



Faculty of Medicine
School of Medical Sciences

DEPARTMENT OF PHARMACOLOGY

PHAR 3101

Drug Discovery, Design and Development

COURSE OUTLINE

SESSION 2, 2018

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Please read this outline in conjunction with the following pages on the [School of Medical Sciences website](#):

- [Advice for Students](#)
- [Learning Resources](#)

(or see "STUDENTS" tab at medicallsciences.med.unsw.edu.au)

PHAR3101 Course Information

Drug Discovery, Design and Development (PHAR3101) is a 3rd year Science course worth six units of credit (6 UOC). The course is usually undertaken as part of a major in Pharmacology for the Bachelor of Science (Adv.) or Bachelor of Medical Sciences or as part of the Bachelor of Medicinal Chemistry. The course builds on the knowledge you have gained in Pharmacology (PHAR2011, PHAR3102 and/or PHAR3251).

OBJECTIVES OF THE COURSE

This course will explore the process of drug development, from target identification to final drug registration. It will present drug development as a process involving target selection, hit discovery using computer-based methods, combinatorial chemistry/high-throughput screening. Lead identification and optimisation via the use of structure activity series and computational methods will be covered. Safety evaluation, bioavailability, clinical trials, and the essentials of intellectual property, regulatory affairs and commercialisation will also be discussed. Along the way, you will learn about screening assays, computer-aided drug design, and toxicology as applied to the development of new medicines.

COURSE CONVENER and LECTURERS:

Course Convener:

Dr. Angela Finch

a.finch@unsw.edu.au

Wallace Wurth Building, level 3E, ph: 9385 1325

Co-Convener:

Dr Johnson Liu

Johnson.liu@unsw.edu.au

Wallace Wurth Building, level 3E,

Students wishing to see the course staff should make an appointment via email as our offices are not readily accessible. We will organize to meet you in a convenient location elsewhere in the building.

Lecturers in this course:

Dr Trudie Binder w.binder@unsw.edu.au

Dr Orin Chisholm o.chisholm@unsw.edu.au

Ms Teresa Domagala Teresa.Domagala@tevapharm.com

Prof Peter Gunning p.gunning@unsw.edu.au

Dr Natasha Kumar natasha.kumar@unsw.edu.au

Dr Alastair Stewart a.stewart@victorchang.edu.au

COURSE STRUCTURE and TEACHING STRATEGIES

Learning activities occur on the following days and times:

- Lectures: Wednesday 11-12 am and Thursday 9-10 am
- Tutorials: Wednesday 9-10 am or 10-11 am
- Practicals: Tuesday 2-5 pm

Students are expected to attend all scheduled activities for their full duration (2 hours of lectures per week and 4 hours of practical and tutorial sessions per week. Students are reminded that UNSW recommends that a 6 units-of-credit course should involve about 125-150 hours of study and learning activities. The formal learning activities are approximately 70 hours throughout the semester and students are expected (and strongly recommended) to do at least the same number of hours of additional study.

Lectures will provide you with the concepts and theory essential for understanding the processes involved in drug development. To assist in the development of research and analytical skills practical classes and tutorials will be held. These classes and tutorials allow students to engage in a more interactive form of learning than is possible in the lectures. The skills you will learn in practical classes are relevant to your professional development.

APPROACH TO LEARNING AND TEACHING

The learning and teaching philosophy underpinning this course is centred on student learning and aims to create an environment which interests and challenges students. The teaching is designed to be relevant and engaging in order to prepare students for future careers.

Although the primary source of information for this course is the material covered in lectures, tutorials, and practical classes, effective learning can be enhanced through self-directed use of other resources such as textbooks and Web based sources. Your practical classes will be directly related to the lectures and it is essential and required to prepare for practical classes before attendance *via* the pre-lab modules. It is up to you to ensure you perform well in each part of the course: preparing for classes; completing assignments; studying for exams and seeking assistance to clarify your understanding.

TEXTBOOK AND READING LIST

Recommended Primary Texts:

- Drug Discovery and Development - Technology in Transition. Hill & Rang. Elsevier Ltd 2nd edition 2013.
- Pharmacology in Drug Discovery: understanding drug response T. P. Kenakin. Elsevier, 2nd Edition 2012.

These textbooks will be available at the UNSW bookshop. They are also available in print and online formats from the library.

Other Resources:

The following electronic journals are accessible *via* the UNSW library.

- Nature Reviews: Drug Discovery.
- Drug discovery today.
- Science online special "Drug discovery" www.sciencemag.org/sciext/drugdisc/
- Pharmacology & Pharmaceutical Medicine Study guide
<http://subjectguides.library.unsw.edu.au/medicine/pharmacology>

Links to additional sources to supplement the material covered in the lectures will be placed on the lecture pages on Moodle.

STUDENT LEARNING OUTCOMES

PHAR3101 will develop those attributes that the Faculty of Science has identified as important for a Science Graduate to attain and the Learning Objectives of the Pharmacology Major.

- A. Research, inquiry and analytical thinking abilities.
- B. Capability and motivation for intellectual development.
- C. Ethical, Social and Professional Understanding.
- D. Communication.
- E. Teamwork, collaborative and management skills.
- F. Information literacy.

Pharmacology Major Learning Outcomes

- i. Demonstrate an understanding of how drugs/therapeutics are developed, work and are used safely.
- ii. Critically analyse, interpret and effectively communicate pharmacology data and literature.
- iii. Design and/or execute experiments or other activities to address pharmacological scenarios.

