

## Section A: Official Development Assistance (ODA) and GCRF strategy

### The strategy

1. Summarise the key aspects of your three year **strategy for development related and GCRF research activity**, including:
  - a. Your institution's strategy and priority objectives for all development related research activity funded through all sources for three years from 2018-19.
  - b. A summary of the key aspects of your three year strategic plan for QR GCRF, in light of the criteria and objectives for the GCRF outlined in the guidance.
  - c. How activity funded through QR GCRF fits into your broader strategy and priorities for all development related research activity.
  - d. How activity funded through QR GCRF relates to the UK strategy for the GCRF.<sup>1</sup>
  - e. How your development-related and GCRF strategies relate to your wider institutional strategy for using QR.
  - f. Likely key barriers and enablers to implementing your strategy.
  - g. The key activities by which you will realise your objectives, such as capacity and capability building; mono-disciplinary, interdisciplinary and collaborative research; generating impact from research; meeting the full economic cost of GCRF activity funded through other sources; rapid response to emergencies with an urgent research need; and pump priming.
  - h. The main developing countries, included in the Development Assistance Committee (DAC) list, which you intend to collaborate with.

Maximum 3,000 words

Some 70% of global cancer deaths occur in low- and middle-income countries (LMICs). The incidence of cancer in LMICs is projected to rise substantially and the annual numbers of deaths to increase from 5.3m in 2012 to 9.1m in 2030. The mission of The Institute of Cancer Research (ICR) is to make the discoveries that defeat cancer. In partnership with The Royal Marsden NHS Trust (RM), ICR's Research Strategy "Making the discoveries: Our strategy to defeat cancer"

<http://d1ijoxngr27nfi.cloudfront.net/default-document-library/icr-royal-marsden-research-strategy-2016-2021.pdf?sfvrsn=0.1851675590200642> focusses on taking discoveries rapidly from the laboratory to the clinic, improving outcomes for patients. The Research Strategy is based on four pillars, "Unravelling cancer's complexity", "Innovative approaches", "Smarter, kinder treatments" and "Making it count". As one of the world's

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<sup>1</sup> UK Strategy for the Global Challenges Research Fund,  
<http://www.rcuk.ac.uk/funding/gcrf/challenges/>

top centres for cancer research and treatment, ICR/RM has already delivered huge benefits for cancer patients in the UK and beyond. For example, the prostate cancer drug abiraterone was discovered at the ICR and is now prolonging the survival of hundreds of thousands of men worldwide. ICR uses QR funding to support staff and infrastructure that, in combination with competitive grant and industrial funding, underpins this discovery research. ICR's GCRF strategy aims to use this research power to deliver better outcomes for cancer patients in LMICs, in support of UN Sustainable Development Goal 3 (Good Health). This GCRF strategy is relevant to all four pillars of the ICR/RM Research Strategy but especially to "Making it count", which aims to deliver better outcomes and improved quality of life for patients by establishing innovative treatments, diagnostics and strategies for prevention as part of routine healthcare.

Owing to differences in environment, diet and genetics, cancer incidence differs markedly between different countries. Therefore, the cancer research that is most relevant to UK patients may be less relevant to those in certain LMICs. We shall focus on a number of key cancer risks in LMICs and propose a GCRF strategy (in partnership with LMIC researchers and other stakeholders) to investigate these cancers and deliver better outcomes for patients in those countries. We have at present limited funds for work related to international development other than the QR GCRF funds, which we have so far used to build on existing international collaborations and to pump-prime projects that we expect to lead to substantial peer-reviewed funding in the future.

Our strategy will be directed to three main research areas:

1. The application of molecular and genetic profiling to the 'stratification' of cancer patients in LMICs and 'personalisation' of their treatments, thus directing scarce resources to the interventions most likely to give the best health outcomes;
2. The development of new targetted interventions for cancers of particular unmet need in LMICs; and
3. The development of care programmes for cancer survivors tailored to the needs of LMICs.

