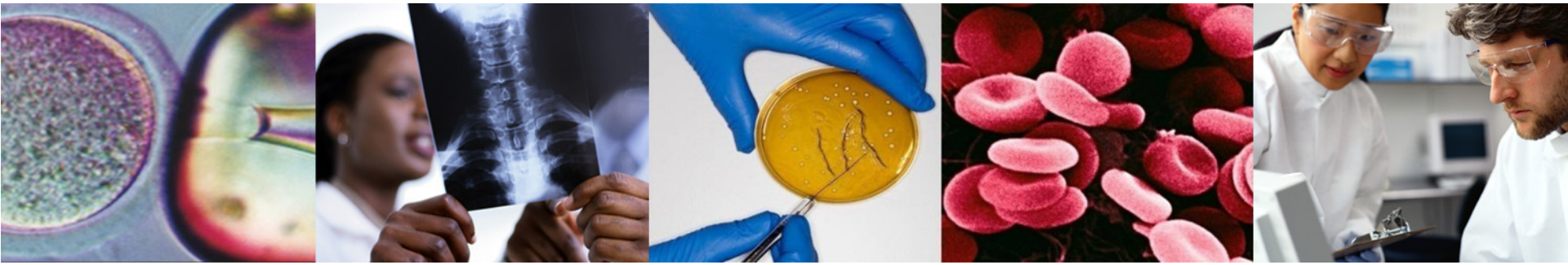


MRC/AstraZeneca Compound Initiative

Chris Watkins
Director, Translational Research and Industry
Medical Research Council

Washington, June 2013

- **About the Medical Research Council**
- The MRC/AZ Initiative – Planned Outcomes
- The MRC/AZ Initiative – Process
- The MRC/AZ Initiative - Outcomes
- The MRC/AZ Initiative – Lessons learnt

About the MRC

Mission-driven: “Encourage and support high-quality research with the aim of improving human health”.

Largest public funder of medical research, in Universities, hospitals, and via intramural programme

MRC research expenditure - £759.4 million in 11/12

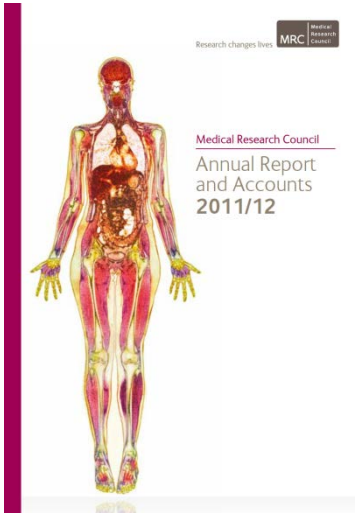
Celebrating centenary this week

MRC investment in research, 2011/12

Largest public funder of medical research, in Universities, hospitals, and via intramural programme

MRC research expenditure - **£759.4 million** in 11/12

- **£354.6m** for more than 440 programmes in MRC research units and institutes.
- **£309.9m** on more than **1,100** grants.
- **£86m** on studentships and fellowships.



Research Changes Lives

MRC Strategic Plan 2009-2014

During 2009-2014 the MRC aims to support medical research which increases the pace of the transition to better health. We will achieve this through:

- Strategic Aim One: **Picking research that delivers**
- Strategic Aim Two: **Research to people**
- Strategic Aim Three: **Going global**
- Strategic Aim Four: **Supporting scientists**

Experimental Medicine

- Important component of MRC's translational strategy
- For MRC: "Investigation undertaken in humans, relating where appropriate to model systems, to identify mechanisms of pathophysiology or disease, or to demonstrate proof-of-concept evidence of the validity and importance of new discoveries or treatments."
- Man as the experimental subject
  - e.g. target validation
  - e.g. Stratified medicine (precision or personalised medicine)
- Requires using safe but selective probes of function/mechanism

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MRC/AstraZeneca: Mechanisms of Disease Initiative

- MRC and AstraZeneca working together in a world-leading initiative to provide access for UK academic researchers to AstraZeneca deprioritised compounds.

