Medicines & Healthcare products Regulatory Agency

CPRD More Dimensions to Data

Independent Scientific Advisory Committee for Medicines and Healthcare products Regulatory Agency (MHRA) database research (ISAC)

15-month Committee Report

1 January 2015 to 31 March 2016

NHS National Institute for Health Research

Contents

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Glossary of acronyms

ADR	Adverse drug reaction
CAG	Confidentiality Advisory Group
CSM	Committee on Safety of Medicines (replaced in 2005 by CHM)
CHM	Commission on Human Medicines
CPRD	Clinical Practice Research Datalink
CPRD GOLD	GP On-Line Database (CPRD's primary care data collection database)
DPA	Data Protection Act 1998
FOIA	Freedom of Information Act 2000
HES	Hospital Episode Statistics
HRA	NHS Health Research Authority
GP	General Practice/practitioner
HSCIC	Health & Social Care Information Centre (now titled NHS Digital)
IDCs	Incremental Data Collections
ISAC	Independent Scientific Advisory Committee for MHRA Database Research
IT	Information Technology
MRC	Medical Research Council
MHRA	Medicines and Healthcare products Regulatory Agency ("the Agency")
NHS	National Health Service
ONS	Office for National Statistics
PEAG	Pharmacovigilance Expert Advisory Group (of the MHRA)
REC	NHS Research Ethics Committee
SEAG	Scientific and Ethical Advisory Group
SPC	Summary of Product Characteristics
UK	United Kingdom
VT	Vision Data Transfer
VRMM	Vigilance and Risk Management of Medicines, a division of the MHRA

Foreword from the Chairman of the MHRA

The Independent Scientific Advisory Committee for MHRA Database Research (ISAC) plays a vital role in ensuring that research using anonymised health data within MHRA databases is appropriately used to support public health, while protecting the confidentiality of patients and the public. I am therefore delighted to present the ISAC Report covering the period January 2015 to March 2016. On this one occasion, the Report encompasses a 15-month timeframe, which will bring the ISAC annual reporting period into line with the Agency's financial year reporting cycle. Future ISAC Annual Reports will run from 1 April to 31 March in the following year.

To date the ISAC's remit has been to review applications to access anonymised health records held by Clinical Practice Research Datalink (CPRD) and Yellow Card data maintained by the MHRA Regulatory Centre. Over the reporting period exciting work was undertaken to facilitate electronic Yellow Card reporting through integration into clinical IT systems used by healthcare professionals. This will improve the recording of adverse drug events, increasing the quantity and quality of data. This 15-month reporting period marks the end of ISAC's responsibilities for reviewing applications for Yellow Card data, which henceforth will be undertaken by Pharmacovigilance Expert Advisory Group (PEAG) of the MHRA. The ISAC activities in the next financial year will consequently exclusively focus on functions that relate to use of CPRD data.

The Agency is reliant on receiving high-quality, representative health data to carry out its medicines vigilance function, as well as supporting a wide range of essential public health research by others. Maintaining public trust in the responsible use of anonymised health data in medical research is therefore crucial to the Agency's role and operations. A summary of the ISAC approved studies undertaken using CPRD, including the named Chief Investigator and co-applicants for each study, is now published on the CPRD website. I believe that this greater transparency is an important step in reassuring the public that their data is being used in research for patient benefit and public good.

The ISAC has received more applications for use of CPRD data in this period than in previous years, and the Committee has dealt with the increase in volume in a professional and timely manner. On behalf of Agency, I wish to express my gratitude to the previous ISAC Chair, Professor Patrick Waller, to the new Chair, Professor Deborah Saltman AM and to all of the ISAC members for their expertise and dedication in ensuring that the ISAC continues to execute its activities to a high standard.

Sir Michael Rawlins
MHRA Chairman

Foreword from the Chair of the ISAC

I took office in February 2016 and have been impressed with the work of the Committee and Secretariat. I am looking forward to continuing to work very closely with the members of the ISAC to improve the health of the public by supporting the use of CPRD data. Coming from a general practice and research epidemiology background, I understand the importance of CPRD data and am delighted to Chair such a diligent and devoted Committee.

The past 15 months has been very busy for the ISAC, with an increase in workload, both in terms of the number of new research protocol submissions to the ISAC, and amendments and resubmissions. This increase demonstrates the importance of the CPRD database to health research and quality health practice. We have reviewed applications coming from all over the world, including Canada, the United States and Europe, demonstrating that the ISAC is able to help shape global public health.

During the reporting period eight new scientific members joined the Committee – Dr Angelyn Bethel, Professor Sinead Brophy, Dr Duncan Edwards, Dr Caroline Jackson, Dr Jennifer Quint, Dr Sara Thomas, Dr Hester Ward and Professor Ian Wong (please see Annex 1 for further details of these members). I would like to thank them for their interest in the work of the Committee, and indeed thank all members of the Committee for their continuing contributions to the ISAC meetings and research protocol reviews submitted to the ISAC for consideration.

I would also like to thank members of the Committee who completed their term of office during the period of this Report, namely Dr David Irvine for his valued contribution to the Committee as Deputy Chair of the ISAC up to June 2015; Professor Jackie Cassell; Professor Richard Martin; Professor Martin Gulliford; Dr Iskander Idris and Dr Ruben Thanacoody. Their longstanding contributions to the success of the Committee and in safeguarding UK public health have been integral to the ISAC's achievements.

I would also like to recognise the excellent support we have received from the ISAC Secretariat and from CPRD throughout the year. In particular I would like to thank the CPRD Director Dr Janet Valentine, for her sage advice and support during my first year. The CPRD Secretariat members, Mrs Tarita Murray-Thomas, Ms Sophia Amjad, Dr James Ellis, Ms Jessie Oyinlola and Dr Wilhelmine Meeraus have provided professional and highly competent support, efficiently managing the large numbers of protocols submitted to the ISAC. I would also like to thank Rebecca Owen for her work supporting the Yellow Card Secretariat. In addition, I would like to thank the CPRD Observational Research team for the role they have played in the assessment of ISAC protocols.

Finally I would like pay tribute to Professor Patrick Waller for his diligent work in shaping the ISAC into a highly professional service during his term of office as ISAC Chair from January 2012 to February 2016. I look forward to stewarding the Committee to another year of success.

Professor Deborah Saltman AM
Chair, Independent Scientific Advisory Committee (ISAC)

1. MHRA Databases

1.1. Introduction to the report

The MHRA is an Executive Agency of the Department of Health. Its role is to protect and promote public health and patient safety by ensuring that medicines, healthcare products and medical equipment meet appropriate standards of safety, quality, performance and effectiveness, and that they are used safely.

