



Department
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Department of Health Response to Raj Long's Independent Report

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Department of Health Response to Raj Long's Independent Report

Prepared by: Members of the Integrated Development Advisory Group

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Background

The Global Action Against Dementia (GAAD) team within the UK Department of Health was set up as part of the UK's leadership in international dementia policy, following the announcement of dementia as a priority of the UK's G8 Presidency. In June 2014 the Department of Health created the Integrated Development initiative as part of GAAD, guided by Raj Long, Senior Regulatory Officer at the Bill and Melinda Gates Foundation, as an external expert. This work assessed what collaborative efforts could be undertaken in the regulatory space to create a more conducive environment for dementia drug development.

Working with the Department of Health and helping to lead the Integrated Development work has given Raj a unique perspective into the dementia drug development pathway. In March 2015 she condensed her learning to date into a series of recommendations, presented at the First World Health Organisation Ministerial Conference on Global Action Against Dementia. These recommendations then formed the basis for an independent report titled [Finding the path for a cure for Dementia: An independent report into an integrated approach to dementia drug development](#), published in July 2015. Alongside the recommendations presented at the WHO Ministerial Conference Raj's report also outlines four key 'actions for change'; directions she feels that the international community need to move in in order to improve the dementia drug pathway. These actions build off the Integrated Development work of the UK Department of Health, and could be the next steps in global effort.

Countries and organisations across the world have shown leadership, commitment and collaboration in all areas of dementia policy. However more needs to be done to make this sustainable and the role for the UK now is to build on the successes of the G8 Presidency to work collaboratively to develop a continuity model. We are keen that Raj Long's recommendations and actions are part of this continued work.

This includes the continued role of patients and those affected by dementia, a key component of the GAAD and UK dementia policies. Engagement with organisations such as Alzheimer's Society as part of the Prime Minister's Challenge on Dementia 2020 has helped to provide a strong patient perspective through their existing networks of those affected by dementia.

In order to fully understand the role that Raj Long's recommendations may have in future dementia policy we brought together a number of officials and organisations from across the spectrum of the work to date to form an 'Advisory Group'. This group met twice, once in August 2015 and once in September 2015, and we also engaged with many members on a one to one basis throughout the intervening period. Their thoughts, guidance, knowledge and expertise have formed the basis of this Governmental response to Raj Long's report.

In doing so it has become clear that no singular blueprint towards an integrated approach currently exists, and that though many organisations and initiatives are attempting to tackle the issues identified by Raj, connections are often missed. Raj's report, and our UK governmental response, has provided an opportunity to draw attention to some of these opportunities for alignment.

This response is not a formal plan for implementation, but will form part of a larger strategy of continuation and facilitation in the UK's role in global dementia work.

1. Action 1: Use the learnings from the regulators to agree principles for facilitating consistent global development pathways

Context

- 1.1. The first of four Actions for Change outlined by Raj Long relates to the regulatory work which makes up the Integrated Development initiative. Across two meetings, and regular calls, regulators from 10 jurisdictions, including the UK Medicines and Healthcare Products Regulatory Agency (MHRA), have identified and progressed five workstreams, each led by an individual regulator.

Workstream	Regulator
Clinical Trial Efficiencies	Swiss Medic
Risk Benefit Balance	Danish Health and Medicines Authority
Multilateral Cooperation	European Medicines Agency
Modelling and Extrapolation	Italian Medicines Agency
Composite End Points	Federal Institute of Drugs and Medical Devices

Discussion

- 1.2. We have engaged with the regulators who are keen to continue this work. They appreciate the role that UK Department of Health has played in facilitating and initiating the workstreams, as well as the unique perspective the Department brings as a leader in global dementia policy and a member of the G7. They however questioned the sustainability of remaining linked to a single country, and were keen for their work to be aligned with global initiatives. It was felt that objectives could be best achieved through a combination of utilising existing agency channels of collaboration and annual workshops focusing on key issues, and aligning with the research community.
- 1.3. Through conversations with Raj Long and the regulators it is clear that sustainability of the programme is the main concern.

