to transfers of value to such recipients (as per Clause 21.9 of the ABPI COP).

Each company providing transfers of value must publish a note summarising the methodologies used by it in preparing the disclosures and identifying each category of transfer of value. The note, including a general summary and/or country specific considerations, must describe the recognition
methodologies applied and should include the treatment of multi-year contracts, VAT and other tax aspects, currency aspects and other issues relating to the timing and amount of transfers of value for the purposes of this Code (as per Clause 21.10 of the ABPI COP).

**Compliance with Data Protection Legislation**

Data protection legislation must be complied with (as per Clause 13.4 of the ABPI COP).

**Notification**

Notification is a statutory requirement and every organisation that processes personal information must notify the Information Commissioner's Office (ICO), unless they are exempt. Failure to notify is a criminal offense.

Notification is the process by which a data controller gives the ICO details about their processing of personal information. The ICO publishes certain details in the register of data controllers, which is available to the public for inspection.

For further information, refer to the following:

- ICO Guidance on the Data Protection Act
- Data Protection Act 1998 (as amended)

**Publish Summary Details and Results of NIS**

Companies must publish the summary details and results of non-interventional studies of marketed medicines in a manner consistent with their parallel obligations with respect to clinical trials (as per Clause 13.3 of the ABPI COP).
Meetings, Hospitality and Sponsorship

Companies must not provide hospitality to members of the health professions and appropriate administrative staff except in association with scientific meetings, promotional meetings, scientific congresses and other such meetings, and training. Meetings must be held in appropriate venues conducive to the main purpose of the event. Hospitality must be strictly limited to the main purpose of the event and must be secondary to the purpose of the meeting ie subsistence only. The level of subsistence offered must be appropriate and not out of proportion to the occasion. The costs involved must not exceed that level which the recipients would normally adopt when paying for themselves. It must not extend beyond members of the health professions or appropriate administrative staff (as per Clause 19.1 of the ABPI COP).

The cost of a meal (including drinks) provided by way of subsistence must not exceed £75 per person, excluding VAT and gratuities (as per Clause 19.2 of the ABPI COP).

Payments may not be made to doctors or groups of doctors or to other prescribers, either directly or indirectly, for rental for rooms to be used for meetings (as per Clause 19.3 of the ABPI COP).

When meetings are sponsored by pharmaceutical companies, that fact must be disclosed in all of the papers relating to the meetings and in any published proceedings. The declaration of sponsorship must be sufficiently prominent to ensure that readers are aware of it at the outset (as per Clause 19.4 of the ABPI COP).

Pharmaceutical companies must publicly disclose financial details of sponsorship of UK health professionals and appropriate administrative staff in relation to attendance at meetings. Sponsorship in this context includes registration fees and the costs of accommodation and travel, both inside and outside the UK (as per Clause 19.5 of the ABPI COP).
Progress Reports

The Chief Investigator should submit a progress report to the relevant Research Ethics Committee (REC) 12 months after the date on which the favourable REC opinion was given. You should complete the forms in typescript and have them signed by the Chief Investigator. A paper copy should be sent to the REC within 30 days of the end of the reporting period.

Refer to:

- NHS Research Ethics Committee (REC) - Annual Progress Reports

Substantial Amendments

If it is proposed to make a substantial amendment to the research, the Chief Investigator should submit a notice of amendment to the relevant REC.

A substantial amendment is any amendment to the terms of the application for ethical review, or to the protocol or other supporting documentation approved by the REC, that is likely to affect to a significant degree:

(a) the safety or physical or mental integrity of the trial participants

(b) the scientific value of the trial

(c) the conduct or management of the trial

The policy of the UK Health Departments is that the statutory provisions relating to substantial amendments to CTIMPs should generally apply to the review of substantial amendments to any research study that has previously been ethically approved by a REC. There will however be some procedural differences, which are indicated in this section. The 35 day clock applies to review of all substantial amendments, except those proposing to include adults lacking capacity for the first time in a non-CTIMP, where 60 days is allowed for the review and the clock may be stopped once to request further information or clarification (see paragraph 12.61) (as per Paragraph 5.8 of NRES SOP, Version 5.1, March 2012).
**Notices of Amendment**

For non-CTIMPs, the NRES Notice of Substantial Amendment form should be used. The form may be submitted by either the sponsor or the Chief Investigator, but should always be authorised by both the Chief Investigator and a representative of the sponsor (as per Paragraph 5.13 of NRES SOP, Version 5.1, March 2012).