The MHRA holds two nationally important patient data sources, namely anonymised primary care data collected by the Clinical Practice Research Datalink (CPRD), and the Yellow Card Scheme database which collects monitoring and safety reports of healthcare products in the UK. This 15-month Report on the work of the Independent Scientific Advisory Committee for MHRA Database Research (ISAC) presents a summary and overview of the operations and outputs of the Committee for the period of 1 January 2015 to 31 March 2016. The role of the Committee is to review the scientific merit of proposals for research using data from the CPRD database, including primary care data linked to other health-related data sets. Up until February 2016 the Committee was also responsible for reviewing proposals to use data from the Yellow Card Scheme database. A description of the data and its uses are described below in Section 1. Details of the ISAC's roles and responsibilities are provided in Section 2 and activities and outputs of the ISAC over this reporting period are described in Section 3.

1.2. Clinical Practice Research Datalink

1.2.1. Background to CPRD

CPRD is a joint venture between the MHRA and the National Institute of Health Research (NIHR) and is based within the MHRA. CPRD operates as a not-for-profit research service aimed at maximising the use of anonymised patient data for public health research. The CPRD database is managed by CPRD on behalf of the Secretary of State for Health.

The primary care database held by CPRD is called GOLD (GP On-Line Database). CPRD GOLD contains the anonymised longitudinal health records collected from primary care (general practices) across the UK. At the end of this reporting period, the database held research quality data for over 20 million patients.

The CPRD GOLD database is used for public health research both nationally and internationally by researchers in academic institutions, regulatory agencies, the NHS, Government organisations and the pharmaceutical industry. Research using CPRD data encompasses disease epidemiology, drug safety, pharmacoepidemiology, drug utilisation, treatment patterns, health outcomes, pharmacoeconomics and health service planning. Since 1988, in excess of 1600 research papers using CPRD data have been published in a wide variety of peer-reviewed scientific journals. These include studies that have contributed to the development of clinical guidelines for important public health issues such as measles, mumps and rubella (MMR) vaccination and selective serotonin reuptake inhibitors (SSRIs).

1.2.2. Permissions and approvals

CPRD must seek annual approval from the Research Ethics Committee and the Confidentiality Advisory Group (CAG), both of the NHS Health Research Authority (HRA), to legally collect and link anonymised patient data without breaching the common law duty of confidentiality. CPRD operates a General Practitioner (GP) opt-in model, whereby a GP practice consents to contribute their anonymised patient records to CPRD. GPs are provided with Fair Processing Notices to inform patients of the right to opt-out of their anonymised data being sent to CPRD for research purposes.

1.2.3. Data collection

CPRD manages the collection of data from GP practices using Vision Primary Care System software or EMIS GP Clinical System software. Once a practice has agreed to contribute data to CPRD, data are transferred to CPRD in an encrypted form via a secure N3 connection. On arrival, the data are verified for integrity and completeness before further processing.

1.2.4. Anonymisation process

CPRD data contains anonymised coded patient level data. No personally identifiable information such as names, addresses, full date of birth and NHS number are transmitted to or held by CPRD. This ensures that the identity of individuals within the database cannot be established by anyone within CPRD or by researchers using CPRD data.

In order to be able to update individual longitudinal patient records on an ongoing basis, it is important that every patient and practice within the database can be distinguished uniquely, so that new information about a specific patient can be added to their longitudinal record. To achieve this, every patient is allocated an encrypted ‘flag’ by the GP system software. The GP is able to re-identify

individual patients using this ‘flag’ however it is not possible for anyone outside the practice to use the ‘flag’ for patient identification. To further protect patient identity, the identities of individual practices are also encrypted so that researchers are unable to determine which practices are contributing data to CPRD. The GP system software also anonymises doctors and practice staff who enter data into their system. As an additional privacy safeguard, the patient ‘flag’ and practice number are encrypted again within CPRD before the anonymised data is supplied to researchers.

1.2.5. Data linkage

CPRD GOLD data from most contributing English practices are linked to other health-related data sources by NHS Digital, previously the Health and Social Care Information Centre (HSCIC). NHS Digital is the only statutory trusted third party in England permitted to undertake this linkage service. The data sets routinely linked to the GOLD data are:

- Hospital Episode Statistics (HES)
    - Inpatient data
    - Outpatient data
    - Accident & Emergency data
    - Diagnostic Imaging Dataset
- The Cancer Registry
- ONS Death Registration Data
- Indices of Deprivation (Townsend scores and Index of Multiple Deprivation).

1.3. The Yellow Card Scheme

Under the Medicines Act 1968, the Commission on Human Medicines (CHM) gives advice to the Licensing Authority (MHRA acting on behalf of the Secretary of State for Health) on the safety, quality or efficacy of medicines and for promoting the collection and investigation of information relating to adverse drug reactions (ADRs). Suspected ADRs in the UK are reported through the UK's spontaneous ADR reporting scheme (the Yellow Card Scheme). The Scheme is voluntary for health professionals and patients, whereas pharmaceutical companies are legally obliged to report serious ADRs to the MHRA. This scheme was set up in 1964 and since then, more than 850,000 UK reports have been received. Approximately 35,000 UK reports of suspected ADRs have been received per year in recent years. Due to a number of initiatives 2015 saw an increase in reports to 40,000.

The Vigilance and Risk Management (VRMM) division of the MHRA is responsible for identifying signals (i.e. warning signs) of possible drug-safety hazards from this information, investigating these and where necessary, conducting risk-benefit analyses to determine whether any action is necessary

to minimise risk. Issues of drug safety may also be brought to the attention of the MHRA from many other sources, and are similarly investigated and acted upon. Information obtained from post-marketing experience may lead to the need for the Marketing Authorisation to be updated in variety of ways. This includes the amendment of the Summary of Product Characteristics (SPC), which may range from restriction of the indication, addition of contraindications or warnings, addition of monitoring requirements or addition to the list of recognised side effects. All changes made to the SPC are reflected in the Patient Information Leaflet that accompanies the medicine.

2. Governance and Management of the ISAC

2.1. Role of the ISAC

The ISAC was established by the Secretary of State for Health in February 2006 to review proposals for research using data from the MHRA's CPRD and Yellow Card Scheme databases.
Over this reporting period the remit of the ISAC was to:

- Consider and provide advice to the MHRA on applications for Yellow Card data[1] which fall outside Freedom of Information provisions, and all research projects which propose the use of data from the Clinical Practice Research Datalink;
- Provide advice at the request of the MHRA on wider aspects of the release of Yellow Card data[2];
- Consider the scientific (medical, statistical/epidemiological and methodological) aspects of protocols;
- Provide advice at the request of the MHRA relating to other ethical or confidentiality issues. This must be considered alongside input from other Committees such as the Confidentiality Advisory Group (CAG).