On completion of this course students should be able to:

- 1. demonstrate an understanding of the steps involved in drug development from bench to bedside.
- 2. apply knowledge of the drug development process and identify challenges and benefits of different approaches to address novel scenarios.
- 3. critically analyse scientific literature and experimental data and communicate their findings.
- 4. show an understanding of teamwork and the contributions of different discipline areas to drug development

See also: [UNSW Graduate Outcomes](#) [Science Graduate Attributes](#)

ASSESSMENT PROCEDURES

- | | |
|---|-------------|
| • Progress exam (50 min duration): | 10 % |
| • Research Manuscript | 20 % |
| • Stages of Drug Design and Development Process | 15 % |
| • End of session examination (2 hours duration) | 55 % |
| • Formative assessment | |

The *practicals and tutorials* are provided to support lecture material and practise analytical skills. The practical classes and tutorials help you to develop graduate attributes A, C, D & E.

You will submit a written report covering four of the practical sessions. The report should be in the form of a scientific communication comprising introduction, methods, results and discussion (see below for instructions). You will work in teams to research the drug discovery process of a given drug and the teamwork involved in that process. These assessment tasks will allow you to develop your research, information literacy, communication and time management skills, as well as allowing you to demonstrate your ability to work in a team and collaborate successfully (Graduate attributes A, B, C, D, E &F) and enable you to demonstrate your mastery of learning outcomes 1, 2, 3 & 4. The marking criteria and instructions are provided below.

A penalty will apply for late submissions of assessment tasks (10% per day).

The *progress examination* will be held during the Wednesday 11 am lecture session in week 6, on the 29th of August. This exam will give you feedback on how you are succeeding in the course. The *progress examination* and *end of session examination* will test not only your knowledge of the process of drug design and development but also your ability to apply the knowledge you have acquired from multiple lectures, practicals and tutorials to drug development scenarios. The examination will be in the format of short and long answer questions. The questions will be based on the material covered in the lectures, practical classes and tutorials. Material covered prior to the progress exam may be examined again in the final exam. The examinations will address graduate attributes A and B and enable you to demonstrate your mastery of learning outcomes 1, 2 & 3. The end of session examination will be held during the official examination period.

The goal of *formative assessment* is to provide ongoing feedback that you can use to improve your learning. Formative assessment tasks help students identify their strengths and weaknesses and therefore the areas they should focus on. The formative assessment will take the form of tutorial questions. Tutorial questions will be posted on Moodle a week before scheduled tutorial sessions and feedback will be provide in the tutorial classes.

COURSE EVALUATION AND DEVELOPMENT

Each year feedback is sought from students about the courses offered in the Department of Pharmacology and continual improvements are made based on this feedback. The UNSW myExperience survey is the way in which student feedback is evaluated and significant changes to the course will be communicated to subsequent cohorts of students. Also, a staff-student liaison group will be set up and students will be invited to become class representatives to seek feedback from their colleagues and meet with academic staff to discuss any issues that arise. Based on feedback given in these meetings changes will be implemented during the course and for future years.

We appreciate student feedback because we are always looking for ways to improve your learning experience in this course. Below is a summary of the feedback from the previous student cohort in this course and our response to how we improved this year's course delivery.

Previous students told us that: They liked the structure and content of the course, especially the real-life examples and that all the components were integrated. Especially that the course covers the Drug Discovery, Design and Development process from start to end providing an understanding of how the industry functions. They commented on the enthusiasm and passion of the teaching staff and that they liked they got to hear from researchers and workers in the field presenting relevant and current content. They commented that the labs were exciting and a highlight for many students was the excursion to the phase I clinical trials unit. They also liked the assessment tasks especially the drug development timeline and thought they were well spaced through the semester.

When asked what could be improved in the course the most frequent responses were regarding allowing more time to complete the manuscript assignment and reduction of the length of the manuscript. Students suggested that more help be provided, possibly in the form of more videos, to help them understand how to use Prism and the other software used in the practical classes. It was also suggested that a peer review component be added to the timeline assignment.

We have responded to this feedback by: The word count of the manuscript has been reduced and extra time allowed for its submission along with an online tutorial being developed to help student to complete this task. More explanation of each step of using the software has been provided in the practical manual along with online "how-to" videos. A peer review component

has been added to the timeline assignment.

GENERAL INFORMATION

The Department of Pharmacology is part of the School of Medical Sciences and is within the Faculty of Medicine. It is located in the Wallace Wurth building. General inquiries can be made at the BABS.SOMS.BEES (B.S.B.) Student Office, located on the Ground Floor Room G27, of the Biosciences Building. Office hours are 9.00 am - 5:00pm.

Professor Margaret Morris is Head of Department and appointments to meet with her may be made via email (m.morris@unsw.edu.au).

There is an honours program conducted by the School. The Honours program is coordinated by Dr Greg Smith (g.smith@unsw.edu.au), Ph: 9385 8075. Any students considering an Honours year should discuss the requirements with the coordinator.

Honours Administrator: Vicky Sawatt (v.sawatt@unsw.edu.au) Ph:9385 8195.

Postgraduate degrees

The Department of Pharmacology offers students the opportunity to enter the following graduate programs:

Course Work Masters: Masters in Pharmaceutical Medicine. For more information contact Dr Orin Chisholm (o.chisholm@unsw.edu.au)

Research Masters: In Pharmacology. Contact the post-graduate co-ordinators A/Prof Pascal Carrive (p.carrive@unsw.edu.au) and Dr Nicole Jones (n.jones@unsw.edu.au)

Doctorate (Ph.D): In Pharmacology. Contact the post-graduate co-ordinators A/Prof Pascal Carrive (p.carrive@unsw.edu.au) and Dr Nicole Jones (n.jones@unsw.edu.au).

Attendance Requirements

For details on the Policy on Class Attendance and Absence see [Advice for Students](#) and the [Policy on Class Attendance and Absence](#).

Attendance at practical classes is compulsory, and must be recorded in the class roll at the start of each class. Arrival more than 15 minutes after the start of the class will be recorded as non-attendance. It is your responsibility to ensure that the demonstrator records your attendance and no discussions will be entered into after the completion of the class. Satisfactory completion of the work set for each class is essential. It should be noted that non-attendance for other than documented medical or other serious reasons, or unsatisfactory performance, for more than 1 practical class during the session may result in an additional practical assessment exam or ineligibility to pass the course. Students who miss practical classes due to illness or for other reasons must submit a copy of medical certificates or other documentation to the course coordinator.