- Refer to the HRA Webpage on Amendments
- HRA Definitions of Substantial and Non-Substantial Amendments

**Safety Reporting Requirements**

**Safety Reporting to RECs**

In research other than CTIMPs, a Serious Adverse Event (SAE) is defined as an untoward occurrence that:

- Results in death;
- Is life-threatening;
- Requires hospitalisation or prolongation of existing hospitalisation;
- Results in persistent or significant disability or incapacity;
- Consists of a congenital anomaly or birth defect; or
- Is otherwise considered medically significant by the investigator.

(as per Paragraph 9.66 of NRES SOP, Version 5.1, March 2012).

An SAE occurring to a research participant should be reported to the main REC where in the opinion of the Chief Investigator the event was:

- “Related” – that is, it resulted from administration of any of the research procedures, and
• “Unexpected” – that is, the type of event is not listed in the protocol as an expected occurrence.

(as per Paragraph 9.67 of NRES SOP, Version 5.1, March 2012).

Reports of related and unexpected SAEs should be submitted within 15 days of the Chief Investigator becoming aware of the event, using the SAE report form for non-CTIMPs published on the NRES website (as per Paragraph 9.68 of NRES SOP, Version 5.1, March 2012).

The Chief Investigator should include a report on the safety of participants in the annual progress report (as per Paragraph 9.69 of NRES SOP, Version 5.1, March 2012).

Individual reports of SAEs should be reviewed at a sub-committee or Committee meeting as per Paragraph 9.70 of NRES SOP, Version 5.1, March 2012).

There is no requirement to provide reports to RECs other than the main REC (as per Paragraph 9.71 of NRES SOP, Version 5.1, March 2012).

Refer to the following NRES webpage for further information and relevant submission forms:

• HRA Guidance on Progress and Safety Reporting
• Non-CTIMP Safety Report to Main REC

Safety Reporting to the MHRA

What are the Key Changes?: The major change for the reporting of suspected ADRs will be the centralised reporting by industry to the Eudravigilance database at the EMA. However this will only come into effect six months after the Eudravigilance functionality has been updated, audited and approved. This is likely to be sometime in 2015 and until then transitional measures will apply (as per the MHRA Guidance on ADR Reporting and Signal Management).
Another major change is the inclusion of reports from patients as valid, reportable ADRs. Also the definition of ADR has been extended to include all reports where harm has occurred to a patient or any reaction that is “noxious and unintended”. This will mean that reports of ADRs that are as a result of error, misuse, abuse and where used off-label should also be reported (as per the MHRA Guidance on ADR Reporting and Signal Management).

For signal management the responsibilities on MAHs are set out in GVP Module IX. This essentially sets out the requirement that MAHs should continuously monitor all available data for the identification of potential safety issues. MAHs will also be required to monitor the Eudravigilance database according to their level of access. Signals should follow a process of validation, prioritisation and assessment, and an audit trail of activities should be kept as part of the quality management system (as per the MHRA Guidance on ADR Reporting and Signal Management).

**What are the Requirements for Post-Authorisation Studies?** GVP Module VI (external link) provides detailed information on the reporting requirements. Essentially all valid serious reports originating from studies, patient support programmes and other data collection systems should be expedited. Reports from observational, non interventional studies using databases such as GPRD should not be reported as ICSRs but should be summarised in the final study report (as per the MHRA Guidance on ADR Reporting and Signal Management).