Example of projects planned for 2018-19 onwards are given in more detail below:

1a. *Clinical and molecular landscapes of triple-negative breast cancer in India and application to improved treatment decisions.* ICR is highly expert in breast cancer (BC) research, having for example discovered one of the BRCA genes that are the major genetic determinants of susceptibility to this disease. BC is the leading cause of cancer-related mortality in females in many Asia-Pacific LMICs including **India**. Furthermore, in the larger metropolitan cities of LMICs, lifestyle changes and poor screening and treatment strategies have contributed to increased BC incidence and mortality. India now has the highest BC mortality/incidence ratio in the world. Unfortunately, the majority of patients in Asia-Pacific countries cannot afford the expensive management that is carried out in developed countries, therefore it is vital that the resources available be used to target the right treatment to the patients most likely to benefit from it. Triple-negative BC (TNBC), so called because the tumours lack three key cell surface receptor proteins, is

an aggressive and recurrent BC sub-type with poor prognosis. In India, TNBCs comprise a substantially higher proportion of BCs than in developed countries (approximately 30% vs. 15-20%). The incidence of TNBC is higher in pre-menopausal and young women in India, similar to that seen in women of African ancestry. The aetiology and molecular basis of this higher incidence of TNBC in young women have remained elusive. In collaboration with St. John's Research Institute in Bangalore, we have been studying the molecular landscapes of TNBCs in pre- and post-menopausal women in three Bangalore hospitals and comparing these data with our experience in the UK. We hypothesise that: (i) there are molecular, histopathological, and prognostic differences in pre- and post-menopausal women with TNBC in India, and (ii) the molecular landscapes of TNBCs in women in India and the UK differ. Preliminary data obtained using Newton Fund support are consistent with these hypotheses. The overall aim is to explain the different disease patterns seen in India and Western countries using modern and clinically applicable profiling strategies to identify differences that can be exploited for personalised medicine approaches. This study will also prime the design and implementation of large-scale genomics studies in India, building research capacity there.

*1b. Genetic predisposition to prostate cancer in the PRACTICAL consortium: increasing participation in developing countries.* Prostate cancer (PC) research is another major strength at ICR. There is evidence for genetic predisposition to PC and this is composed of common and rare variants. The common variants have been studied mainly in European Caucasian populations, and over 75% of the variants known to date have been found by ICR. We have created and lead an international consortium, PRACTICAL, which consists of 126 groups with access to 200,000 samples, to identify further genetic variants and use them to stratify populations into groups of differing PC risk. Assessing the risk of aggressive as opposed to indolent PC is vital because all the interventions we have carry risks of serious side-effects so must be reserved for those patients likely to develop life-threatening disease. Participation of LMICs in PRACTICAL has so far been limited but needs to be increased, because the structure of genetic variation differs geographically – i.e. the current research does not meet the needs of LMICs. Extension of PRACTICAL to LMICs also offers an opportunity to build capacity in genetic medicine in the target countries. Using GCRF QR funds we have therefore initiated PRACTICAL studies in **Brazil** and **Lebanon**, and research capacity building in **Nepal** with a view to its inclusion in the future. The prostate is the second most common site of cancer in males in Lebanon and its incidence is increasing. The long-term aim is to be able to tailor PC screening and targeted intervention to those in LMICs most likely to benefit.

*2. Characterisation of epidermal growth factor receptor inhibitor resistance and new therapies for lung cancer in Asia.* The lung is the most common site of lethal cancer worldwide. The prevalence of mutations in Epidermal Growth Factor Receptor (EGFR) in lung cancer disproportionately affects patients from developing countries, including China, Vietnam, the Philippines and Thailand. EGRF is a protein on the surface of human cells that can receive signals for the cells to grow and proliferate: when its gene is mutated, this signalling can become unregulated, and cancer can result. A study in 7 Asian countries showed that EGFR mutation frequency in the Kinh (Vietnamese),

Chinese, Filipino and Thai ethnicities ranged from 50–64% of all lung adenocarcinomas, compared with 20% in Caucasian populations. In response to these EGFR mutations, EGRF inhibitor therapy was developed, but now ~10–15% of lung cancer patients exhibit resistance to these drugs and palliative care is often the sole remaining option. Most of these patients have so-called 'Exon 20 insertions' in their tumours and an inferior prognosis. In this project, we shall address this unmet clinical need by characterising the molecular alterations associated with Exon 20 insertion mutant tumours from **China** (where there are an estimated 30,000 lung cancer patients with Exon 20 insertions) compared with other sensitising EGFR mutations. Defining these alterations in cellular signalling pathways will facilitate the identification of new therapeutic targets for this difficult-to-treat subgroup of patients in LMICs.