Practical Classes

The practical class is an opportunity for students to develop graduate attribute C by behaving in an ethical, socially responsible and professional manner within the practical class.

Students must take due care with biological and hazardous material and make sure all equipment is left clean and functional. In the interests of safety, special attention should be paid to any precautionary measures recommended in the notes. If any accidents or incidents occur they should be reported immediately to the demonstrator in charge of the class who will record the incident and recommend what further action is required.

For more details see [Advice for Students-Practical Classes](#)

Special Consideration

You can apply for special consideration when illness or other circumstances beyond your control interfere with your assessment performance. Except in unusual circumstances, the duration of circumstances impacting academic work must be more than 3 consecutive days, or a total of 5 days within the teaching period.

You must make formal application for Special Consideration as soon as practicable after the problem occurs and within 3 working days of the assessment to which it refers.

The application for all special consideration regardless of the percentage of the final grade it contributes must be made through Online Services in myUNSW (My Student Profile tab > My Student Services > Online Services > Special Consideration).

Please see [UNSW-Special Consideration](#) and [Student Advice-Special Consideration](#)

If you unavoidably miss the progress exam in PHAR3101, you must lodge an application with UNSW Student Central for special consideration. If your request for consideration is granted an alternative assessment will be organised which may take the form of a supplementary exam or increased weighting of the final exam.

The supplementary exams for the School of Medical Sciences in Semester 2, 2018 will be held on the 8th of December to 15th of December 2018.

Student Support Services

Details of the available student support services can be found at [Student Advice-Student support services](#).

Appeal Procedures

Details can be found at [Student-Advice-Reviews and Appeals](#)

Academic Integrity and Plagiarism

The School of Medical Sciences will not tolerate plagiarism in submitted written work. The University regards this as academic misconduct and imposes severe penalties. Evidence of plagiarism in submitted assignments, etc. will be thoroughly investigated and may be penalised by the award of a score of zero for the assessable work. Flagrant plagiarism will be directly referred to the Director of Integrity for disciplinary action under UNSW rules.

The [UNSW Student Code](#) outlines the standard of conduct expected of students with respect to their academic integrity and plagiarism.

More details of what constitutes plagiarism can be found [here](#)

Drug Discovery, Design and Development

LECTURE and PRACTICAL OUTLINES

The course is divided into 4 main themes covering the drug development process from bench to bedside.

1. Target Selection & Validation
2. Lead Identification & Optimisation
3. Pre-Clinical & Clinical Development
4. Registration & Commercialisation

1. Target Selection & Validation

Drug Discovery & Development: Choosing the project

This lecture will present the process of drug discovery and development, outlining the journey from test tube to patient treatment. It will introduce terminology used in drug discovery and development programs and discuss the role of multidiscipline teams in this lengthy, expensive, and complicated process. It will explore the factors that are considered when making the initial decision of whether or not to embark on a new drug discovery project.

Novel Target Identification and Validation

In this lecture, the role of genomics and bioinformatics in target selection will be introduced. The use of genetic approaches to identify target candidates, genomics and proteomics will be covered. Also covered will be the role of bioinformatics in the analysis of nucleic acid sequence, protein sequence and structure, expression databases and functional pathway data contained in databases.

Target Validation and Drug Validation Practicals

Drug discovery teams (groups of 2-3 students) will validate a potential drug target, tropomyosin Tm5NM1/Tm3.1, for the treatment of cancer. This novel target is suggested to control the proliferation of cancer cells. Having validated the target drug validation for Tm5NM1/TM3.1 will be carried out to verify specificity and desired impact on cell function.

1. Target Validation

Aims:

- To investigate changes in the actin cytoskeleton when the expression levels of Tm5NM1/Tm3.1 is knocked down using small interfering RNA (siRNA).
- To investigate the impact of Tm5NM1 knockdown on tumour cell growth using a clonogenic colony forming assay.

2. Drug Validation

Aims:

- To investigate changes in the actin cytoskeleton when cells are incubated with the anti-tropomyosin compound TR100
- To investigate the impact of the anti-tropomyosin compound TR100 on tumour cell growth and determine the effective concentration (EC₅₀) using cell viability assays.

Gene Technology in Target Identification and Validation

This lecture will build on the previous lecture with a focus on the technology used to further our understanding of the molecular basis of human diseases. It will cover the technical advances in target identification and validation being made such as sophisticated gene profiling technologies (eg DNA microarrays), bioinformatics approaches (eg gene expression databases allowing for in silico discovery of therapeutic targets) and the potential use for gene expression silencing (eg RNAi) to screen for target identification, looking at the benefits and

limitations of each approach. We will also examine transgenic animal models as key tools in functional genomics, for the generation of human disease models and validation of new drugs comparing the advantages and limitations of these models.

Target Selection

This lecture will discuss the key issues in target selection and discuss the rationale for decision making. We will explore the advantages and disadvantages of different proteins/nucleic acids as drug targets. The qualities that make a good drug target will be covered including: contribution to a biological pathway involved in the pathophysiology of a disease, functional and structural information about the target and that the target is “druggable” will be covered.

2. Lead Identification & Optimisation

Hit Identification

This lecture will examine the types of assays that can be used to screen for hits as well as test compounds during lead optimization. We will compare different assay formats, such as biochemical versus cell based, homogenous versus heterogeneous, and target versus phenotypic assays. The advantages and disadvantages of each assay type will be explored.