- 1.4. The advisory group considered different ways in which the regulators might be encouraged and supported to continue their activity. They identified synergies with other existing pieces of work or initiatives, but there was a consensus that none of these were focused on the same challenges that the Integrated Development programme has identified, or on dementia specifically. Examples suggested included the International Pharmaceutical Regulatory Forum, and the International Coalition of Medicines Regulatory Agencies.
- 1.5. The suggestion was raised by the Organisation for Economic Co-operation and Development (OECD) and the World Health Organisation (WHO) that the make-up of the regulators should be expanded to also include medicines regulators from lower-middle income countries (LMICs) which would help to ensure the sustainability of the integrated approach globally.
- 1.6. OECD have offered to develop a proposal for facilitating the regulator work going forward, and this is an idea worth exploration, given what we have heard from regulators about the importance of global reach.
- 1.7. We heard suggestions that the outputs of the regulator led workstreams developed as part of the Integrated Development initiative should be applied more broadly to general regulatory issues. In particular, that there could be alignment with work that the Office of Life Sciences' are progressing through the Accelerated Access Review. Alzheimer's Research UK are currently working on a reaction to the Accelerated Access Review, highlighting dementia as a potential 'case study'. ARUK also have a broader interest in work with regulators through their work on medical access. The European Commission also highlighted that they were open to considering ways in which the ideas and outputs from the regulator's work could be brought to the Commission Expert Group on Safe and Timely Access to Medicines for Patients (STAMP).
- 1.8. There was consensus around the importance of the regulator work continuing, and an enthusiasm to ensure that this was appropriately supported in the future, recognising that the UK Department of Health may not be able to continue in the role it has played. There was a suggestion that Raj's leadership of this work is important, and that it would be helpful if her relationship with the regulators could be maintained, but also that the regulator's work could benefit from closer alignment with broader innovation and development.
- 1.9. To this end ARUK have developed a second proposal, suggesting they facilitate the regulator work as part of a broader strategy of global dementia work.

Next Steps

- 1.10. In response to Raj Long's first Action for Change:
 - MHRA will continue to be part of the regulator work.

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- The Department of Health will support ARUK in the development of their proposal, and explore how this could align with a wider continuity strategy.
- This will include engaging with OECD around the role they could play in facilitating the existing work.
- The UK Government welcomes any other steps that the EC, WHO, OECD and others take to support the extension to a wider breadth of regulatory jurisdictions.
- Through the Accelerated Access Review, the Office of Life Sciences will explore the potential for applying learning from the outputs of the regulators work, for example utilising existing routes of conversation with ARUK.

2. Action 2: Understand and agree on the gaps in the basic science (both amyloid and non-amyloid approaches) and take action to address these.

Context

- 2.1. Raj's second Action for Change can be seen as a response to the limitations of the current scientific knowledge around dementia. It builds on the idea that the challenges in dementia drug development cannot be solved through regulatory measures alone. Raj suggests that the global research community should come together in the same way as regulators have for the Integrated Development initiative, in order to try and identify the key gaps in the scientific understanding of the condition, and to take action to address these, for example through a 'single blueprint' or a set of 'universal guidelines'.

Discussion

- 2.2. The UK Department of Health is committed to research prioritisation and sharing. [The Prime Minister's Challenge on Dementia to 2020](#) outlines our objective to contribute to an international framework for dementia research, enabling closer collaboration and cooperation between researchers on the use of research resources, alongside expansion of the global dementia research agenda and filling research gaps identified.
- 2.3. The second Integrated Development meeting of regulators facilitated by the Department of Health, included a half-day discussion led by academics on the amyloid and non-amyloid approaches to dementia research. It is felt that greater understanding by the regulators of the range of basic science approaches to developing new treatments should be encouraged in the future.
- 2.4. The advisory group considered whether the Integrated Development model of a 'coalition of minds' was transferable to the research community. It was broadly felt that there are existing channels working in this area, and that Raj's ideas may be realised if incorporated into these, as a common strategic research agenda. For example it was noted that The EU Joint Programme – Neurodegenerative Disease Research (JPND) and the US National Institute on Ageing already share common objectives and will take initial steps to work in closer alignment. Moreover there is scope for JPND to expand globally. These are conversations for the relevant national research agencies and related bodies to progress.
- 2.5. The UK has established the Dementias Platform UK to underpin the coordination and alignment of dementia research at the national level. This academic-industry programme encompasses the establishment of big data resources, preclinical technology platforms, and clinical phenotyping and intervention. In addition, UK scientists have been closely involved in