*3. Unmet needs in women following primary BC treatment in two African countries: the feasibility of implementing holistic needs assessments, care plans and treatment summaries.* A large proportion of women who have had BC face unmet needs at the end of primary treatment, which can be physical, psychological, social, spiritual or financial. The UK National Cancer Survivorship Initiative (NCSI) has therefore designed the Recovery Package, a set of tools to improve holistic assessment and management of people living with or beyond cancer, and improved communication with primary care. This consists of a Holistic Needs Assessment (HNA) and resulting care plan, a treatment summary, access to a health and wellbeing event and a Cancer Care Review in Primary Care. Cancer survivorship is however a new concept in LMICs. It is important to develop this part of the cancer care continuum to improve cancer outcomes and quality of life in those living with and beyond cancer, and to generate survivors to advocate for improvements in cancer care. We are therefore using GCRF QR funds to study those coming through two centres in **Ghana** and **Tanzania** to identify unmet needs using the NCSI HNA and compare this with retrospective data already published from our UK centre. The average age at diagnosis of BC patients in Africa is significantly lower than in the UK but the mortality/incidence ratio significantly higher, so this issue is especially important in African LMICs. The feasibility of generating a care plan from the HNA and of producing a treatment summary to be shared with the patient and future health care professionals involved with the women's care is being assessed and services available to women living beyond BC in the two African countries scoped. Recognising the different needs and capacities of LMICs, particular emphasis will be placed upon using novel ways to support patients, such as peer-to-peer support and the engagement of civil society partners.

Key activities from the projects described above will fall under the headings of capacity and capability building; mono-disciplinary, interdisciplinary and collaborative research (not easily funded by other GCRF delivery partners or other grant-funding sources); generating impact from research, and pump-priming small projects.

The capacity/capability building, research and impact generation from the projects described above meet the UK GCRF strategy in the following ways:

- (i) by building capability of and capacity for research on LMIC problems in both the UK and the chosen partner countries;
- (ii) by addressing, through excellent research, some key and so far intractable health challenges of LMICs as identified by those LMICs - namely certain debilitating and lethal cancers;
- (iii) by working towards innovative solutions for these challenges - for example cheap, accessible and sustainable testing systems to allow cancer patient stratification and better targetting of interventions;
- (iv) by facilitating the participation of some of our experts who would not have previously been significantly involved in research relevant to the challenges of LMICs;
- (v) by creating the potential for impact in LMICs spread across different income levels and three continents; and
- (vi) by developing equitable, sustainable partnerships with LMIC collaborators and stakeholders, for example a long-term capability-building relationship with Nepali hospitals.

The main, likely barriers to our activities are listed below:

- (i) Limited research infrastructure in some of the partner LMICs, hampering their ability to collaborate effectively;
- (ii) Physical distance between the ICR and the partners, risking poor coordination;
- (iii) Different practices in accounting, human resources, research ethics, etc. in the LMICs, making it difficult to ensure accountability of expenditure by the partners.

The key enablers that will allow us to overcome these pitfalls include:

- (i) Calibrating research expectations to the level of sophistication of the partner. For example, our Lebanese partner (the American University of Beirut) will be capable of carrying out the gene sequence analysis required on site, whereas Nepal lacks such expertise and we shall build up the required capability via a programme of visiting fellowships for Nepalese physicians/scientists at ICR/RM.
- (ii) It will be necessary to ensure good contacts with the collaborators and stakeholders in the partner LMICs to ensure relevance of the research and optimal delivery of the benefits. In recognition however of the significant and increasing contribution of air travel to global climate change, and the fact that LMICs are most vulnerable to the latter's adverse effects, intercontinental travel will be kept to a minimum. Fortunately, remote face-to-face communication has improved greatly in recent years and will be used alongside conventional telephone and e-mail for collaborative meetings. Where travel is essential, trips will be combined (e.g. multiple research and teaching visits, conferences, etc.) as far as possible.
- (iii) The use of tailored 'due diligence' questionnaires covering the key points of assurance. Small institutes receiving low amounts of funding can be held to less exacting standards than larger ones receiving more funds, while still maintaining adequate oversight. In the case of Nepal, we shall disburse the fellowship funding via the Britain-Nepal Medical Trust (BNMT) that already has the appropriate relationships and safeguards.