High Throughput Screening

The introduction of new technologies, such as high throughput screening (HTS), which can experimentally test hundreds of thousands of compounds a day, has resulted in a more rapid identification of promising drug candidates and reduced drug development costs. This lecture covers assay development and the qualities needed in a screening assay. The role of high throughput screening and the advantages and challenges it brings to the drug discovery process will be discussed.

Hit Optimisation Practicals:

Drug discovery teams (groups of 3-4 students) will test a series of structurally related compounds to determine their affinity, potency and efficacy at the human β_2 adrenoceptor. This data will allow for the identification of structural requirements for high affinity, potent full agonists.

1. Hit Optimisation: Radioligand Binding Assays

Aims:

- To determine the affinity, association rate and dissociation rate of [³H]-dihydroalprenolol ([³H]-DHA), a non-selective β -adrenoceptor (β -AR) antagonist, for human β_2 -adrenoceptors (β_2 -AR) transiently expressed in COS-7 cells.
- To characterize the β_2 -AR affinity of a series of compounds based on SOMS-1, a hit identified from a library of compounds as having β_2 -AR affinity.

2. Hit Optimisation: cAMP BRET assay

Aims:

- To investigate the structural basis of ligand potency and efficacy of a series of compounds (SOMS 1 – 11) for human β_2 -adrenoceptors (β_2 -AR) expressed in CHO-K1 cells. This data will be obtained using a BRET CAMYEL cAMP biosensor.

3. Hit Optimisation: Structure-Activity Relationships (Data Analysis)

Aims:

- To investigate the structural basis of β_2 AR affinity, potency and efficacy of a series of compounds (SOMS 1 – 11).
- To determine the physicochemical properties, lipophilicity and drug-likeness of a series of compounds (SOMS 1 – 11)

4. Computational Drug Design

Aims:

- To characterize the amino acids that contribute to affinity, potency and efficacy of a series of β_2 -AR compounds based on SOMS-1, a hit identified from a library of compounds as having β_2 -AR affinity.
- To predict receptor-ligand interactions that will improve compound affinity, potency and/or efficacy

How to Write a Scientific Paper (online practical)

Scientific communication is key to the advancement of scientific knowledge. The style in which scientific articles are written can seem at odds to other styles of writing you have been taught and are practiced at using. Scientific writing generally follows a specific format, broken down into sections. However, this format varies to some extent across scientific fields. Articles published in biomedical research journals have the following sections: (i) a title, to inform and attract readers, (ii) an abstract summarising the paper, (iii) an introduction to the topic and the hypotheses to be tested, (iv) a description of methods, (v) results section where the data is presented, and finally, (vi) a discussion that places the research in the context of the broader research field.

Although writing scientific reports can be daunting, the aim of this lesson is to help demystify this process and give you practice and guidance of what to put in each section.

Sources of Active Compounds

This lecture will explore the various sources of compounds that can be used to produce libraries for screening. These sources include isolation of compounds from natural sources, combinatorial methods of organic synthesis; fragment based approaches, and privileged motifs. The advantage and disadvantages of each source will be discussed. The use of ethnopharmacology to identify new therapeutic scaffolds and drug repurposing will also be examined.

Ligand-Based Drug Design

To improve the properties of a potential drug, structure-activity relationships are established to identify structural moieties that contribute to the binding and activity of a compound. Computational methods will be discussed in this lecture which can be used to model and predict these properties, and to screen databases for new leads. These methods include quantitative structure-activity relationship (QSAR) and pharmacophore determination. A pharmacophore defines the structural features and geometry of a drug that impart biological activity.

Structural Biology in Drug Development

A fundamental requirement of structure-based drug design (also termed rational drug design) is knowledge of the 3-dimensional structure of the target, generally a protein, sometimes a nucleic acid, occasionally a protein-nucleic acid complex. In this lecture, we will explore the experimental methods available for determining these structures, focusing on X-ray crystallography, NMR spectroscopy, and mass spectrometry and role they play in drug discovery and development.

Structure-Based Drug Design

Where the detailed three-dimensional structure of the protein target is available, structure-based computer-aided drug design methods can be utilised to identify and modify lead compounds. If the protein structure is not available, then computer models, based on structures of similar proteins, can be prepared and are suitable for structure-based drug design. This lecture will introduce structure-based drug design and protein modelling methods.

Intellectual Property

The basic principles underlying the protection of intellectual property will be discussed, focussing on the legal issues relevant to the patenting of pharmaceutical agents. We will discuss the types of patents available and what can be protected, the notions of disclosure, prior art, innovation, challenges, and what needs to be included in a patent application.

Case Studies in Drug Discovery

In this lecture we will look at the path that some drugs travelled to get to the clinical. This lecture will highlight the challenges and triumphs the drug discovery and development teams faced.

Bioavailability

This lecture will explore the importance of pharmacokinetics in the clinical actions of a drug and how compound structure and chemical properties effect drug absorption, distribution, metabolism and elimination. We will focus on what properties of a compound need to be optimized to improve oral availability, metabolic stability and membrane permeability. We will look at the available tools to predict these desirable qualities. We will also discuss the specialized case of drugs targeting the central nervous system and what is required to get them pass the blood brain barrier.

Pro-drugs and Drug Delivery

An inactive derivative of a known active drug may be called a prodrug and requires transformation within the body in order to release the active drug. Prodrugs can provide improved physiochemical properties such as solubility and enhanced delivery characteristics and / or therapeutic effect. This lecture outlines barriers to drug action, pro-drugs as drug delivery systems, and the application of pharmacokinetics and pharmacodynamics in drug delivery.

3. Pre-Clinical & Clinical Development

Pre-clinical Toxicology: *In Vitro*

In this lecture the role of *in vitro* toxicity tests in assessing the safety of new drugs will be addressed. How the *in vitro* toxicity tests that are required by the world's regulatory bodies, including tests for genotoxicity and cytotoxicity, are performed will be discussed. The role of Good Laboratory Practice in performing these tests will also be covered.