international programmes, such as JPND, Centres of Excellence in Neurodegeneration (COEN) and the Innovative Medicines Initiative (IMI). The commitment to continue to be a part of this work is part of the Dementia Challenge to 2020.

- 2.6. Work has also already been instigated by the WHO and the OECD, who carried out research prioritisation and gap analysis exercises in 2014, comparing activity across the G7 countries. WHO will continue to support the global sharing of scientific evidence through the Global Dementia Observatory and OECD is facilitating a three year comparative study of dementia indicators across member states.
- 2.7. In relation to the concept of 'universal' guidelines, and the scope of this as a feasible output, there was agreement that the idea was helpful, and that this should be explored by the scientific community, alongside the work being taken forward by regulators as part of Action 1.
- 2.8. There are however difficulties in this approach as dementia is a series of complex and potentially overlapping diseases. It was suggested that further discussion around the use of appropriate end points could be a logical starting point.
- 2.9. The US Alzheimer's Association and the Foundation Plan Alzheimer's are working together to set up a research think tank in early 2016, as part of a programme called Global Alzheimer's Leadership Series (GoALS). The think tank aims to identify gaps in the research science, aligning with Raj's report.
- 2.10. Focused collaboration along existing lines was seen as the best way of getting close to a 'blueprint'. This aligns with the on-going work on the Dementia Challenge to 2020 commitment to an international framework.

Next Steps

- 2.11. In response to Raj Long's second Action for Change:
 - The Department of Health Dementia Policy team and R&D will continue to engage with the dementia research community, ensuring that opportunities for alignment internationally are incorporated into the delivery of The Prime Minister's Dementia Challenge to 2020.
 - Through our support for the WHO Observatory on Dementia the Department of Health supports the on-going collection, sharing and analysis of dementia research on a global level.
 - We welcome the fact that Raj's suggestions will be taken forward as part of existing work, such as that being led by JPND, Alzheimer's Association and Foundation Plan Alzheimer's.

3. Action 3: Support the assessment of the necessary clinical evidence required in dementia development programmes for regulatory assessment.

Context

- 3.1. Raj's third Action for Change calls for international alignment and alliance around the drug development pathway. She suggests that there should be better sharing of data in cases where a drug has failed during development and that pathways should be more receptive to alternative models, for example that development pathways should support combination therapies and not just monotherapy.

Discussion

- 3.2. This Action was discussed with interest by the advisory group. Stakeholders working globally or multinationally, such as the WHO, could identify examples of industry, academics and regulators working in a more open way, to share experiences of success and failure, where there was a culture of trust. As an example The Council for International Organizations of Medical Sciences (CIOMS) is an international, non-governmental, non-profit organization established jointly by WHO and UNESCO in 1949. Through its membership, CIOMS is representative of a substantial proportion of the biomedical scientific community. In 2013, the membership of CIOMS included 49 international, national and associate member organizations, representing many of the biomedical disciplines, national academies of sciences and medical research councils. This was countered though with the recognition that for many in the industry, incentivisation and competition are ongoing issues that could diminish the success of these ideals. There are a number of key challenges and opportunities and these will need to be explored further before plan to implement this recommendation can be made.
- 3.3. It was also noted that lack of information sharing around failures is not purely down to an industry policy against data sharing, but also reflective of the lack of procedures to store and access such data.
- 3.4. New university based dementia institutes being set up by ARUK will include data sharing as a key objective. These will build on the principles explored through the Dementia Consortium; an initiative set up by ARUK and MRC Technology, and use an approach to dementia research and clinical development which closely aligns with many of Raj's principles around drug development.
- 3.5. Alongside this MRC Technology are also leading on an initiative called NeuroMap which provides research charities with opportunities to fund stalled