- Aimed at increasing better understanding of mechanisms of human disease and development of potential therapeutic interventions

- Transformational in stimulating relationships between academia and industry

MRC/AstraZeneca: Mechanisms of Disease Initiative - Intentions

- Using compounds as tools to probe mechanisms of disease
  - Gaining a better understanding of underlying biology
  - Target validation
  - Revealing novel therapeutic opportunities
- Not screening of compound library
- Hypothesis-testing, not hypothesis-generating
- Not supporting research that should be done by AZ, including repurposing of specific compounds
- Collaborative projects between academic and AZ researchers
- Use of template agreements wherever possible (MICA, mICRA)

MRC/AstraZeneca: Mechanisms of Disease Initiative - How the compounds were selected

- Detailed discussion between MRC and AZ

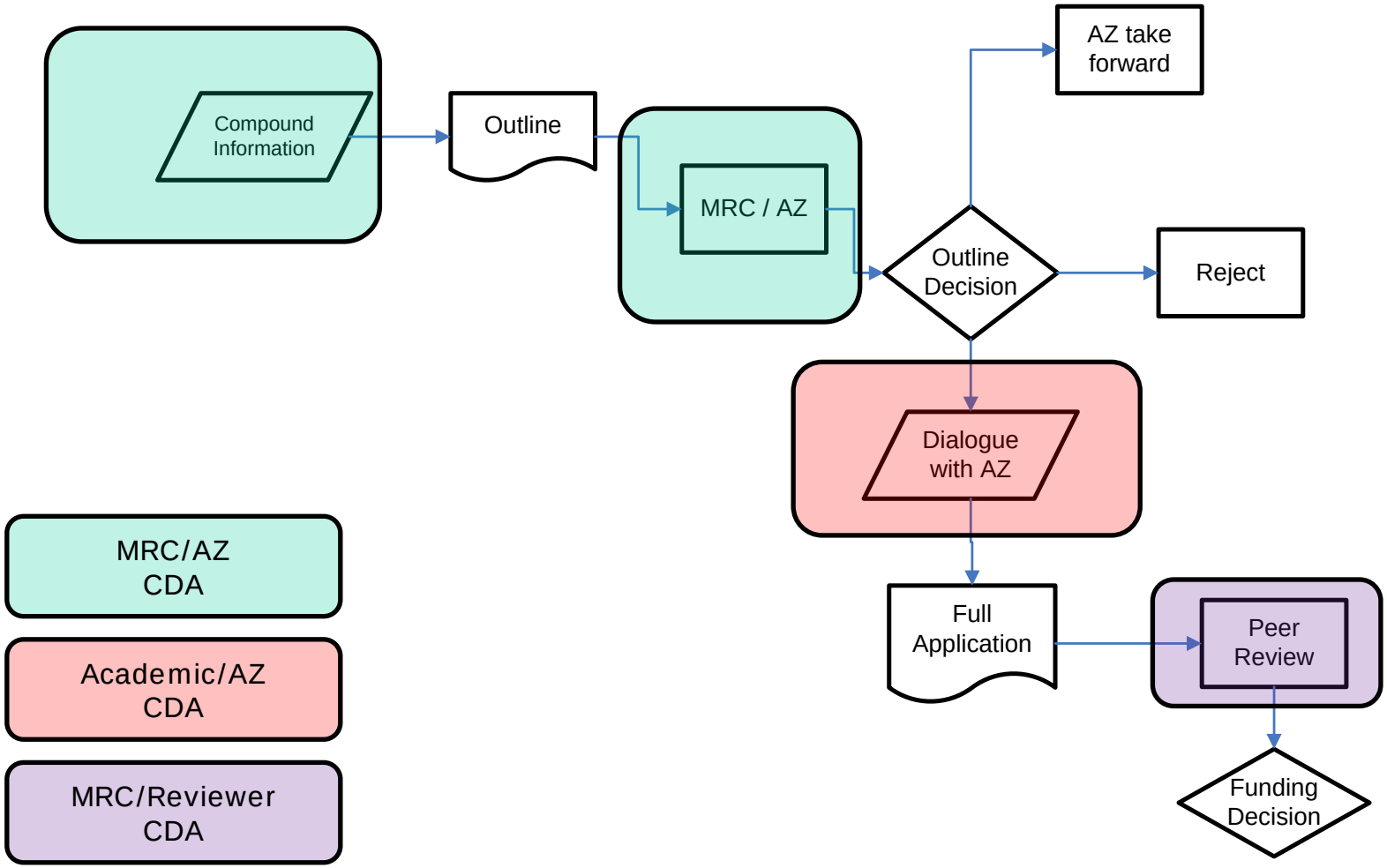
- Focused on deprioritised compounds
  - Relatively well-worked up molecules
  - Would not risk compromising active AZ programmes
  - MRC able to support research which otherwise would not have been undertaken