Pre-clinical Toxicology: *In Vivo*

The role of *in vivo* toxicity tests in establishing the safety of new drugs will be discussed in this lecture. The different types of *in vivo* tests in general toxicity testing, and when they are required to be performed by the regulatory bodies will be covered. The suite of safety pharmacology tests that is required will also be discussed.

Pre-clinical Toxicology Practical: Ames test

The assessment of the genotoxicity is the first step in the safety assessment of a compound. Lead compounds with optimised affinity, potency and efficacy will be assessed to determine their genotoxicity using an Ames Test.

Aims:

- To assess the *in vitro* genotoxicity of potential lead compounds being developed for a variety of indications, including COPD. Genotoxicity will be determined using *Salmonella typhimurium* TA100 in an Ames Test. Enzymatic bioactivation with liver S9 fraction will be demonstrated.

Clinical Trials

The regulation of therapeutic products and the phases (I-IV) of clinical trial that a drug must pass through before registration will be covered in this lecture.

Clinical Trial Design

This lecture will cover clinical trial design. The components of clinical trial design to be discussed will be: aims, design, controls and placebo, blinding, randomisation procedures, sample size, statistics, endpoints and ethics.

Ethics of Human and Animal Experimentation

In this lecture we will discuss the ethical conduct of biomedical research, including the policies governing biomedical and animal research in Australia. The role of institutional human ethics committees and what constitutes informed consent will be discussed. The general principles for the care and use of animals for scientific purposes and the 3 R's, replacement, reduction and refinement will be covered and the role of institutional animal ethics committees will be covered. Regulations to limit any harm and distress to research subjects, and research integrity will be discussed.

Phase I Clinical Trials Centre Site Visit

In this practical class we will be visiting the Scientia Clinical Research facility. This newly opened facility conducts early and later phase clinical trials. We will be shown the inner workings of a trial centre, meet with clinical researchers, and discuss the process of getting a patient on a trial. To develop an understanding of phase I clinical trials, you will also communicate and collaborate in a team to design and conduct a clinical trial.

4. Registration & Commercialisation

Biopharmaceuticals

This lecture will introduce therapeutic proteins, also called biopharmaceuticals or biologics. In general, this includes vaccines, blood, blood components or derivatives, plasma derivatives, recombinant DNA (rDNA) products, monoclonal antibody, therapeutic serum, toxin, antitoxin, cell and gene therapy products involved in the prevention, treatment or cure of a disease or condition of human beings. A subset of these, monoclonal antibodies, antibody substitutes and fusion proteins (cytokine fusions and receptor fusions) follow a similar workflow to that employed for small molecule drugs and some of the similarities and differences in discovery and development will be highlighted.

Regulatory Affairs

The role of regulatory affairs in the therapeutics industry will be discussed. The regulatory systems in Australia and the legal basis for the regulation of therapeutic products will be covered. We will discuss why the therapeutics industry is so highly regulated and the role of the regulatory affairs professional in ensuring optimal product indications and maintenance of products on the market.

Commercial Considerations: Marketing and Phase IV

Commercial considerations in drug development will be covered from target discovery, indication selection and lead identification, through safety assessments, clinical trials and marketing. What drives decisions (Go/No-Go), time-scales, program planning and the interactive perspectives of different groups in small and large pharma companies will be covered.

Careers in Drug Discovery

This workshop will take place during the practical time slot in week 12. Invited guests working in different phases of the drug development process will talk about their career path and provide insight into the jobs they do.

PHAR3101 Drug Discovery, Design and Development – Timetable 2018

Wk	Start. Mon	Practical Tuesday 2-5pm WW	Tutorial Wed 9am or 10 am AGSM LG06	Lecture 1 Wednesday 11am WWLG02	Lecture 2 Thursday 9am LG02
1	23/7	Drug discovery process A. Finch		The drug discovery process: Choosing the project A. Finch	Novel target identification and validation P. Gunning
2	30/7	Target validation P. Gunning	The drug discovery process: Choosing the project	Gene technology in target ID and Validation N. Kumar	Target Selection A. Finch
3	6/8	Drug validation P. Gunning	Target selection and validation	Hit identification A. Finch	High-throughput screening A. Finch
4	13/8	Hit optimisation: radioligand binding A. Finch	Hit optimisation & HTS screening	Sources of active compounds A. Finch	Ligand-based drug design A. Finch
5	20/8	Hit optimisation: cAMP A. Finch	Structure Activity Relationships	Structural biology in drug development A. Stewart	Structure-based drug design A. Finch
6	27/8	Hit optimisation: data analysis A. Finch		Progress Exam	
7	3/9	Computational Drug discovery A. Finch	Structural based drug discovery	Intellectual property A. Finch	Case studies in drug discovery A. Finch
8	10/9	How to write of scientific paper (online activity) A. Finch	Sources of active compounds & Intellectual Property	Bioavailability A. Finch	Pro-drugs and drug delivery T. Binder
9	17/9		Drug Delivery and Bioavailability	Pre-clinical toxicology – <i>in vitro</i> N. Kumar	Pre-clinical toxicology – <i>in vivo</i> N. Kumar
Mid-semester break					
10	1/10	Preclinical toxicology: Ames test 1 N. Kumar	Pre-clinical toxicology	Clinical trials N. Kumar	Clinical trial design N. Kumar
11	8/10	Preclinical toxicology: Ames test 2 N. Kumar	Clinical trial design	Ethics of human and animal experimentation N. Kumar	Biopharmaceuticals T. Domagala
12	15/10	Phase I Clinical Trials A. Finch & N. Kumar	Drug discovery process	Regulatory Affairs O Chisholm	Commercialisation: marketing and phase 4 O. Chisholm
13	23/10	Careers in Drug Discovery A. Finch	Biopharmaceuticals & Regulatory Affairs		

Assessment Tasks

Task	Due Date
Stages of Drug Design and Development Process	
Therapeutic product development history timeline (1 st submission)	Monday 13 th August, 9 am
Peer review of Therapeutic product development history timelines	Monday 20 th August, 9 am
Therapeutic product development history timeline (Final submission)	Monday 3 rd September, 9am
Teamwork in the stages of the drug discovery and development process	Monday 23 rd October, 9am
Progress Exam	Wednesday, 29 th August, 11 am
Research Manuscript	Monday 1 st October, 9 am
Final Examination	Official exam period
Formative tasks	Each tutorial

Formative Assessment

The goal of formative assessment is to provide ongoing feedback that you can use to improve your learning. Formative assessment tasks help students identify their strengths and weaknesses and therefore the areas they should focus on.