**During the Transition Period, what will the MHRA's Reporting Requirements for Companies be?**

The provisions for company reporting requirements to the MHRA is as follows:

<table>
<thead>
<tr>
<th></th>
<th>Current provisions</th>
<th>Transitional period</th>
<th>Post-transitional period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious UK ADR reports</td>
<td></td>
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</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Category</th>
<th>Professional</th>
<th>Consumer</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Health professional</strong></td>
<td>Within 15 days</td>
<td>Within 15 days</td>
<td>Not required by MHRA. To EudraVigilance within 15 days</td>
</tr>
<tr>
<td><strong>Consumer</strong></td>
<td>Not applicable</td>
<td>Within 15 days</td>
<td>Not required by MHRA. To EudraVigilance within 15 days</td>
</tr>
<tr>
<td><strong>Non-serious UK ADR reports</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health professional</td>
<td>Not applicable</td>
<td>Not required by MHRA</td>
<td>Not required by MHRA. To EudraVigilance within 90 days</td>
</tr>
<tr>
<td>Consumer</td>
<td>Not applicable</td>
<td>Not required by MHRA</td>
<td>Not required by MHRA. To EudraVigilance within 90 days</td>
</tr>
<tr>
<td><strong>Serious non-UK EU ADR reports</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health professional</td>
<td>Within 15 days (for black triangle products) and products authorised via MR/DC or Centralised procedures where UK is Reference Member State or Rapporteur.</td>
<td>As current provisions*</td>
<td>Not required by MHRA. To EudraVigilance within 15 days</td>
</tr>
<tr>
<td>Consumer</td>
<td>Not applicable</td>
<td>Not required by MHRA</td>
<td>Not required by MHRA. To EudraVigilance within 15 days</td>
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<td><strong>Non-serious non-UK EU ADR reports</strong></td>
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<td></td>
<td></td>
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<tr>
<td>Health professional</td>
<td>Not applicable</td>
<td>Not required by MHRA</td>
<td>Not required by MHRA. To EudraVigilance within 90 days</td>
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<tr>
<td>Consumer</td>
<td>Not applicable</td>
<td>Not required by MHRA</td>
<td>Not required by MHRA. To EudraVigilance within 90 days</td>
</tr>
<tr>
<td><strong>Serious third country (from outside EU) ADR reports</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health professional</td>
<td>Unexpected ADRs within 15 days (MHRA will also accept expected ADRs)</td>
<td>As current provisions*</td>
<td>Not required by MHRA. To EudraVigilance within 15 days</td>
</tr>
<tr>
<td>Consumer</td>
<td>Not applicable</td>
<td>Not required by MHRA</td>
<td>Not required by MHRA. To EudraVigilance within 15 days</td>
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</tbody>
</table>
Non-serious third country (from outside EU) ADR reports

<table>
<thead>
<tr>
<th>Health professional</th>
<th>Not applicable</th>
<th>Not required by MHRA</th>
<th>Not required by MHRA.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consumer</td>
<td>Not applicable</td>
<td>Not required by MHRA</td>
<td>Not required by MHRA.</td>
</tr>
</tbody>
</table>

Please note that this table is an updated version from that published in the annexes of the consultation document of the Transposition of Pharmacovigilance Directive (published Dec 6 2011); non-serious cases should not be reported to EudraVigilance during the transitional period (as per the MHRA Guidance on ADR Reporting and Signal Management).

*For reporting of serious health professional reports from outside the UK MAHs should submit these to MHRA until they are no longer requested to do so. This may be before full functionality of EudraVigilance has been established. Work on the dictionary of medicinal products is ongoing at the EMA and when we are confident this enables accurate analyses of these data on EudraVigilance for effective use in signal detection we will lift this requirement

**If companies wish, or find it easier, to send us non-UK serious consumer reports we will be happy to accept them but this is not mandatory

Please note that this table is an updated version from that published in the annexes of the consultation document of the Transposition of Pharmacovigilance Directive (published Dec 6 2011); non-serious cases should not be reported to EudraVigilance during the transitional period.