- Issues over company knowledge and information on deprioritised compounds
  - e.g. Investigator Brochure
  - Risk/benefit ratio for novel patient groups (toxicology, formulation, etc)

MRC/AstraZeneca: Mechanisms of Disease Initiative - Release of information

- Balance between confidentiality and sufficient information to attract the best research proposals
  - Data around nature of target, specificity and selectivity
  - Toxicological information
  - Where already tested
- Structures of the compounds not necessary
- Protecting IP of potential applicants
- More detailed information shared under confidentiality agreements between researchers and AZ

MRC/AstraZeneca: Mechanisms of Disease Initiative - protecting information



MRC/AstraZeneca: Mechanisms of Disease Initiative - Intellectual Property issues

- AstraZeneca retain the intellectual property (IP) on the chemical composition of the compounds.
- Any IP resulting from the research from the studies will be retained by the research organisations and AstraZeneca will be able to negotiate this once the studies have completed.
- All results from the studies will be published within 6 months of the end of the work.

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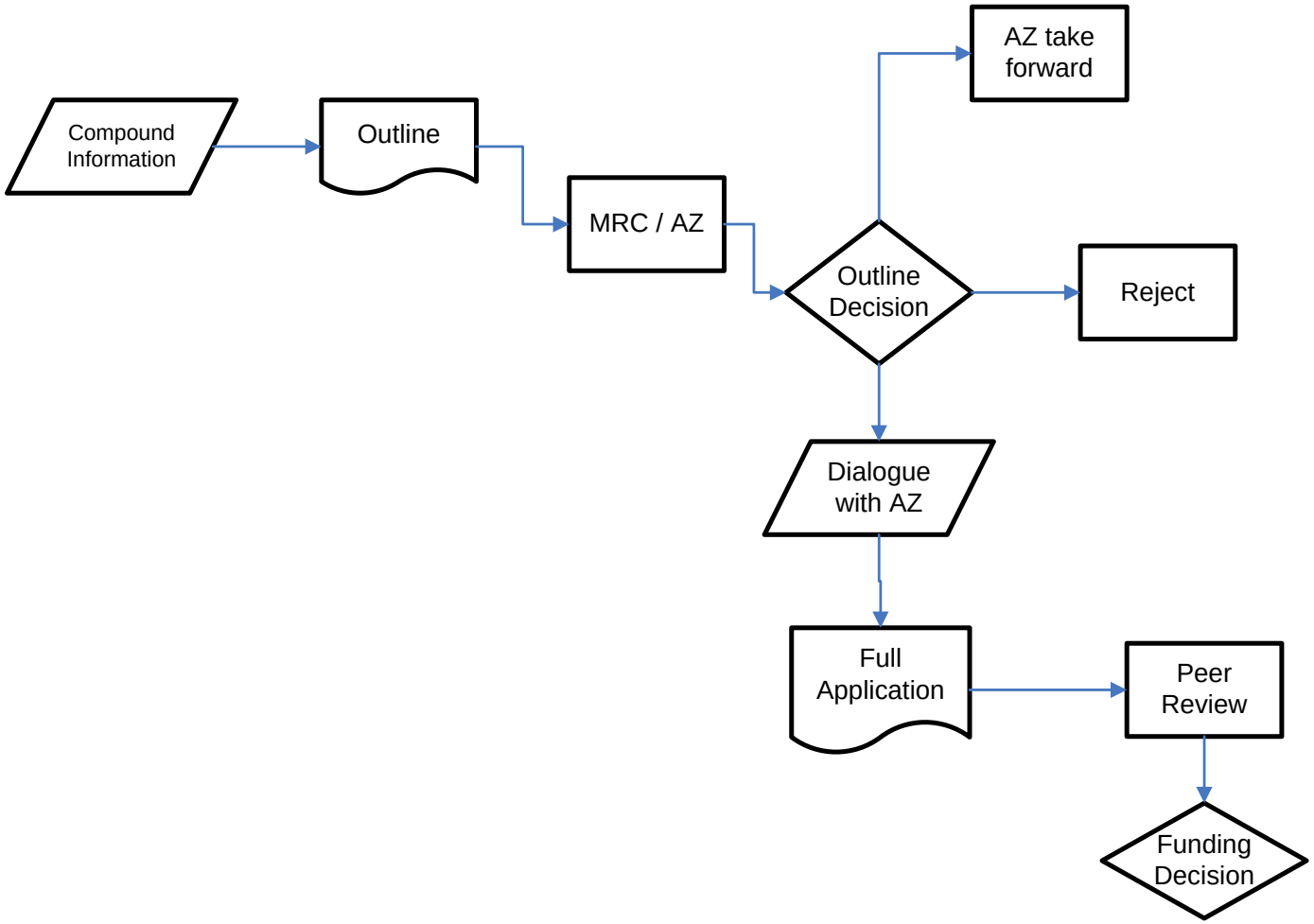
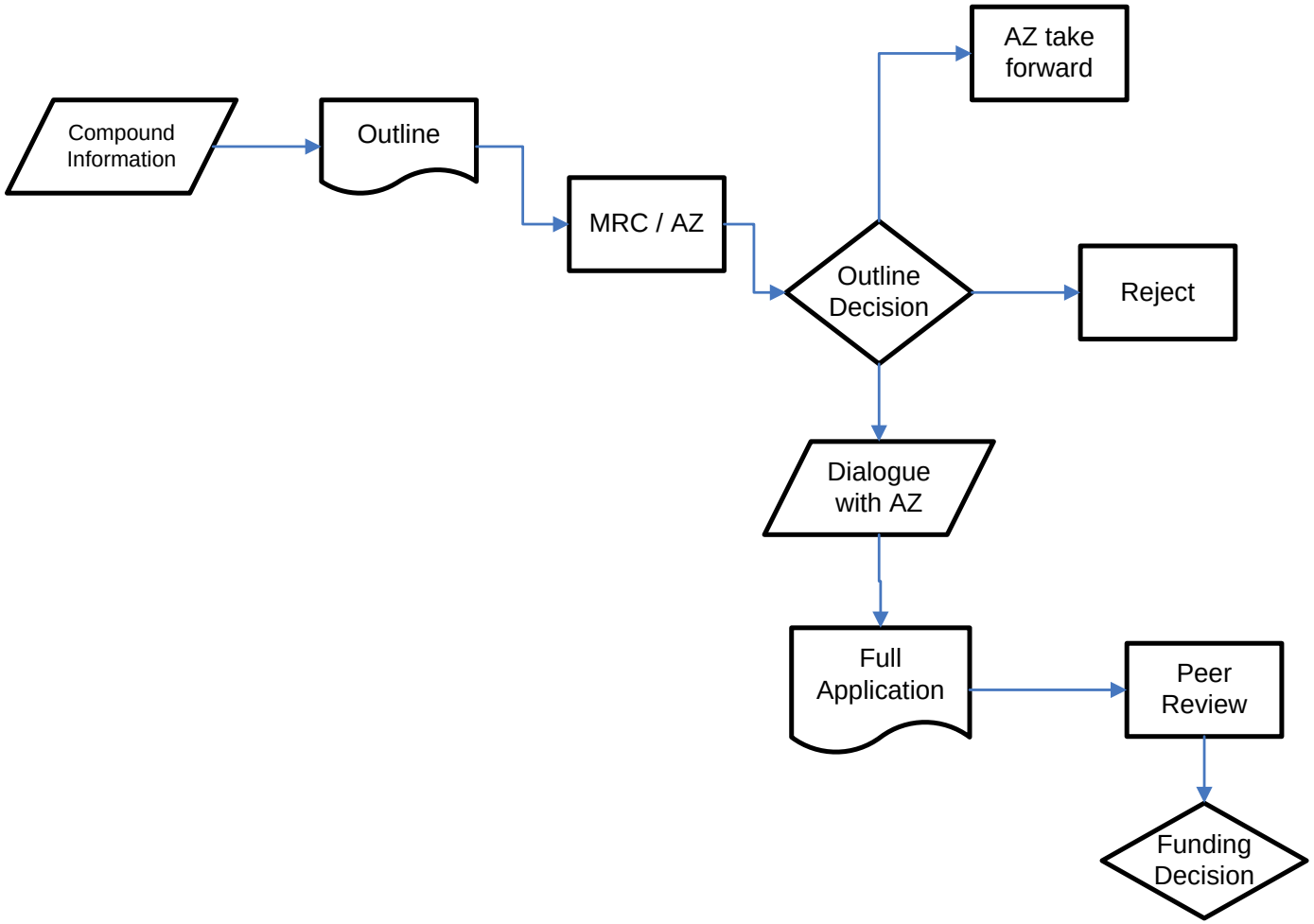
MRC/AstraZeneca: Mechanisms of Disease Initiative - Process Steps