Exams

The questions will be based on the material covered in the lectures, practical classes and tutorials.

Progress examination (10%) will be held in the lecture slot at **11 am on Wednesday the 29th of August**. This exam will give you feedback on how you are succeeding in the course. This examination consists of two parts (A & B):

- Part A consists of 3 short answer questions, each worth 10 marks. Answer 2 of these questions. If you answer more than 2 questions, only the first 2 will be marked
- Part B consists of 2 long answer questions, each worth 20 marks. Answer 1 of these questions. If you answer more than 1 question, only the first 1 will be marked.

Final Examination (55%) will be held in the official exam period.

The examination consists of two parts (A & B)

- Part A consists of 6 short answer questions, each worth 10 marks. Answer 3 of these questions. If you answer more than 3 questions, only the first 3 will be marked.
- Part B consists of 6 long answer questions, each worth 20 marks. Answer 4 of these questions. If you answer more than 4 questions, only the first 4 will be marked

Material covered prior to the progress exam may be again examined in the final exam.

Research Manuscript

You research team (Somsceuticals Respiratory Disease Division) is working on a draft of a manuscript using the data you have collected on the SOMS compounds during the practicals in weeks 4-7. The team leader has sent you a draft that has the introduction and methods completed, your task is to now write the results and discussion of the paper. Word limit 2000±200 words (excluding references, tables, figures and figure legends).

The manuscript is to be submitted to the “journal editor” (through the Moodle site) by **9 am, 1st of October 2018**. A 10% penalty (per working day) will apply for late submissions.

The manuscript needs to contain the following sections:

1. Title, Authors & Addresses
2. Introduction
3. Methods
4. Results
5. Discussion and conclusions
6. List of references
7. Tables
8. Figures and Legends

Title, Authors and Addresses

The title should contain no more than 150 characters (including spaces) and should not consist of more than one sentence. It must clearly indicate the subject matter of the paper. Titles should indicate broadly what the paper is about. Following the title the name (and student number) and address (Respiratory Disease Division, Somsceuticals, NSW, Australia) of the author should be given.

Results

The results section includes:

- i. A written description in paragraph format of the experimental results. When results are reported, the mean results with standard errors, and the number of observations, and statistical significance should be given. Conclusions or interpretation of results should not be presented.
- ii. A graph and figure legend of the competition binding data (do not include the saturation binding, temperature or time course graphs)
- iii. A graph and figure legend of the mean % maximum isopertenolol response data
- iv. A table of the K_i and affinity relative to SOMS-1 values for each compound
- v. A table of Mean Log $EC_{50} \pm SE$, mean EC_{50} , Δ and relative potency for each compound
- vi. A table of Molecular Properties data (*ie* $m\text{LogP}$, MW, $n\text{rotb}$, TPSA)
- vii. A table of π data for each R group
- viii. You may also include data from week 7's practical if you wish, in table or figure form.

Tables: Each table should have a brief descriptive title. Each column should have a heading and the units of measurement should be given in parentheses in the heading. Use either scientific notation or general number format not both in a given column. Limit numbers to 2 decimal places. Tables should be self-explanatory, with necessary descriptions of each heading provided underneath the table.

Figures and Legends

Figure legends should explain the figures in sufficient detail that, whenever possible, they can be

understood without reference to the text. A very brief description of the experimental method, including “n’s” and statistical measurements should be included. Do not summarise your results in the figure legend.

Discussion and Conclusions

The purpose of the discussion is to present a brief interpretation of the results with reference to other scientific studies. Repeating the results should be avoided. The main conclusions should be conveyed in a final paragraph with a clear statement of how the study advances knowledge and understanding in the field.

Your discussion should address the following points:

1. What relationship if any exists between each of the functional groups and the potency, affinity and efficacy of each compound? *TIP: to do this you need to compare compounds that only differ at one R group.*
2. Is there a relationship between π of specific functional groups and potency, efficacy and affinity of the compounds?
3. Do the molecular interactions identified in the docking of the ligands with of the β_2 -adrenoceptor explain your results? What are the known important interactions that the β_2 -adrenoceptor ligands make with the receptor and how do they compare to what you found?
4. How do your findings compare to other research on β_2 -adrenoceptor ligands?
5. Do the compounds have suitable lead-like or drug like qualities? *Hint: think about the likely route of administration of the drug.*
6. Have you identified a suitable drug candidate for further development?

Citations

In the text, references to other work should take the form: (Bolton and Kitamura, 1983) or ‘Bolton and Kitamura (1983) showed that...’

References

The reference list at the end of the manuscript must be arranged alphabetically according to the surname of the first author. When the surnames of first authors are identical, the alphabetical order of the surnames of subsequent authors takes precedence over the year of publication. The authors’ names are followed by the year of publication in brackets. If more than one paper by the same authors in one year is cited, a, b, c, etc. are placed after the year of publication, both in the text and in the list of references. All authors should be quoted for papers with up to six authors; for papers with more than six authors, the first six should be quoted followed by *et al.* For example:

Journal Reference

Connor M, Kitchen I (2006). Has the sun set on κ_3 -opioid receptors? *Br J Pharmacol* 147: 349–350.