2.1.1. Review of CPRD research protocols

When reviewing CPRD protocols the Committee considers whether:

- The CPRD database is a suitable database with which to conduct the research;
- There are no major scientific concerns with the medical, statistical, epidemiological or methodological aspects of the study:
    - The methodology is considered appropriate, including consideration of possible bias and confounding;
    - There is a well-defined hypothesis or clear question to be addressed where appropriate;
- There is compliance with the requirement to ensure protection of practice and patient confidentiality.

2.1.2. CPRD protocol risk review

The purpose of the Committee's review of research protocols is to ensure that investigators using data for research have feasible plans that do not raise governance concerns and reach an acceptable scientific standard. In this context the ISAC provides a timely, high-quality peer review of protocols

[1] Responsibilities transferred to PEAG on 19th February 2016

[2] Responsibilities transferred to PEAG on 19th February 2016

whilst recognising that the quality of the research ultimately remains the responsibility of the applicants. Protocols are systematically assessed for potential scientific and governance issues taking into account the nature of the study and the potential implications for public health. The system for protocol assessment changed during the reporting period.

Between April and June 2015, protocols were rated by the ISAC Chair and CPRD Secretariat as low, medium or high risk. Basic epidemiology or drug utilisation studies which often do not raise significant concerns tended to be rated as low risk and were reviewed independently by the ISAC Chair and CPRD Secretariat. More complex hypothesis testing drug safety studies and research proposing new or novel methodologies were generally rated as high risk, even when they appeared to be well-designed. These were reviewed by the ISAC Chair and by two (or, exceptionally, three) ISAC members with the most appropriate expertise in the area.

From July 2015 onwards, the risk rating of protocols was simplified to categorise each application with either a low or high risk rating. The CPRD Observational Research team also became involved in the protocol reviewing process. Protocols rated as low risk were reviewed independently by both the ISAC Chair and at least one nominated CPRD Researcher. Protocols rated as high risk were reviewed independently by the ISAC Chair, at least one ISAC member and one CPRD Researcher. By using this approach the Committee was better able to focus its resources efficiently on those protocols raising the most concern and draw on the technical and methodological expertise of CPRD Researchers who know and understand the data sources well.

2.1.3. Review of Yellow Card protocols

To support compliance with the Data Protection Act 1998 (DPA) and the Freedom of Information Act 2000 (FOIA) requests for Yellow Card Scheme data were divided into ‘Category I’ requests that were generally releasable under the FOIA and not prohibited from release by the DPA and ‘Category II’ requests that were subject to FOIA exemptions and the restrictions of the DPA.

Until February 2016, the Committee’s role was to review scientific aspects of requests for Category II data. The Committee did not have access to the data being requested, but considered whether or not the MHRA should collate and supply these data, with due consideration towards the founding principles of the Yellow Card Scheme (presented in Annex 1).

When reviewing Yellow Card applications the Committee considered whether:

- The methodology of the study was sound;
- Yellow Card data could address the hypothesis;
- The study was of potential scientific value and/or had significant public health implications;

- The use of other data sources could, together with Yellow Card data, identify patients or reporters;
- Ethical review from an NHS research ethics committee (REC) was required; and
- There were any FOI/DPA reasons why data should not be released.

The Yellow Card review process followed a risk rating process analogous to that of CPRD protocol risk review, as explained above.

As of 19th February 2016, all applications to access Yellow Card data were passed to the Pharmacovigilance Expert Advisory Group (PEAG) of the MHRA, which ended Yellow Card responsibilities of the ISAC over the remaining period of this Report.

2.2. Membership

The ISAC membership falls into two key categories: scientific and lay members. Scientific members provide advice on the medical, statistical/epidemiological and methodological aspects of protocols submitted to the Committee for review. Lay members provide advice on protocols seeking additional information from GPs, patients and practices, and where there may be potential governance issues associated with a study.

2.2.1. Membership over the reporting period

At the end of the reporting period, ISAC membership consisted of 21 scientific members and two lay members. A total of 27 scientific members served on the Committee inclusive of membership turnover (i.e. members whose terms of office ended, members whose terms continued and new appointees to the ISAC). Lay membership remained constant with two members on the Committee throughout the reporting period. Membership of the ISAC between 21st April 2015 and 31st March 2016 is listed in Annex 2.

2.2.2. Appointment of members

Responsibility for the recruitment and appointment of members altered during the period of this Report. The Chair and members of the ISAC were previously appointed by the Department of Health Appointments Commission (formerly the NHS Appointments Commission) for a three-year term, after which each term might be renewed on a three-year basis up to a maximum of ten years.

From October 2015, the appointment procedures changed. ISAC members are now appointed directly by the MHRA. New members are appointed for an initial two-year term, which may be extended for a

further two years, to a maximum four-year appointment. The duties of the ISAC members are be found in Annex 3.

2.2.3. Declarations of interest

Members of the ISAC are required to declare any relevant interests or relationships with the pharmaceutical industry and any other interests that may affect their impartiality or be perceived as doing so. Declarations must include interests of their immediate family members (e.g. spouse). Declarations must be made on appointment and the MHRA must be notified immediately of any changes. Failure to comply may result in removal of an individual from the Committee.

Furthermore, members are asked to declare any potential conflicts of interest relevant to individual protocols at the time of protocol review. This allows interests to be taken into account during protocol evaluation, reducing potential bias in connection with these interests. ISAC members are excluded from participation in the review of protocols and applications arising from their own academic department. The Deputy Chair is responsible in cases where the Chair has a direct conflict of interest or is unavailable. A register of members' declared interests can be found in Annex 4.

2.3. Meetings of the Committee

2.3.1. Physical meetings

Committee meetings where members meet in person are held quarterly. Over the reporting period, the Committee met five times on the following dates: 20 January 2015, 14 April 2015, 8 July 2015, 21 October 2015 and 19 January 2016. The ISAC meetings were held at the MHRA offices located at 151 Buckingham Palace Road, Victoria, London SW1W 9SZ.

2.3.2. Member meeting expenses

Members are entitled to claim a set fee for each physical meeting attended. In 2015 and 2016 Committee members were entitled to claim £174 for preparation and attendance per meeting. In addition, members are entitled to claim travel and subsistence expenses as for the following:

- Reasonable travel expenses to and from home to the meeting venue;
- Reasonable travel and subsistence expenses incurred as part of ISAC work away from the normal venue;
- Particular travelling costs incurred by disabled members;

- Other reasonable expenses incurred e.g. locum costs, child care and overnight stay, subject to agreed MHRA limits.

The Chair is remunerated by the MHRA on a pro-rata basis for ISAC duties and does not receive payment or expenses for ISAC meeting attendance.