MRC/AstraZeneca: Mechanisms of Disease Initiative - Call details

- Over 100 Outline applications submitted which were assessed on the following criteria:
  - Fit to remit
  - Strength of scientific rationale
  - Feasibility of proposal - with regards to asset availability and supply
  - Novelty - whether such studies are already on-going within AstraZeneca
  - Design of any clinical trial proposed (length, subject numbers, endpoints)
  - Appropriateness of risk-benefit for patients enrolled in any proposed clinical studies, based on known safety & tolerability profiles of the compound & mechanism
- 25 applications invited to submit full proposal.
- Funding announcements in November 2012.

MRC/AstraZeneca: Mechanisms of Disease Initiative - Process Steps



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MRC/AstraZeneca: Mechanisms of Disease Initiative - Funding Decisions

- **£7M** funding awarded for **15** collaborative projects (**8** clinical and **7** preclinical) in **October 2012** (Initiative announced in December 2011, opened in April 2012)
- Research areas range from common illnesses to orphan diseases.
- Including:

  - University of Bristol: investigating whether a compound originally evaluated for the treatment of prostate cancer can delay the progression of Alzheimer's disease.

  - University of Manchester: a small clinical trial of a new treatment for chronic cough using a compound developed to treat heartburn.

  - Royal Veterinary College, University of London: re-purposing a lung disease drug to treat muscular dystrophies.

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MRC/AstraZeneca: Mechanisms of Disease Initiative - Why it works

- True collaboration as AstraZeneca are full co-applicants on all of the proposals and will invest time and contributions in kind.
- AstraZeneca benefit through gaining access to a large pool of researchers they may not have been aware of previously.
- Researchers benefit by gaining access not just to the compounds but the toxicological and safety data which is not in the public domain.
- Through working together, researchers and AstraZeneca can capitalise upon their unique strengths to improve understanding of mechanisms of human disease and aid the development of potential therapeutic interventions

MRC/AstraZeneca: Mechanisms of Disease Initiative - Final Perspectives

- A lot of planning before announcement
- Use of templates really helpful
- Balancing level of information in public domain with confidentiality and interaction with company researchers
- Use of deprioritised compounds
- Initiative very well received
- Other companies very interested

Model Industry Collaborative Research Agreement (mICRA)

Prospective development of template agreement

Universities already familiar with template, endorsed by many key stakeholders

All 15 project agreements signed within 3 months of funding decision

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MRC/AstraZeneca: Mechanisms of Disease Initiative - the people responsible

MRC

- Chris Watkins
- Jo Latimer
- Louise Armstrong
- Amy-Rose Mayes

AstraZeneca

- Clive Morris
- Don Frail
- Chris Wilks
- Graham Wilkinson
- + colleagues

Any Questions?

Chris Watkins

Medical Research Council
chris.watkins@headoffice.mrc.ac.uk
www.mrc.ac.uk