Book Reference

McGrath, JC, Daly CJ (2005). Imaging adrenergic receptors and their function: the use of fluorescent ligands and receptors to visualize adrenergic receptors. In: Perez DM (ed). *The Adrenergic Receptors, in the 21st Century*. Humana Press: New Jersey, pp 65–72.

Formatting and Technical Instructions

Times New Roman font, size 12, with 1.5 line-spacing throughout the manuscript. Margins at top and bottom and both sides should be 3 cm. *The text should **not** be in two columns.*

PRACTICAL REPORT: MARKING CRITERIA

	Exemplary (>8.5)	Very Good (8.4-7.5)	Good (7.4-6.5)	Satisfactory (6.4-5.0)	Unacceptable (<5.0)
Title and Formatting _____ x 0.5	Title clearly indicates the subject matter of the paper. Name and student number and departmental address given. Correct formatting. Word count 2000 ± 200.	Title indicates the subject matter of the paper. Name and student number and departmental address given. Minor errors in formatting. Word count 2000 ± 200.	Title indicates the subject matter of the paper. Name and student number and departmental address given. Errors in formatting. Word count 2000 ± 200.	Title does not indicate the subject matter of the paper. Name and student number and departmental address given. Errors in formatting. Word count > 2200.	Title, author's name and/or address not given. Formatting requirements not followed. Word count >2200 or <1800.
Results _____ x 2	Excellent description of the experimental results. No conclusions or interpretation of results presented.	Good description of the experimental results. No conclusions or interpretation of results presented.	Good description of the experimental results. Lacks some required detail. No conclusions or interpretation of results presented.	Description of the experimental results lacks required detail. Some conclusions or interpretation of results presented.	No description of results. Results not written in paragraph style.
Tables, Figures & Legends _____ x 1.5	Graph axes labelled, and units of measurement given. Legends explain the figures in sufficient detail that they can be understood without reference to the text. Tables self-explanatory, with necessary descriptions provided in footnotes underneath the table. Data analysis was performed correctly	Graph axes labelled, and units of measurement given. Legends explain the figures in sufficient detail that they can be understood without reference to the text. Tables self-explanatory, with footnotes underneath the table. A few minor errors in data presentation. Minor errors in data analysis.	Graph axes labelled, and units of measurement given. Not all legends explain the figures in sufficient detail that they can be understood without reference to the text. Most tables self-explanatory, with footnotes underneath the table. Some minor errors in data presentation. A few errors or omissions in data analysis	Most graph axes labelled, and units of measurement given. Not all legends explain the figures in sufficient detail that they can be understood without reference to the text. Most tables are self-explanatory. Some significant errors in data presentation. Some errors or omissions in data analysis.	Results poorly presented or missing. Graph axes not labelled and units of measurement absent. Legends do not explain the figures in sufficient detail that they can be understood without reference to the text. Tables are not self-explanatory. Errors in data analysis. Some data analysis not presented
Discussion & Conclusion _____ x 4	Discussion is clear and succinct. Extensive interpretation of the results with reference to previous scientific studies. No re-statement of the results. Main conclusions conveyed in a final paragraph.	Good interpretation of the results, greater reference to previous scientific studies needed. Some re-statement of the results. Main conclusions conveyed in a final paragraph.	Some interpretation of the results, greater reference to previous scientific studies needed. Minor errors in interpretation of the results. Some re-statement of the results. Conclusions conveyed in a final paragraph.	Some interpretation of the results, greater reference to previous scientific studies needed. Errors in interpretation of the results. Some re-statement of the results. Some conclusions conveyed in a final paragraph.	No interpretation of the results with reference to previous scientific studies given. Results presented. Main conclusions not conveyed in a final paragraph.
Referencing _____ x 1	In-text citations and reference list follow BJP conventions. Relevant information selected. A wide range of references used.	In-text citations and reference list follow BJP conventions. Relevant information selected. A wider range of references needed.	In-text citations and reference list follow BJP conventions, with minor errors. Relevant information selected. A wider range of references needed.	In-text citations and/or reference do not follow BJP conventions. Relevant information selected. A wider range of references needed.	BJP conventions not followed. Non-peer reviewed sources used. Information in introduction and discussion not referenced. Wider range of references needed.
Writing Conventions _____ x 1	Excellent sentence structure, correct grammar and word usage. Sentences and paragraphs well connected. Appropriate written expression-using discipline specific vocabulary and formal not oral language. Has been proof read.	Good sentence structure, correct grammar and word usage. Sentences and paragraphs well connected. Appropriate written expression- using discipline specific vocabulary and formal not oral language. Proof reading needed to eliminate minor errors.	Good sentence structure, correct grammar & word usage. Most sentences/paragraphs well connected. Appropriate written expression-better use of discipline specific vocabulary & formal language needed. Proof reading needed.	Poor sentence structure, grammar & word usage. Sentences & paragraphs not well connected. Appropriate written expression-better use of discipline specific vocabulary & formal language needed. Proof reading needed.	Use of paragraphs and improved sentence structure needed. The report is difficult to read due to poor grammar and word usage. No evidence of proof reading.
TOTAL /100					

Stages of Drug Design and Development Process

Part A: Therapeutic product development history (10%)

1. Each team will produce a timeline of the drug design and development process of their assigned drug, highlighting the major milestones in the journey that the drug took from bench to bedside. This should include at least one entry for the following stages of the drug design and development process for the given drug: (A) Target Selection, (B) Lead Discovery, (C) Preclinical Development, (D) Clinical Trials, and (E) Registration. *See below for more details of each section*

You can be creative as you like in producing your timeline, using any medium to produce your timeline (e.g. a video, an animation, infographic) with the overall aim to educate a peer audience about the major milestones along the path the drug took from bench to bedside. Some suggestions are to use online timeline production freeware, a video, an animation, drawing program etc.

