



APPENDICES C-G

APPENDIX C: BIOMEDICAL RESEARCH ACTIVITY CLASSIFICATION SYSTEM

1. BASIC RESEARCH

- 1.1 General biological processes mechanisms functions
 - 1.1.1 Underpinning biological studies assessing normal function / development / processes
 - 1.1.2 Infrastructure supporting basic biology studies
- 1.2 Etiology of disease / dysfunction / pathogenesis
 - 1.2.1 Clinical (observational) studies: epidemiology / natural history / longitudinal / cross-sectional / assessment of clinical data for novel targets / genotype-phenotype assessments
 - 1.2.2 Biological pathway / mechanistic elucidation of disease (cellular)
 - 1.2.3 Elucidation of endophenotypic pathways / complications (systems)
 - 1.2.4 Target discovery
 - 1.2.4.1 Discover new genes / gene products
 - 1.2.4.2 Functional genomics / annotation/ functional classification / expression data
 - 1.2.4.3 Transcriptional control / epigenetic regulation / imprinting
 - 1.2.4.4 Translational control / post-translational modification
 - 1.2.5 Target validation
 - 1.2.5.1 *In vitro* validation, cellular assays and models
 - 1.2.5.2 Development of animal models / model organisms
 - 1.2.5.3 *In vivo* validation, assays and animal models / pre-clinical proof-of-concept
 - 1.2.6 Etiological factors related to physical environment
 - 1.2.7 Psychological / social / economic factors
 - 1.2.8 Infrastructure supporting etiology studies and basic research

2. TREATMENT DEVELOPMENT

- 2.1 Lead discovery
 - 2.1.1 Assay development *in vitro* / cell / tissue based models
 - 2.1.2 Assay development *in vivo* animal models
 - 2.1.3 Assay development HTS
 - 2.1.4 Primary screening of compound libraries for hits / leads
 - 2.1.5 *In silico* screening / CADD / SBDD
 - 2.1.6 Chemical synthesis / combinatorial chemistry for hits / leads
 - 2.1.7 Selective optimization of side activities; assessment of clinical data for known side activities of compounds
- 2.2 Lead validation
 - 2.2.1 Secondary screening of hits/leads – Potency / dose-response
 - 2.2.2 Secondary screening of hits/leads – Counter-screening and selectivity

- 2.2.3 Secondary screening of hits/leads – Mechanism of action
- 2.2.4 Secondary screening of hits/leads – *in silico* CADD / SAR / QSAR
- 2.3 Lead optimization
 - 2.3.1 Lead optimization – Medicinal chemistry
 - 2.3.2 Lead optimization – PK/PD / ADME / bioavailability / BBB permeability
 - 2.3.3 Lead optimization – Toxicity P450 / HERG / CACO – *in vitro*
 - 2.3.4 Lead optimization – Toxicity LD50 *in vivo*
 - 2.3.5 Lead optimization – Dosing / formulation / delivery
- 2.4 Pre-clinical drug development, small molecule
 - 2.4.1 Drug development – Pre-clinical data to IND submission
 - 2.4.2 Drug development – Process development / CMC / API
 - 2.4.3 Drug development – Reformulation
- 2.5 Pre-clinical development, gene & cell-based therapies / biologicals / vaccines
 - 2.5.1 Drug development – Pre-clinical data to IND submission
 - 2.5.2 Drug development – Process development / CMC / API
 - 2.5.3 Drug development – Reformulation
- 2.6 Other interventions development
 - 2.6.1 Devices – Testing *in vivo*
 - 2.6.2 Surgical interventions – Testing *in vivo*
 - 2.6.3 Radiotherapy development – Testing *in vivo*
 - 2.6.4 Psychological/behavioral interventions – testing *in vivo*
 - 2.6.5 Physical Therapy – Testing *in vivo*
 - 2.6.6 Complementary medicine / therapies – Testing *in vivo*
- 2.7 Infrastructure supporting treatment development
- 3. TREATMENT EVALUATION (IN MAN)
 - 3.1 Pharmaceutical Evaluation (Phases I-IV)
 - 3.1.1 Phase I – Safety and dosing
 - 3.1.2 Phase II – Proof of efficacy
 - 3.1.3 Phase III – Large scale clinical trial
 - 3.1.4 NDA / Phase IV – Post-marketing surveillance
 - 3.2 Gene Therapy / cell-based therapies / biological
 - 3.2.1 Phase I – Safety and dosing
 - 3.2.2 Phase II – Proof of efficacy
 - 3.2.3 Phase III – Large scale clinical trial
 - 3.3 NDA / Phase IV – Post-marketing surveillance
 - 3.4 Other Interventions (clinical studies in man)
 - 3.4.1 Clinical study – Nutrition and nutraceuticals
 - 3.4.2 Clinical study – Complementary medicines / therapies
 - 3.4.3 Clinical study – Radiotherapies
 - 3.4.4 Clinical study – Devices