2.3.3. Virtual working between meetings

Review of almost all CPRD and Yellow Card research protocol submissions was performed virtually on a continuous basis throughout the reporting period. Reviews were undertaken by ISAC members and by Yellow Card and CPRD staff and are described further in section 2.5. All phases of protocol review were overseen and signed off by the Chair.

2.4. Secretariat

In the reporting period, the ISAC was serviced and supported by two distinct Secretariats of Agency employees due to the distinct requirements for processing and reviewing protocols submitted to access CPRD data and Yellow Card data.

The CPRD Secretariat supported processing of research protocols requesting access to CPRD data and provided administrative support for the wider activities of the Committee. The Yellow Card Secretariat covered research proposing use of Yellow Card data and was staffed by the VRMM division of the MHRA.

The separation of Secretariat roles was to ensure that discussions and outcomes arising from the review of CPRD protocols did not influence decision-making by regulatory staff from VRMM, which examined Yellow Card protocols only. Applications for use of the two different MHRA databases were submitted via separate email mailboxes.

2.5. Appeals process

If applicants disagree with the outcome of an ISAC decision and this cannot be resolved by minor revision of the application or by resubmission, applicants can appeal the Committee's decision. The appeal process can be found in Annex 5.

2.6. Transparency of ISAC approved research protocols

A new Agency policy to publish summary information about ISAC approved research protocols on the CPRD website was implemented in July 2015. Information is published a minimum of three months after applicants receive the requested data for their research from CPRD. Further information on the ISAC approved studies can be found at https://www.cprd.com/ISAC/datause.asp .

2.7. Publication of ISAC approved studies

The findings of many studies approved by the ISAC are published in peer-reviewed scientific journals. A comprehensive list of all publications using or referencing CPRD data can be found on the CPRD website: https://www.cprd.com/bibliography/.

2.8. Publication of the ISAC activities

Summary minutes of ISAC meetings are published on both the CPRD and MHRA websites once the full minutes have been agreed by the Committee. The summary of ISAC minutes are available at https://www.cprd.com/ISAC/Minutes.asp.

The annual reports of the ISAC are made available on both the MHRA and CPRD websites, at https://www.gov.uk/government/groups/independent-scientific-advisory-committee-for-mhra-database-research and https://www.cprd.com/ISAC/Minutes.asp.

3. Activities and Outputs

3.1. Research protocols: applications and approvals

3.1.1. Summary of applications and approvals for use of CPRD data

During the reporting period a total of 329 research protocols requesting use of CPRD data were reviewed by the Committee. This figure represents both new applications submitted during this reporting period, as well as resubmitted applications that were initially submitted for ISAC review in previous reporting periods. A total of 242 protocols were approved by the ISAC during the reporting period. Of the 329 applications reviewed by the ISAC, 220 applications requested linked data.

Table 1 presents the proportional breakdown of 242 ISAC approved research protocols by lead investigator's organisational affiliation. In instances where a lead investigator has two organisational affiliations, both of these affiliations have been recorded. Table 1 shows that the majority of ISAC approved protocols were submitted by researchers based in academic organisations.

Table 1: Number of protocols approved by lead investigator's organisational affiliation

Lead Investigator's Organisational Affiliation	Number of Approved Protocols[3]
Academia	170
Pharmaceutical company	32
Research Services Provider	31
Government	11
Charity	2
National Health Service	2

Classification of the 242 approved protocols by study type is shown in Table 2. As these categories are not mutually exclusive, the number of approved protocols by study type is greater than the total number of 242 individual protocols approved by the ISAC. Where more than one type of study is involved with a single protocol, the protocol is classified as 'Combined'.

[3] The number of approved protocols linked to organisational affiliation shown is greater than total number of 242 protocols approved due to some lead investigators listing more than one organisational affiliation.

Table 2: ISAC approved protocols by study type

Study Type	Number of Approved Protocols[4]
Disease Epidemiology	81
Adverse Drug Reactions/ Drug Safety	41
Drug Use	24
Public Health	27
Drug Effectiveness	6
Combined and Other Types[5]	150

The value of research using primary care data can be significantly augmented by linking to other data sources. Of the 329 applications to the ISAC over the reporting period, 220 (67%) included requests to link to other data sets. A single protocol may request linkage to more than one data set. Table 3 illustrates the number of individual requests for linkage to routinely-linked data sets and for bespoke data linkage. The highest proportion of requests was for linkage to Hospital Episode Statistics Inpatient data.

Table 3: Requests for data sets to be linked to CPRD data

Data set requested for linkage	No. of Requests[6]
Routine data linkage	
Hospital Episode Statistics (HES) – Inpatient	198
Townsend / Index of Multiple Deprivation (IMD) score	153
Office for National Statistics – Death Registration Data	118
Hospital Episode Statistics (HES) – Outpatient	47
Cancer Registry Data	6
Bespoke data linkage	
Myocardial Ischaemia National Audit Project (MINAP)	13
Hospital Treatment Insights	3
Other data sets	18

[4] Study type classification is not mutually exclusive

[5] Study types described here as 'Combined and Other Types' include protocols classified by more than one study type.

[6] Number of linkage requests will be greater than number of approved individual protocols as a single approved protocol may request linkage to more than one data set

3.1.2. Summary of applications and approvals for use of Yellow Card data

During the reporting period there were two new Yellow Card applications, both of which were approved by the Committee.

3.2. Wider activities of the Committee

3.2.1. Revision of existing protocol submission guidance

Updated guidance to applicants was published on the CPRD website in July 2015 in conjunction with an updated application form. A new Curriculum Vitae (CV) system was also introduced in July 2015 to aid the ISAC in identifying expertise and conflicts of interests of applicants. A total of 815 CVs were processed between July 2015 and March 2016 by the CPRD Secretariat.

3.3. Audit project of ISAC protocol outcomes

The ISAC concluded their work auditing publications arising from ISAC approved applications. The findings from this exercise would be presented at a future user group meeting.

Annex 1 – Fundamental principles of the Yellow Card Scheme

Sir Derrick Dunlop, who was Chairman of the Committee on Safety of Drugs (CSD) when the Yellow Card Scheme was launched in 1964, set out five basic principles which have stood the test of time:

- A voluntary scheme based on the good will of reporters
- The collation of reports of ADRs without a causal link needing to be established
- Reporters are encouraged to report without delay
- All reports are held in complete confidence by the MHRA and CSM
- The data are never to be used for disciplinary purposes or for enquiries about prescribing cost.