*For reporting of serious health professional reports from outside the UK MAHs should submit these to MHRA until they are no longer requested to do so. This may be before full functionality of EudraVigilance has been established. Work on the dictionary of medicinal products is ongoing at the EMA and when we are confident this enables accurate analyses of these data on EudraVigilance for effective use in signal detection we will lift this requirement

**If companies wish, or find it easier, to send us non-UK serious consumer reports we will be happy to accept them but this is not mandatory

End of Trial Notifications

The policy from NRES is that the requirement to notify the main REC of conclusion or early termination should also apply to all other research with a favourable opinion. In the case of non-CTIMPs, reports should be submitted in the form prescribed by NRES and published on the website as per Paragraph 9.83 of NRES SOP, Version 5.1, March 2012).
The Clinical Trials Regulations provide that the sponsor should notify the MHRA and the main REC in writing that a CTIMP has ended within 90 days of the conclusion of the trial. In the case of an international trial, guidance from the European Commission is that the sponsor is only required to notify the conclusion of the trial as a whole. Where the UK arm of a trial ends in advance of the conclusion in all Member States, this may be notified voluntarily (the form for declaring the end of the trial should not be used in this case) as per Paragraph 9.79 of NRES SOP, Version 5.1, March 2012).

If the trial is terminated early, the sponsor should notify the main REC within 15 days of the date of termination. An explanation of the reasons for early termination should be given as per Paragraph 9.80 of NRES SOP, Version 5.1, March 2012).

The definition of the conclusion of the research should be provided in the protocol and any change to this definition should be notified as a substantial amendment. The end of the research should be defined in relation to the collection of all data required to answer the research questions in the protocol. Where a clinical trial protocol requires follow-up monitoring and data collection to meet secondary or tertiary endpoints, the end of trial should be the final data capture rather than the last treatment visit as per Paragraph 9.81 of NRES SOP, Version 5.1, March 2012).

The Chief Investigator should notify the Committee in writing that the research has ended within 90 days of its conclusion. The conclusion of the research is defined as the final date or event specified in the protocol, not the completion of data analysis or publication of the results.

If the research is terminated early, the Chief Investigator should notify the Committee within 15 days of the date of termination. An explanation of the reasons for early termination should be given.

Reports of conclusion or early termination should be submitted in the form prescribed by NRES and published on the website:

- End of Study Notification - Studies Other than Clinical Trials of Investigational Medicinal Products
Analysis and Retention of Study Results

The study results must be analysed and summaries must be made available within a reasonable period to the Company’s Scientific Service, which shall maintain records of such reports (as per Clause 13.4 of the ABPI COP).

Dissemination of Summary Reports

The summary report should be sent to health professionals who participated in the study (as per Clause 13.3 of the ABPI COP).

A summary of the final report on the research should be provided to the relevant REC within 12 months of the conclusion of the study. This should include information on whether the study achieved its objectives, the main findings, and arrangements for publication or dissemination of the research including any feedback to participants should be submitted in the form prescribed by NRES and published on the website:

- End of Study Notification - Studies Other than Clinical Trials of Investigational Medicinal Products

Notification of Important Benefit-Risk Information

If the study results are important for the assessment of benefit-risk, the summary report should be immediately forwarded to the relevant competent authority (as per Clause 13.4 of the ABPI COP).

Market Research

Market research is the collection and analysis of information and must be unbiased and non-promotional. The use to which the statistics or information
is put may be promotional. The two phases must be kept distinct (as per the Supplementary Information for Clause 12.2 of the ABPI COP).

Attention is drawn to the Legal & Ethical Guidelines for Healthcare Market Research produced by the British Healthcare Business Intelligence Association in consultation with the ABPI (as per the Supplementary Information for Clause 12.2 of the ABPI COP).

Market research material should be examined to ensure that it does not contravene the Code (as per the Supplementary Information for Clause 12.2 of the ABPI COP).

Where market research is carried out by an agency on behalf of a pharmaceutical company, the agency must reveal the name of its client to the Prescription Medicines Code of Practice Authority when the Authority requests it to do so. When commissioning market research, a company must take steps to ensure that its identity would be so made known to the Authority should a request for that information be made (as per the Supplementary Information for Clause 12.2 of the ABPI COP).

Other Non-interventional Studies of Marketed Products

According to the supplementary information which has been provided for Clause 13 in the ABPI COP:

“Companies are encouraged to comply with Clause 13.4 for all other types of studies covered by Clause 13.2, including epidemiological studies and
registries and other studies that are retrospective in nature. In any case, such studies are subject to Clause 18.7.

17 Contracts between companies and institutions, organisations or associations of health professionals under which such institutions, organisations or associations provide any type of services on behalf of companies (or any other type of funding by the company not otherwise covered by the Code) are only allowed if such services (or other funding):

• comply with Clause 18.4 or are provided for the purpose of supporting research
• do not constitute an inducement to prescribe, supply, administer, recommend, buy or sell any medicine.