2. Provide details of the main intended **outcomes and impacts** of your strategy.

Maximum 500 words

In most LMIC settings, cancer interventions are applied empirically without *a priori* determination of the optimal treatment regime for the particular patient and tumour. This results in sub-optimal use of scarce health-care resources and inferior outcomes to those that might be achieved in the UK. A key, anticipated outcome of our research is the development of patient stratification methods based on new knowledge of the genetic predispositions and molecular features of patients and their tumours as well as the clinical pictures of the patients. Deployment of inexpensive tests and increased understanding should allow treatment regimes to be tailored to patients with resulting gains in quality of life and life expectancy and consequent social and economic benefits.

In some cases, for example EGFR-mutant lung cancers in Asia-Pacific countries, treatment options for cancers common in LMICs are unsatisfactory and the anticipated outcomes of our research are new small-molecule or biologic (e.g. antibody-based) treatments targetted at the tumour cells carrying those properties. Provided these agents can be made inexpensively, this has the potential to enhance the therapeutic armoury available to LMIC health-care professionals in the management of lung cancer.

Survival of an episode of cancer does not necessarily signify an end to the health-care needs of the patient. Our research on BC survivorship for example could result in more holistic management of recovering cancer patients, resulting in improved health and wellbeing outcomes and increased return to work and caring duties. Empowering women who have survived BC is relevant to UN Sustainable Development Goal 5 (Gender equality) as well as Goal 3. It is hoped that this methodology can be extended to other LMICs and cancer types.

A major outcome of our strategy in general and all of the projects individually will be the development of our capacity to carry out research relevant to cancer in LMICs. These capacity-building outcomes will include:

- (i) increased number and depth of collaborations between ICR and LMIC researchers,
- (ii) increased engagement of ICR researchers with various health-care stakeholders in LMICs such as government departments, health-care professionals, patient groups and the local biotech/pharma industry, and
- (iii) increased awareness among ICR researchers of the cancer challenges most relevant to LMICs and potential ways of bringing our research power to bear on getting better outcomes for cancer patients in LMICs.

The research will also contribute to research training and capacity building in the partner LMICs and promote the development of targeted screening and precision medicine, possibly boosting local biotech industries.

The overall impact of our GCRF-related research will therefore be measurable scientific, educational, health-care and resultant socio-economic gains in a range of LMICs. In addition, it will boost the ICR's capacity to do the research that will "Make it count" for patients in LIMCs.

### **Management of GCRF**

3. How will your HEI **monitor** and **evaluate** its progress and compliance in ODA and GCRF activity, including assessing geographical distribution of activity, outputs, outcomes and economic and social impacts?

Please describe the policies, procedures and approach you have in place to measure progress, evaluate outcomes, identify lessons learned, and ensure ODA compliance.

Maximum 1,500 words

The strategic direction of the ICR's GCRF research will be managed by the **Research Leadership Board** (RLB) of the ICR, which is a committee that oversees research strategy in general. The RLB is composed of the Chief Executive Officer (CEO, acting as both Vice-Chancellor and Director of Research), senior academics including all (8) Heads of Division, and certain senior research administrators. The RLB has approved this strategy document and will receive annual reports on GCRF progress compiled by the Research Support Unit based on submissions from the lead researchers. Reports will include details of outcomes and impact so far including comment from LMIC partners and stakeholders. Feedback from this oversight will be transmitted both formally and informally to the researchers and also used in the preparation of the annual report to Research England.

Decisions on allocation of QR GCRF funding for each academic year will be taken by a panel of 5 senior academics (**GCRF panel**), based on progress reports and plans from the research leads. These decisions will be ratified by the RLB.

In order to obtain independent and unbiased oversight, monitoring and evaluation will also be performed by a panel of two external experts in research related to the challenges of LMICs (**Advisory Board**). Provisional agreement to serve on the board has so far been obtained from Shirley Hodgson, Emeritus Professor of Genetics, St. George's Hospital Medical School and Hon. Consultant, Leicester Genetics Service.