Annex 2 – Membership over 2015/16 and member biographies

Professor Patrick Waller BMedSci MD MPH FRCP Ed. FFPM FBPharmacolS (Outgoing Chair) (Retired as Chair on 29 February 2016)
Honorary Professor, Faculty of Epidemiology and Public Health, London School of Hygiene and Tropical Medicine

Professor Deborah Saltman AM (Chair) MBBS MD MRCGP FRACGP FAFPHM GAICD. (Appointed as Chair on 18 January 2016)

Professor Richard Stevens (Deputy Chair) BA MSc PhD (Appointed as Deputy Chair February 2016)
Associate Professor, Medical Statistics Group, Nuffield Dept of Primary Care Health Sciences, University of Oxford

Mr David Irvine BSc, MSc, CStat (Deputy Chair) (Resigned 30 June 2015)

Dr Angelyn Bethel MD (Appointed 1 January 2016)
Deputy Director, University of Oxford Diabetes Trials Unit

Dr Krishnan Bhaskaran MSc PhD (Reappointed 2 January 2016)
Senior Lecturer in Statistical Epidemiology, Department of Non-Communicable Diseases Epidemiology, London School of Hygiene and Tropical Medicine, London

Professor Sinead Brophy BSc PhD (Appointed 15 December 2015)
Professor of CIPHER, College of Medicines, Swansea University

Dr Benjamin Cairns BA BSc PhD (Reappointed 2 January 2016)
Senior Statistical Epidemiologist, Cancer Epidemiology Unit, University of Oxford

Professor Jacqueline Cassell FFPH FRCP MD MSc DipGUM DFFP (Resigned 7 December 2015)
Professor of Primary Care Epidemiology, Brighton and Sussex Medical School

Dr Christopher Edwards BSc (Hons) PhD MIPEM (Reappointed 2 January 2016)
Consultant Medical Physicist, Aneurin Bevan University Health Board, St Woolos Hospital in Newport, South Wales

Dr Duncan Edwards BSc, MB BS, MRCGP (Appointed 1 January 2016)
NIHR Doctoral Research Fellow and GP, Department of Public Health and Primary Care, The School of Clinical Medicine, University of Cambridge

Professor Martin Gulliford MA FRCP FFPH (Retired as a member on 28 November 2015)
Professor in Public Health at King's College London

Professor Peter Helms MBBS PhD FRCP FRCPCH FFSEM (Appointed 1 January 2015)
Emeritus Professor of Child Health, University of Aberdeen

Dr Iskandar Idris BMedSci BMBS FRCP (London & Edin) DM (Retired as a member on 1 January 2015)
Associate Professor in Diabetes and Honorary Consultant Physician, University of Nottingham & Royal Derby Hospital

Dr Caroline Jackson BSc, MSC, PhD (Appointed 1 January 2016)
Chancellor's Fellow, Institute of Population Health Sciences and Informatics, University of Edinburgh

Professor Umesh T Kadam MRCGP MPhil MSc PhD FFPH (Reappointed 15 November 2013)
Professor of Health Services Research & Clinical Epidemiology, Keele University, Staffordshire

Dr Wendy Knibb MSc (Econ.) PhD (Health Econ.) (Appointed 1 October 2014)
Independent Health Economics consultant

Professor Benjamin A Lipsky MD FACP FIDSA FRCP (Appointed 1 January 2015)
Deputy Director, Graduate Entry Course, University of Oxford Medical School

Dr Emily McFadden MA (Cantab) MSc PhD (Appointed 1 October 2014)
Senior Statistical Epidemiologist – Nuffield Department of Primary Care Health Sciences, University of Oxford

Ms Sally Malin BA (Hons) MA (Cantab) MSc (Econ) (Lay member) (Reappointed 2 January 2016)

Professor Richard Martin BMedSci BM BS MRCGP FFPH MSc PhD (Retired as a member on 28 November 2015)
Professor in Clinical Epidemiology, School of Social and Community Medicine, University of Bristol

Professor Simon Mitchell MD MRCP FRCPCH DCH DRCOG (Reappointed 15 November 2013)
Consultant Neonatologist, Newborn Intensive Care Unit, St Mary's Hospital, Manchester

Professor Keith Neal (Reappointed 1 October 2014)

Emeritus Professor in the Epidemiology of Infectious Diseases, University of Nottingham and Consultant Epidemiologist, for the Field Epidemiology Service, Public Health England

Dr Jennifer Quint PhD (Appointed 15 December 2015)

Clinical Senior Lecturer Respiratory Epidemiology, National Heart and Lung Institute, Imperial College London

Ms Marcia Saunders BA MA MSc (Lay member) (Reappointed 29 November 2014)

Chair, North West London Local Education and Training Board

Dr Ruben Thanacoody MD FRCP (Edin.) (Retired as a member on 14 November 2015)

Senior Lecturer in Clinical Pharmacology, University of Newcastle-upon-Tyne

Dr Sara Thomas PhD (Appointed 1 December 2015)

Clinical Senior Lecturer (Epidemiology) Faculty of Epidemiology and Population Health, London School of Hygiene & Tropical Medicine

Dr Hester Ward (Appointed 1 January 2016)

Consultant in Public Health Medicine (Health Informatics)

Professor Ian Wong (Appointed 14 December 2015)

Chair in Pharmacy Practice, UCL School of Pharmacy.

Member biographies

Professor Patrick Waller is an Honorary Professor in the Faculty of Epidemiology and Public Health at the London School of Hygiene and Tropical Medicine. After graduating in medicine from Sheffield University in 1980, he trained in clinical pharmacology and epidemiology. From 1988-1990 he was Senior Research Fellow at the Drug Safety Research Unit in Southampton. He then moved to the Medicines Control Agency in London where he became Head of the Pharmacovigilance Assessment Group. From 1998 to 2000 he was a UK delegate to the EC's drug regulatory committee and Chairman of its Pharmacovigilance Working Party. From 2002 to 2011 he was an independent consultant in pharmacovigilance and pharmacoepidemiology. From January 2012 to February 2016 he was Chair of the ISAC.

Professor Deborah Saltman AM is the Chair of the ISAC. Previously she was a clinical and scientific advisor and consultant within the medical communications and pharmacoeconomics arena. She holds positions as Honorary Professor in the Faculty of Medicine at Imperial College and the University of Sydney and is Visiting Professor at the University of Technology, Sydney. She has extensive experience in databases and database research, HTA assessments, health research, postgraduate medical education and medical publishing.

Deborah was made a member of the Order of Australia in 2004, and is a recipient of the Rose Hunt Medal from the RCGP (UK 2006). She is also a Notable Australian Doctor and has a doctorate in general practice as well as Fellowships of the RACGP, RCGP, RACP (Public Health Faculty). She is also a graduate of the Australian Institute of Company Directors. An active member of several professional organisations, Deborah is currently working with the UK Council of Psychotherapists to develop a new Code of Ethics.