Pharmaceutical companies must publicly disclose details of transfers of value made to such institutions, organisations or associations.
Additional Resources

**Country-specific eLearning Module**

CHCUK now offer an eLearning Module for the UK that explores the country-specific requirements when conducting non-interventional studies in the UK and looks specifically at:

- Regulatory classification
- Regulatory framework, the applicable legislation and guidelines
- Approval requirements and timeframes
- Submission documents
- Who is responsible for what?
- Practical considerations when conducting non-interventional studies
- Requirements for non-interventional studies that intend to collect, store and/or analyse human tissue samples
- Industry best practice

**Course Format**

The course:

- Takes approximately 20 minutes to complete
- Is cloud-based and can be accessed from any computer (Mac, Pc etc), as well as smartphones and tablets.
- Has an audio commentary
Includes PDFs of all the training materials

Includes a certificate of completion that is automatically issued to all participants who complete the course

Comprehensive Country-Specific Reports

Please bear in mind that the two ‘NIS Europe’ reports are a very high level overview of the regulatory and operational considerations in each country and are merely a summary of the more comprehensive and detailed country-specific reports that we prepare for each country.

These latter reports are designed as operational manuals for projects teams and provide and are intended to complement-supplement the eLearning modules.

The reports contain:

- Approximately 100 to 200 pages of information specific to the conduct of all types of non-interventional studies in the country of interest
- Hyperlinks to all of the referenced materials
- Detailed and comprehensive information covering:
  - Regulatory classification of studies
  - Applicable applicable legislation and guidelines
  - Regulatory roadmap(s)
  - Data privacy requirements and considerations
  - Approval requirements and timeframes
  - Submission documents
  - Who is responsible for what?
  - Practical considerations when conducting non-interventional studies
Requirements for non-interventional studies that intend to collect, store and/or analyse human tissue samples

Industry best practice

Who Would Benefit from the eLearning Courses and Comprehensive Reports?

The courses and reports are intended for anyone involved in the oversight or operational aspects of non-interventional studies, such as:

- Medical Affairs Groups/ Company Affiliates
- Clinical Operations Teams
- Project Managers
- CRAs
- Quality Assurance Personnel
- Regulatory Affairs Personnel

Try Before You Buy!

Don’t just take our word for it! Our NIS Considerations (UK - 2013) eLearning module and comprehensive country-specific report are now both free to access so that you see for yourself what we offer.
Further Information and/or Free Demonstration

If you would like further details, or would like to request a free demo then please contact us at:

Email: info@chcuk.co.uk

Phone: +44 1997 42 33 11

website: www.chcuk.co.uk
## UK - Useful Links

<table>
<thead>
<tr>
<th>Useful Links</th>
<th>Accessed From</th>
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</thead>
<tbody>
<tr>
<td>Association of British Pharmaceutical Industries (ABPI)</td>
<td><a href="http://www.abpi.org.uk/Pages/default.aspx">http://www.abpi.org.uk/Pages/default.aspx</a></td>
</tr>
<tr>
<td>Health Research Authority (HRA)</td>
<td><a href="http://www.hra.nhs.uk/">http://www.hra.nhs.uk/</a></td>
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<tr>
<td>HRA Resources Page</td>
<td><a href="http://www.hra.nhs.uk/resources/">http://www.hra.nhs.uk/resources/</a></td>
</tr>
<tr>
<td>Information Commissioner's Office (ICO)</td>
<td><a href="http://www.ico.org.uk">http://www.ico.org.uk</a></td>
</tr>
<tr>
<td>Integrated Research Application System (IRAS)</td>
<td><a href="https://www.myresearchproject.org.uk">https://www.myresearchproject.org.uk</a></td>
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<tr>
<td>National Institute for Health Research - Model Clinical trial Agreements</td>
<td><a href="http://www.nihr.ac.uk/industry/Pages/model_clinical_trials_agreement.aspx">http://www.nihr.ac.uk/industry/Pages/model_clinical_trials_agreement.aspx</a></td>
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