assets. The assets are identified by industry, and are progressed under the condition that data on failure is shared. Both Alzheimer's Society and ARUK are already involved in NeuroMap, and this will feed into future drug development initiatives, including actions taken on Raj's recommendations. There is scope to explore alignment with the Dementia Discovery Fund as this work progresses.

- 3.6. Other initiatives in this area include the Global Alzheimer's Platform launched in 2013 by the Global CEO initiative (CEOi) on Alzheimer's Disease and the New York Academy of Sciences (NYAS).
- 3.7. UK academics are leading in the European Prevention of Alzheimer's Dementia Consortium (EPAD) which is working to develop a better infrastructure for clinical trials, including publically available cohorts of trial data developed from a register of 24,000 participants.
- 3.8. The DPUK has been established as an open-science resource, with data emerging from the programme to be released to the community to inform patient selection (stratification) for future clinical trials. It aims to build a major trials readiness cohort that will enable the early testing of new or repurposed interventions.
- 3.9. As with the previous Action, the concept that Raj has outlined is likely to apply to drug development more widely and the OLS Accelerated Access Review will be following the progress of the work in dementia as a demonstrator for wider application.
- 3.10. The advisory group reassured us that work is progressing in this area, and welcomed Raj's unique perspective.

Next Steps

- 3.11. In response to Raj Long's third Action for Change:
 - Acknowledging the developing work in this area the UK Department of Health will not explore new initiatives at this time.
 - We encourage existing initiatives to explore opportunities for future alignment, such as the potential alignment between NeuroMAP and the Dementia Discovery Fund, and the existing collaboration between DPUK and the EPAD.
 - Through the Prime Minister's Challenge on Dementia to 2020 we will work with British academics as they continue to play a role in these initiatives.
 - We are supportive of the work which ARUK, Alzheimer's Society, MRC Technology and other partners are already progressing, and which will be aligned with efforts globally to improve drug development.

4. Action 4: International Dementia Advisory Platform (IDAP).

Context

- 4.1. The fourth Action for Change suggested by Raj brings together the ideas contained within the first three.
- 4.2. She suggests the creation of an international platform which would bring together leading experts from all stages of dementia drug development to guide candidates through the process, offering the best possible advice at each stage.
- 4.3. The platform would provide a streamlining of academic and expert advice utilised throughout the regulatory process and incorporating the outputs of Action 1, although not including regulators within it. .

Discussion

- 4.4. At this time the idea is very much at concept stage, and work would be needed to explore the detail and logistics.
- 4.5. Discussions with UK academics leading on EPAD have shown that there is a desire to build research initiatives into a global platform.
- 4.6. From the start of our discussions ARUK have been very interested in the potential model offered by the IDAP, and saw interactions with their existing work. They have offered to scope out feasibility and develop a model for the IDAP. Their early thoughts include that it could link to the WDC, and that Raj's involvement in both could be a link to global dementia policy.
- 4.7. They also intend to use the scoping stage of this work to explore Raj's recommendations in more detail, building on the discussions of the Advisory Group, and leadership of the Department of Health to date.
- 4.8. ARUK work closely with industry, through a number of difference initiatives, for example the Dementia Consortium, and this would provide a useful framework if ARUK were to roll out the IDAP. The advisory group questioned whether large pharmaceutical companies would utilise a new source of expert advice, given their familiarity with their own advisory networks, and ARUK have proposed to carry out a scoping and feasibility exercise on this issue alongside developing the concept.
- 4.9. The UK Government led Dementia Discovery Fund was seen to have a connection to the concept of the IDAP as a potential 'customer', however it was not seen that the two platforms would be linked.
- 4.10. Some members of the advisory group suggested it might be more effective to focus on one specific disease rather than the full breadth of dementia, at least in the initial stages of introducing an IDAP.
- 4.11. The IDAP could provide a mechanism to bring together all four of the Actions for Change that Raj has suggested. The ideas put forward by the regulators