Professor Richard Stevens is deputy director of the statistics group at the Nuffield Department of Primary Care Health Sciences (NDPCHS) in Oxford, and a fellow of Kellogg College, Oxford. His previous experience includes eight years at the Oxford Centre for Diabetes, Endocrinology and Metabolism, where he worked with the UK Prospective Diabetes Study group on the epidemiology and computer modelling of the cardiovascular complications of type 2 diabetes, and three years with the Cancer Research UK Epidemiology unit, where he studied pancreatic cancer in the Million Women Study cohort. His current research interests are in statistical models for the monitoring of chronic diseases such as diabetes, hypertension and chronic kidney disease. He was appointed Deputy Chair of ISAC in March 2016.

David Irvine joined the Medicines and Healthcare Products Regulatory Agency (MHRA) in 2005 as a pharmacoepidemiologist, his career having previously covered statistical and occupational epidemiological work for the Medical Research Council, British Petroleum, the Ministry of Defence and British Airways Health Services. Following retirement from the MHRA in 2010 he provided consultancy in pharmacoepidemiology to the Pharmaceutical company Takeda ending in 2014.

Dr Angelyn Bethel is Assistant Professor of Diabetes Endocrinology at the University of Oxford and is the Deputy Director of the University of Oxford Diabetes Trials Unit (DTU), a fully registered UKCRC Clinical Trials Unit and an internationally recognised Academic Research Organisation. At the DTU, she provides clinical and strategic oversight for ongoing multicenter cardiovascular outcomes trials in diabetes. Dr. Bethel is the primary investigator for GLINT, has served as the Academic Clinical Lead for Trial Evaluating Cardiovascular Outcomes with Sitagliptin, EXenatide Study of Cardiovascular Event Lowering, and Acarbose Cardiovascular Evaluation and has worked closely with the Translational Research Group at DTU, serving as a primary investigator and clinical advisor for a wide range of early phase clinical studies.

Dr Krishnan Bhaskaran is a Senior Lecturer in Statistical Epidemiology at the London School of Hygiene and Tropical Medicine (LSHTM). He graduated from Sheffield University with a BSc Hons in Mathematics in 1999. After taking an MSc in Medical Statistics at Leicester University in 2000-2001, he joined the MRC Clinical Trials Unit, and stayed there for six years, working on a variety of HIV trials and observational studies, with an emphasis on HIV seroconverters (individuals with well estimated dates of HIV infection). In October 2010, on gaining his PhD at LSHTM for a project looking at environmental risk factors for heart disease, he joined the Department of Non-Communicable Diseases Epidemiology as a lecturer. He currently holds a National Institute for Health Research postdoctoral fellowship and is investigating questions around cancer pharmacoepidemiology using routinely collected healthcare data. He teaches on the LSHTM MSc Epidemiology and is the course director for the LSHTM Short Course in Practical Pharmacoepidemiology. He also teaches basic statistics to undergraduate UCL medical students.

Professor Sinead Brophy is Professor of Public Health Informatics at Swansea University. She has over 20 years of experience working with large data sets and linkage of routine data for digital epidemiology, and longer term follow-up of interventions and natural experiments. She is Deputy Director of the National Centre of Population Health and Wellbeing and Lead of Informatics, Pharmacoepidemiology lead (CIPHER – Centre for the Improvement of Population Health through E-records Research) within the FARR Institute. She also has expertise in developing electronic cohort studies.

Dr Benjamin Cairns is Senior Statistical Epidemiologist in the Cancer Epidemiology Unit at the University of Oxford. He studies the causes of cardiovascular diseases and cancer, mostly in the Million Women Study, a study of the health and lifestyle of more than a million UK women. He also teaches statistics and epidemiology in the University of Oxford's undergraduate Medical Sciences and postgraduate Global Health programmes.

Professor Jackie Cassell is Director of Research, Chair in Primary Care Epidemiology and Honorary Consultant in Public Health at Brighton and Sussex Medical School. She leads a multidisciplinary programme of research funded by the Wellcome Trust on the production of electronic data and analysis of free text. Jackie is editor of the journal Sexually Transmitted Infections and serves on the Scientific Advisory Group to the MRC Methodology Research Panel. She was previously a Senior Clinical Research Fellow at University College London. Jackie leads a programme of health services research in the field of sexually transmitted infections in HIV, and is interested in broadening the public health uses of primary care databases.

Dr Christopher Edwards obtained a first degree in Health Physics, then spent a brief time in industry as a Nuclear Power instrumentation engineer. He then obtained a PhD in high frequency ultrasound for skin imaging from the University of Manchester Institute of Science and Technology. This was followed by 15 years as a research lecturer in Skin Bioengineering in the Dermatology department of the University of Wales, College of Medicine. Here his post involved the design, construction and use of instruments to measure skin properties, and he had a special interest in photobiology of the skin. He gained much experience in the design, running and analysis of clinical research trials. For the last 14 years he has run the phototherapy service in Newport, and has continued his research into phototherapies, while continuing to develop the popular Newport Phototherapy Course. He is a member of the Radiation Protection Special Standing Advisory Group, a Welsh Assembly Government advisory sub-committee. He is a committee member of the British Photodermatology Group and is co-author on the national guidelines on minimum standards for phototherapy and ultraviolet dosimetry in phototherapy. He is Health Board lead for research education and advises on research methodologies and statistics. He chairs the Intellectual Property Group. He is the Laser Protection Advisor to Aneurin Bevan University Health Board.

Dr Duncan Edwards is an NIHR Doctoral Research Fellow at the University of Cambridge and GP in South Norfolk. He graduated from Royal Free and University College London Medical School in 2005. After working as a junior doctor in London and East Anglia, he undertook general practice training combined with an academic clinical fellowship at the University of Cambridge between 2007 and 2011 before he joined Grove Surgery, Thetford as a GP partner in 2011. From 2013-5 he was a

board member of South Norfolk CCG. His own research is focused on the prevention and treatment of stroke and cardiovascular disease in the primary care setting.

Professor Martin Gulliford is Professor of Public Health at King's College London. He is active in CPRD-based research and is interested in the design and analysis of studies with clustered data, access to health care and diabetes care.

Professor Peter Helms is Emeritus Professor of Child Health University of Aberdeen and previous Consultant Paediatrician in the Royal Aberdeen Children's Hospital. He contributes to a number of national and international bodies and professional organisations in the areas childhood respiratory health and disease, sports and exercise medicine, and clinical pharmacology. He is immediate past Director of the Scottish Medicines for Children Network and co-chair of the European Research Network hosted at the European Medicines Agency (Enpr-EMA). His current research interests include the early expression of respiratory illness and paediatric pharmacoepidemiology.