Annual reports from the researchers will be assessed by the Advisory Board and that Board's report submitted to the RLB to contribute to the annual evaluation and setting of priorities for the coming year. The Advisory Board members will also act as a 'sounding board' for the researchers with regard to the development of the individual projects, especially with regard to ensuring GCRF compliance and maximising impact.

One of the lead researchers (Dr. S. Stanway) runs an annual meeting on 'Cancer Control in LMICs' and this will offer an opportunity for wider evaluation of the progress of the ICR's GCRF programme. It is envisaged that QR GCRF funding may contribute to sustaining this meeting depending on the funds allocated.

The ICR's GCRF research will be subject to the institute's usual research governance policies such as those on Clinical Research, Good Research Practice and Research Integrity. Clinical and vertebrate animal research will also be subject to oversight by the appropriate ethics committees.

The GCRF component of QR funding will be accounted for separately and subject to the same stringent financial controls as grant funding. Partners in LMICs will be required to submit detailed and well-justified invoices that match the agreed budgets. GCRF QR spending will be overseen by the Director of Finance.

## **Section B: Use of QR GCRF 2018-19 allocation and future QR GCRF priorities**

4. Please complete the table in Annex A2 detailing the expected spending and activities for QR GCRF in the academic year 2018-19. Note that the total QR GCRF spending must equal the indicative allocation (available in Annex C), and all activities must be ODA-compliant for strategies to be assessed as ODA-compliant overall.

5. Please add here any explanatory notes on how you have completed the table in Annex A2 that will help inform assessment of ODA compliance.

Maximum 200 words

Table A gives details of the four projects described in detail in section 1 with likely budgets, DAC countries involved, benefits to those countries and outputs/impacts. These projects and budgets are representative of our strategy but the precise deployment of GCRF funds will be subject to final approval as described in section 3 above. Committed additional funding for these projects is also indicated: this is expected to be added to during 2018-19. In addition to this, existing project funding underpins the research of our GCRF Strategy: this is mentioned in the table but does not contribute to the total because it covers non-GCRF activities as well.

6. How would your **priorities and activities** for 2018-19 QR GCRF change if the funding level differs from that outlined in indicative allocations? Please include detail of how priorities will change with increases and decreases to QR GCRF funding, and details of how each priority meets ODA criteria.

Maximum 500 words



In the ICR's case the level of spending is modest and the number of projects limited to 4 or thereabouts. If necessary, priority will be given to projects that (i) are closest to delivery of meaningful outcomes for LMICs and therefore best meet GCRF/ODA criteria and (ii) best demonstrate research excellence in the context of the ICR/RM Research Strategy. This will be decided as described in section 3. Further budget flexibility should be available through the programme of capability-building fellowships with Nepali physicians/scientists, in that there is an adequate supply of candidates so the number of fellowships can be adjusted up or down in response to changes in QR GCRF allocation. Use of QR GCRF funds for increasing engagement of ICR scientists with international development challenges and/or networking meetings to develop and sustain partnerships (e.g. Cancer Control in LMICs meeting) will be pursued if funds allow but as a lower priority than the research outlined above.

7. Based on indicative funding allocations, what are your **priorities** for QR GCRF activity in 2019-20? Please include detail of how priorities will change with increases and decreases to QR GCRF funding, and details of how each priority meets ODA criteria.

Maximum 1,000 words

Priorities for 2019-20 will be decided on a similar basis as for 2018-19, also taking into account the assessment of progress and plans by the Advisory Board and RLB. The GCRF Panel will decide the allocations for the ongoing and any new projects, subject to confirmation by the RLB. It is anticipated that 2016-17 and 2017-18 QR GCRF funds will act as pump-priming and in some cases additional (GCRF or non-GCRF) funding will be obtained for follow-on activities on these projects, freeing QR GCRF funds for further project pump-priming. It is hoped that this will allow at least one new project to begin in 2019-20 and one in 2020-21.

8. Based on indicative funding allocations, what are your **priorities** for QR GCRF activity in 2020-21? Please include detail of how priorities will change with increases and decreases to QR GCRF funding, and details of how each priority meets ODA criteria.

Maximum 1,000 words

Priorities for 2020-21 will be decided on a similar basis as for 2019-20: see above, section 7 for details.