2. Each student will then provide feedback on the effectiveness of two other groups timeline in educating them about the major milestones and challenges faced for the drug in question. Each student will review 2 timelines and will be assessed on their effective use of the RISE model of feedback.
3. The groups will then update their timeline for final submission and grading and write a summary (<250 words) of how they used the feedback they received to improve their timeline.
4. Team members will also provide an assessment of each members contribution to the team for this component of the assignment and this will be used to moderate each individual's grade.

Part B: Teamwork in the drug discovery and development process (5%)

1. Each student team will produce an infographic to educate a peer audience that explores teamwork in the pharmaceutical industry. This could include the use of cross-functional teams, the roles within teams at each stage of the process and how they work together in or across each stage of the drug design and development process.
2. Team members will also provide an assessment of each members contribution to the team for this component of the assignment and this will be used to moderate each individual's grade.

Part A: Therapeutic product development history timeline

Criteria	Exemplary (5)	Very Good (4)	Good (3)	Improvement Needed (2)	Unacceptable (1)
Quality of content x 1.5	Included events are important and interesting. No major details are missing.	The included events are important or interesting. One or two major events are missing.	Most of the included events are important or interesting. Some major events are missing.	Some events included are trivial, and/or major events are missing.	Most of the major events are missing, and/or too many trivial events are included.
Accuracy of Content x 1.5	Facts are accurate for all events reported on the timeline.	Facts are accurate for almost all events reported on the timeline.	Facts are accurate for most of the events reported on the timeline.	Facts are accurate for some of the events reported on the timeline.	Facts are often inaccurate for the events reported on the timeline.
Referencing x 1	The data and facts presented are evidence based from reliable sources. Source of all material is cited appropriately.	The data and facts presented are evidence based from reliable sources. Most sources of the material are cited appropriately.	Most of the data and facts presented are evidence based from reliable sources. Most sources of the material are cited appropriately.	Some of the data and facts presented are evidence based from reliable sources. Several sources of the material are not cited or cited inappropriately.	Extensive use of non-peer reviewed sources. Information provided not cited appropriately.
Audio and/or visual aids x 2	Audio/visual material engages the audience. All graphics are effective and balanced with text use. The audio/visual components greatly enhanced the timeline.	Audio/visual material engages the audience. Most of the graphics are effective and balanced with text use. The audio/visual components enhanced the timeline.	Audio/visual material engages the audience. Some of the graphics are not effective or balanced with text use. The audio/visual components add to the timeline.	Audio/visual material conveys the material but does not grab the interest of the audience. The ratio of graphics & text is not balanced.	Audio/visual material does not enhance the presentation or was missing.
1st submission x 0.5	Completed to a very high standard of presentation.	Completed to a high standard of presentation.	Completed to a good standard of presentation.	Complete but of a poor standard of presentation.	Incomplete.
Response to feedback x 1.5	A thoughtful and considered response to feedback received. Incorporated feedback to improve final product. <250 words. No grammatical and spelling errors.	A considered response to feedback received. Incorporated most of the feedback appropriately to improve final product. <250 words. No grammatical and spelling errors.	A concise response to feedback. Partially incorporate feedback. Exceed the word limit, or with a few grammatical or spelling errors.	A concise response to feedback. Partially incorporate feedback. Grammatical and spelling errors appeared frequently.	Provide no or poor response to feedback.
Peer Review x 2	Provided positive and constructive critique of the work, employ the four stages of the RISE model to great effect.	Provided positive and/or constructive critique of the work, employ the four stages of the RISE model.	Provided positive and/or constructive critique of the work, did not effectively employ the four stages of the RISE model.	Failed to provide positive and/or constructive critique of the work, did not employ the four stages of the RISE model.	Provided no critique of the work.

Part B: Teamwork in the drug discovery and development process

Criteria	Exemplary (5)	Very Good (4)	Good (3)	Improvement Needed (2)	Unacceptable (1)
Message Clarity x 2	The topic and message of the infographic are clear and easily understood; it strongly educates the viewer on the role of teamwork in the pharmaceutical industry	The topic and message of the infographic are mostly clear and easily understood; it educates the viewer on the role of teamwork in the pharmaceutical industry	The topic and message of the infographic are mostly easily understood; it educates the viewer to some extent on the role of teamwork in the pharmaceutical industry	The topic and message of the infographic are not easily understood; it superficially informs the viewer of the role of teamwork in the pharmaceutical industry	The topic and message of the infographic are not easily understood; it does not inform the viewer of the role of teamwork in the pharmaceutical industry
Details X 1	Details support and enhance the main idea without distracting from the main message.	Details support the main idea without distracting from the main message.	Details support the main idea but are sometimes distracting from the main message	Details either lacking or distract from the main message.	Lacks detail to support the main message
Referencing x 0.5	The data and facts presented are evidence based from reliable sources. Source of all material is cited appropriately.	The data and facts presented are evidence based from reliable sources. Most sources of the material are cited appropriately.	Most of the data and facts presented are evidence based from reliable sources. Most sources of the material are cited appropriately	Some of the data and facts presented are evidence based from reliable sources. Several sources of the material are not cited or cited inappropriately	Extensive use of non-peer reviewed sources. Information provided not cited appropriately.
Graphics x 1.5	The graphics used strongly convey the information. Graphics engage the audience. All graphics are effective and balanced with text use. The graphic components greatly enhance the delivery of the content.	The graphics used convey the information. Most of the graphics are effective and balanced with text use. The graphic components enhance the delivery of the content.	The graphics used mostly convey the information. Some of the graphics are effective and balanced with text use. The graphic components somewhat enhance the delivery of the content.	The graphics used convey the information but does not grab the interest of the audience. The ratio of graphics & text is not balanced. The graphic components detract from the delivery of the content.	The graphics do not enhance the presentation or are missing. The graphic components detract from the delivery of the content