Dr Iskandar Idris is an Associate Professor in Diabetes and Vascular Medicine at the University of Nottingham and Honorary Consultant Physician at the Royal Derby Hospital. He is currently the Training Programme Director for Specialist Training in Diabetes and Endocrinology at the East Midlands postgraduate deanery. He has ongoing academic and research interests in the field of obesity and vascular complications of diabetes and novel strategies for managing hyperglycaemia and vascular risks in patients with diabetes. Within the University of Nottingham, he has strong research links with the Division of Vascular Medicine and the MRC arthritis UK for musculoskeletal research and ageing. He has published widely in the field of diabetes, pharmacology and vascular complications.

Dr Caroline Jackson is a Chancellor's Fellow in the Population Health Sciences and Informatics Institute at the University of Edinburgh. After graduating in Biological Sciences (Hons. Immunology) she embarked on a career in epidemiology, obtaining her MSc in Epidemiology from the London School of Hygiene and Tropical Medicine and her PhD from University of Edinburgh in 2009. Her research interests include cardiovascular disease, multimorbidity (including mental and physical health co-morbidity) and health inequalities, using observational and routinely collected linked data. Prior to her current post, she was as a research associate at the University of Edinburgh, a MRC Career Development fellow with the Scottish Collaboration for Public Health Research and Policy and, most recently, a post-doctoral fellow in the School of Public Health at the University of Queensland.

Professor Umesh Kadam is Professor of Health Services Research & Clinical Epidemiology, Keele University. He is research active in the field of musculoskeletal disorders, comorbidity and ageing,

and has a particular interest in using general practice databases and linkage methods for characterising the course of diseases and common symptoms in primary care.

Dr Wendy Knibb was a Senior Lecturer in Health Economics at the University of Surrey from 2003 to 2014. She is currently an independent Health Economics consultant. Having graduated (1st class) in Economics with Politics, she took an MSc in Economics and subsequently a PhD in Health Economics from the University of Surrey. She has extensive knowledge of research in both Health Economics and also evaluative studies. She was seconded to the Department of Health SE part-time for three years (2008 – 2011) to advise on Health Economics and evaluative techniques. She has been an active member of the European Health Management Association for many years and has led a special interest group on their behalf. She has sat on a commissioning panel for the National Institute for Health Research and has also chaired an NHS Research Ethics Committee.

Professor Benjamin Lipsky is a Teaching Associate at Green Templeton College (University of Oxford), Visiting Professor of Medicine at the University of Geneva and Professor of Medicine Emeritus at the University of Washington. After graduating from Cornell University School of Medicine (New York) he trained in internal medicine and infectious diseases at the University of Washington (Seattle), where he was appointed to the faculty in 1978 (based at the VA Puget Sound Health Care System) and rose to Full Professor in 2000. He was an active clinician, served as an Infectious Diseases and Internal Medicine consultant, Chair of Infection Control, Hospital Epidemiologist, Director of the Primary Care Clinic and a member of the Investigational Review Board. He is now collaborating on various research projects (mainly involving diabetic foot infections) and is setting up a clinical research program at the Hospital of the University of Geneva.

Dr Emily McFadden is a Senior Statistical Epidemiologist in the Nuffield Department of Primary Care Health Sciences at the University of Oxford, where she also lectures in Study Design and Research Methods for the postgraduate Evidence Based Health Care programme, and in Medical Statistics for the undergraduate Medical Sciences programme. Her current research focuses on monitoring chronic conditions in primary care. She graduated from the University of Cambridge with an MA in Natural Sciences and Biological Anthropology, and from the London School of Hygiene and Tropical Medicine with an MSc in Epidemiology. She completed her PhD in 2009 at the University of Cambridge in the Department of Public Health and Primary Care. From 2009 to 2012 she worked as a Research Fellow in Epidemiology and Medical Statistics at the Institute of Cancer Research.

Sally Malin has worked in public policy (NHS and criminal justice) for over 30 years in strategic, academic and operational roles. She chaired Barnet PCT (2003 to 2008). Currently Independent Board Member of Health Education North West London; also Lay representative on Health Education

England Medical Advisory Group; on the MBBS 2020 Curriculum Committee, King's College London; and on the Credentialing Working Group, General Medical Council.

Professor Richard Martin is Professor in Clinical Epidemiology, School of Social and Community Medicine, University of Bristol and Honorary Consultant in Public Health at North Bristol NHS Trust. He has a longstanding interest in pharmacoepidemiology and the research potential of automated general practice databases, first developed as an academic general practitioner in London and Southampton.

Professor Simon Mitchell is a consultant neonatal paediatrician at St Mary's Hospital, Manchester. His research interests include genetic factors in the aetiology of cerebral palsy, dosage and administration of neonatal vitamin K prophylaxis and the clinical effects of intrauterine growth restriction. He is a member of the British Paediatric Surveillance Unit Executive Committee and Chair of Central Manchester Research Ethics Committee.

Professor Keith Neal is an Emeritus Professor in the Epidemiology of Infectious Diseases (University of Nottingham) and currently working as a consultant epidemiologist for Field Epidemiology Services (Public Health England). After graduating in medicine from Southampton University in 1980, he trained in infectious diseases and public health. His research interests include hepatitis C, invasive meningococcal disease and gastro-intestinal infections.

Dr Jennifer Quint is a Clinical Senior Lecturer in Respiratory Epidemiology at the National Heart and Lung Institute, Imperial College and Honorary Consultant Physician in Respiratory Medicine at Royal Brompton Hospital, London. Dr Quint's research interests centre on the use of electronic health records to study chronic obstructive pulmonary disease (COPD) as well as other chronic respiratory diseases including bronchiectasis and asthma. The majority of her work has been on exacerbations of COPD, exploring both the effect of COPD exacerbations on vascular outcomes and the relationship between environmental factors and exacerbations of COPD. Additionally she has undertaken several pieces of work in validation of identification of respiratory diseases in electronic health records.

Marcia Saunders is Independent Chair of Health Education North West London (Local Education and Training Board). Previously a PCT and SHA chair, her main career was in social services senior management and policy analysis. She is a member of the Governors and Pro Chancellor of De Montfort University, a lay assessor for the General Medical Council, and an honorary member of the Royal Pharmaceutical Society. She holds degrees from Cornell University, the University of Chicago and Bristol University.

Dr Ruben Thanacoody is Consultant Physician, Royal Victoria Infirmary, Newcastle Upon Tyne Hospitals NHS Trust. He has a longstanding interest in pharmacovigilance and is involved in Yellow Card Centre (Northern and Yorkshire). His research interests include drug-induced QT prolongation and adverse reactions to acetylcysteine.