- 3.4.5 Clinical study – Surgical interventions
- 3.4.6 Clinical study – Psychological / behavioral / communication
- 3.4.7 Clinical study – Physical therapy
- 3.5 Infrastructure supporting clinical treatment evaluation

- 4. DETECTION, DIAGNOSTICS & IMAGING
 - 4.1 Discovery and validation of markers, imaging reagents & diagnostic technologies
 - 4.2 Clinical development of markers, surrogate markers, reagents and technologies
 - 4.3 Infrastructure supporting detection, diagnostics & imaging

- 5. PRIMARY PREVENTION & RISK FACTOR MANAGEMENT
 - 5.1 Primary prevention / interventions to modify behavior / well being
 - 5.2 Interventions to alter physical / biological / environmental risk
 - 5.3 Vaccination
 - 5.4 Infrastructure supporting primary prevention

- 6. DISEASE MANAGEMENT
 - 6.1 Individual care needs / palliative care
 - 6.2 End of life care
 - 6.3 Healthcare management and decision making
 - 6.4 Infrastructure supporting disease management

- 7. HEALTHCARE SERVICES, POLICY AND METHODOLOGY
 - 7.1 Organization and delivery services
 - 7.2 Health and welfare economics (pharmacoeconomics)
 - 7.3 Ethics and policy research
 - 7.4 Research design and methodology
 - 7.5 Infrastructure supporting healthcare services and delivery

APPENDIX D: ABBREVIATIONS

'000s	Thousands
ADME	Absorption, distribution, metabolism & excretion
API	Active pharmaceutical ingredient
BBB	Blood brain barrier
CADD	Computer-aided drug design
CBD	Corticobasal Degeneration
CDMRP	Congressionally directed medical research programs (US)
CIHR	Canadian Institutes of Health Research
CMC	Chemistry, manufacturing & controls
CORDIS	Community Research & Development Information Services (EU)
FTD	Frontotemporal dementia
FULD	Frontotemporal lobar degeneration
FULD-U	Frontotemporal lobar degeneration with ubiquitinated inclusions
HRB	Health Research Board (Ireland)
IND	Investigational New Drug
MM	Millions
MRC	Medical Research Council (UK)
NCI	National Cancer Institute (NIH, US)
NCRR	National Center for Research Resources (NIH, US)
NDA	New Drug Application
NEI	National Eye Institute (NIH, US)
NHGRI	National Human Genome Research Institute
NHLBI	National Heart, Lung & Blood Institute (NIH, US)
NHMRC	National Health & Medical Research Council (Australia)
NIA	National Institute on Aging (NIH, US)
NIAID	National Institute of Allergy and Infectious Diseases (NIH, US)
NIAMS	National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIH, US)
NICHD	National Institute of Child Health and Human Development (NIH, US)
NIDA	National Institute on Drug Abuse (NIH, US)
NIDCD	National Institute on Deafness and Other Communication Disorders (NIH, US)
NIEHS	National Institute of Environmental Health Sciences (NIH, US)
NIGMS	National Institute General Medical Sciences (NIH, US)
NIH	National Institutes of Health
NIMH	National Institute of Mental Health (NIH, US)
NINDS	National Institute of Neurological Disorders and Stroke (NIH, US)
PNA	Progressive Nonfluent Aphasia
PSP	Progressive Supranuclear Palsy
SBDD	Structure-based drug design
SD	Semantic dementia
VCP	Valosin-containing protein

APPENDIX E: RESEARCH FUNDING CONSULTANTS

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