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(Action 1), improved basic science (Action 2) and more streamlined regulatory assessment (Action 3) could all provide the technical insight and mechanisms that will enable an IDAP to be a success. ARUK will aim to incorporate this thinking into their scoping and development work.

- 4.12. Through this Advisory Group process the UK Department of Health has been able to start conversations around integrated current efforts, which will be taken forward as part of next steps in this area.

Next Steps

- 4.13. In response to Raj Long's fourth Action for Change:

- The UK Government welcome ARUK's scoping of the IDAP, and see them as an appropriate organisation to take forward this work

Conclusion

The UK Government is grateful to Raj Long for her time and expertise. Without her specialist skills and knowledge the Integrated Development work would not have progressed as far as it has. It is through her support that we have been able to convene regulators from ten jurisdictions, and enable them to give their own time and resources voluntarily to the initiative. This is not work which could have been done with the authority of the UK Department of Health alone.

It is clear that this work should continue, and that the outputs of this ground-breaking initiative could go beyond the scope of tackling dementia alone. The Office for Life Sciences will make use of the learning within the Accelerated Access Review to consider this further.

The independent report which Raj has published goes further than just the Department of Health's facilitation of Integrated Development. It calls for actions to be taken by a range of stakeholders. In order for the regulator led work to be sustainable it needs to align with these global efforts, maintaining a direct link to global institutions such as the World Dementia Council (WDC), OECD and WHO.

We are pleased to have been able to take this opportunity to explore Raj's recommendations with stakeholders and organisations in these areas, and to open up opportunities for future alignment and collaboration.

Given ARUK's willingness to take forward scoping around Raj's recommended actions, in particular the IDAP, we believe the next steps in coordination of this work is best placed with ARUK. Through their existing connections to data sharing innovation, research networks and funding mechanisms, including the Dementia Discovery Fund, they are in a position to align this work as part of a wider programme.

Alongside this our Dementia Policy team will continue to work with Alzheimer's Society to ensure that the patient perspective is considered as part of dementia research and drug development. We look forward to increased efforts in this space.

To date we have worked closely with G7 countries, and welcome the continuation of a link between the work of regulators and the WDC, through Raj, as part of the wider sustainable model for continued global action on dementia.

We will therefore facilitate the continuation of Integrated Development exploring options with ARUK, aligning with their exploration of Raj's IDAP model, and OECD.

As part of our commitment to the Prime Ministers Challenge on Dementia to 2020 we will ensure that we maintain our leading role in research against dementia, feeding into existing networks which will take forward Raj's thoughts and ideas. Our support and participation in the setting-up of the WHO Dementia Observatory will also ensure these remain a priority.

The UK Government is committed to working towards finding a cure or disease modifying therapy for dementia by 2025, and will continue to work in alignment across the drug development space.

ANNEX A: Membership of the Integrated Development Advisory Group

Alzheimer's Society

Alzheimer's Research UK (ARUK)

Department of Health

- Dementia Discovery Fund
- Dementia Policy
- Global Action Against Dementia
- NICE and MHRA Sponsor Team
- Office of Life Sciences
- Research Finance and Programmes

EU Joint Programme- Neurodegenerative Disease Research (JPND)

European Commission

- eHealth and HTA
- Medicinal products-authorisations, EMA
- Programme Management and Diseases

Medical Research Council (MRC)

National Institute for Health Research (NIHR)

National Institute of Ageing (NIA)

Organisation for Economic Co-operation and Development (OECD)

University of Newcastle

World Health Organisation (WHO)

We have also engaged with:

Alzheimer's Association

CEOi

MRC Technology