Dr Sara Thomas is a Clinical Associate Professor in Epidemiology at the London School of Hygiene and Tropical Medicine. Her research focuses on the epidemiology of infections, immune-mediated disorders, vaccines and disorders of pregnancy, and much of this work involves use of linked electronic health records. She currently leads the Electronic Health Records Theme of the Health Protection Research Unit in Immunisation, a research collaboration between LSHTM and Public Health England. She also teaches epidemiological methods on a number of MSc and short courses at LSHTM, and she is the Programme Content Director of the LSHTM MSc in Epidemiology by Distance Learning.

Dr Hester Ward is a Consultant in Public Health Medicine at Information Services Division (ISD) & Health Protection Scotland (HPS), NHS National Services Scotland, an Honorary Reader at the University of Edinburgh and member of the Farr Institute. Hester provides public health leadership and expertise in the production and use of information and intelligence to benefit the health of the population of Scotland. Her focus is on primary care, health and social care integration, unscheduled care, dementia, with a focus on Creutzfeldt-Jakob disease (CJD), and research and innovation (strategy and governance).

Professor Ian Wong is the Head of Research at the Department of Practice and Policy at the UCL School of Pharmacy in London. Prior to his appointment, Professor Wong was the first Professor of Pharmacy at the University of Hong Kong and served as a board member of the Medicines Regulatory Authority of Hong Kong (Pharmacy and Poisons Board). Professor Wong was the founding director of the Centre for Paediatrics Pharmacy Research (2002 to 2011) at UCL and Great Ormond Street Hospital for Children. He was also the former co-director of the Centre for Safe Medication Practice and Research at the University of Hong Kong (2012 to 2015).

Annex 3 – Duties of ISAC members

1. Provide formal and informal advice to MHRA between meetings. Applications will be circulated electronically to ensure they are reviewed within 14 days and most CPRD applications will have to be decided without committee members meeting in person.
2. Attend all scheduled and unscheduled meetings of the Committee.
3. Consider, comment and contribute by their individual expertise and judgement as appropriate on all agenda items and to assist the Committee to frame clear and unequivocal advice to MHRA in accordance with the Committee's terms of reference.
4. Be able and be prepared to speak on a range of relevant issues and not just their own areas of specialism.
5. Develop an understanding of the types and uses of data contained in the CPRD and Yellow Card databases and understand how and when release of data (in particular Yellow Card data) could lead to patients being identified if applications are not robust scientifically.

Annex 4 – Declaration of Interests

Member's declared current Personal and Non-Personal Interests over 2015/16:

	Personal Interests		Non Personal Interests		
MEMBER	**Name Of Company**	**Nature Of Interest**	**Name Of Company**	**Nature Of Interest**	**Whether Current**
Prof Deborah Saltman	None	n/a	None	n/a	
Prof Richard Stevens	None	n/a	None	n/a	
Prof Patrick Waller	None	n/a	None	n/a	
Mr David Irvine	None	n/a	None	n/a	
Dr Angelyn Bethel	None	n/a	Merck Sharp & Dohme	Department receives research funding	Yes
			Boehringer Ingelheim	Consultancy	Yes
			NovoNordisk	Consultancy	Yes
			GlaxoSmithKline	Fee-paid work	Yes
			AstraZeneca	Department receives research funding	Yes
Dr Krishnan Bhaskaran	None	n/a	None	n/a	
Prof Sinead Brophy	None	n/a	None	n/a	
Dr Benjamin Cairns	None	n/a	None	n/a	
Prof Jacqueline Cassell	None	n/a	None	n/a	
Dr Christopher Edwards	None	n/a	None	n/a	

	Personal Interests		Non Personal Interests		
MEMBER	**Name Of Company**	**Nature Of Interest**	**Name Of Company**	**Nature Of Interest**	**Whether Current**
Dr Duncan Edwards	None	n/a	None	n/a	
Prof Martin Gulliford	None	n/a	None	n/a	
Prof Peter Helms	None	n/a	None	n/a	
Dr Iskandar Idris	MSD	Speaker fees	None	n/a	
	Eli Lilly	Research funding			
	Novo Nordisk	Advisory board			
Dr Caroline Jackson	None	n/a	None	n/a	
Prof Umesh Kadam	None	n/a	None	n/a	
Dr Wendy Knibb	None	n/a	None	n/a	
Prof Benjamin Lipsky	KCI/Acelity	Consultancy	None	n/a	Yes
	Dipexium	Consultancy			Yes
	Debiopharm	Consultancy			Yes
	Microbion	Consultancy			Yes
	Genentech	Consultancy			Yes
Dr Emily McFadden	None	n/a	None	n/a	
Ms Sally Malin	None	n/a	None	n/a	
Prof Richard Martin	None	n/a	None	n/a	
Prof Simon Mitchell	None	n/a	None	n/a	
Prof Keith Neal	None	n/a	None	n/a	

	Personal Interests		Non Personal Interests		
MEMBER	**Name Of Company**	**Nature Of Interest**	**Name Of Company**	**Nature Of Interest**	**Whether Current**
Dr Jennifer Quint	AstraZeneca	Consultancy	None	n/a	Yes
	GlaxoSmithKline	Grants & consultancy			Yes
	IMS	Consultancy			Yes
Ms Marcia Saunders	None	n/a	None	n/a	
Dr Ruben Thanacoody	None	n/a	None	n/a	
Dr Sara Thomas PhD	None	n/a	None	n/a	
Dr Hester Ward	Raptor Pharmaceuticals	Spouse: One off Advisory Board meeting attendance in 2016 (fee paid)	None	n/a	Yes
	Lamellar Biomedical Ltd	Spouse is medical advisor to the Board			Yes
	Elsevier	Spouse is editor on three medical text books (co-editor on 1)			Yes

	Personal Interests		Non Personal Interests		
MEMBER	**Name Of Company**	**Nature Of Interest**	**Name Of Company**	**Nature Of Interest**	**Whether Current**
Prof Ian Wong	Therakind in London	Founder of the company with shares and salary.	Pfizer	Research Grant	Yes / Yes
	Healthcare Innovation Technology Service In London	Director of the company, receives fee occasionally.			No
	Jacobson Pharmaceutical in Hong Kong	Consultancy with fee.			Yes

Annex 5 – ISAC Appeal process

If the MHRA accepts the advice of ISAC to turn down an application for data, the unsuccessful applicant will be sent a letter setting out the reasons why. The applicant will be told that he/she has 28 days from the date of the letter to make representations, and that these should be made in writing to the Yellow Card/CPRD ISAC Secretary. The applicant will be informed that once this 28 day period has expired, he/she will have to make a fresh application. If an appeal is to be carried out, the Licensing Authority will appoint a person or persons to undertake a review of the documentation. A letter will be sent to the applicant with the outcome of the appeal. The decision of the Licensing Authority will be final.