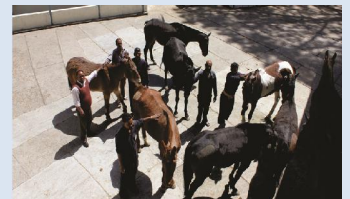


**GENERAL INSTRUCTIONS
AND
COURSE CURRICULUM**

**POST GRADUATE DIPLOMA
VACCINOLOGY &
IMMUNOBIOLOGICALS**



Effective from:
JULY 2018



Course offered by

CENTRAL RESEARCH INSTITUTE, KASALI

KASALI-173204 (H.P.), INDIA

CENTRAL RESEARCH INSTITUTE, KASALI
KASALI-173204

POST-GRADUATE DIPLOMA PROGRAMME ON
VACCINOLOGY & IMMUNOBIOLOGICALS [PGD-VI]

GENERAL INSTRUCTIONS/GUIDELINES FOR EXECUTION OF CURRICULUM

1. The Post-Graduate Diploma programme on Vaccinology & Immunobiologicals [PGD-VI] will be of one year duration spread over two semesters.
2. There will be eight courses to be taught and examined under PGD-VI program. In the first and second semester, there will be four courses each including one project course consisting of Project Report, Seminar and Viva-Voce in each semester.
3. The distribution of marks in theory, practical and internal assessment in various courses has been given in the OUTLINES OF COURSES FOR POST-GRADUATE DIPLOMA ON VACCINOLOGY AND IMMUNOBIOLOGICALS.
4. The split for Internal Assessment component will be: i) Two Internal Assessment tests of 10 marks each (20 Multiple choice questions, each question shall carry 0.5 marks in each test) in each course. Remaining 10 marks will include Class Seminar (5 marks) and Class Attendance (5 marks). The criteria to be followed to award marks shall be: i) up to 75% lectures including condonation of lectures as per Ordinances: Zero mark, ii) without condonation of lectures up to 75%: 1.0 mark; iii) 76-80% lectures: 2.0 marks, iv) 81-85% lectures: 3.0 marks; v) 86-90% lectures: 4.0 marks; and vi) 91% and above lectures: 5.0 marks.
5. For Internal Assessment, the teacher teaching the course will examine the students in his/her subject by giving multiple choice questions (MCQ)-based examination covering the syllabus/topics taught in the classes. The Head of Department/ Chairperson of the department offering the programme will notify the date sheet for Internal Assessment test(s) at the beginning of semester/academic calendar. In case a student is absent in the internal assessment test, the student will explain in writing the reason of his/ her absence to the Head of Department/ Chairperson of the Department. Such case(s), if any will be discussed in the Departmental Council/Staff Council, and if it finds the reason given by the student valid, it may recommend to the Head of Department/ Chairperson of the programme to allow the student to sit in such test separately.
6. The candidate who regularly attends teaching/ practical classes and maintains 75% attendance in each of the courses/ practical shall be permitted to sit in the semester examinations.
7. Any candidate who intends to participate in intra-university or inter-university cultural/ sports/ extracurricular function(s) shall get her/ his name recommended by the Head of Department/ Chairperson for being considered for any such participation(s) and benefit(s) if any, thereof.
8. The project work will be in the specialized area of the vaccine, antisera preparation, diagnostic reagent manufacturing and animal care. The project work will start from the onset of each semester. The students will submit the project report by the due date

specified / notified by the Head of Department/ Chairperson. The Faculty/ Departmental Council will evaluate these reports. There will be a viva-voce examination on the project report conducted by the Departmental Council. If the Head of Department/ Chairperson of the programme feels, he/ she may invite an External Expert for evaluation of the reports. The evaluation of the project report and seminar/viva voce will be of 30 and 20 marks, respectively.

9. The candidate has to secure minimum pass marks individually in Theory paper, Practical as well as Internal Assessment in concerned course. A candidate thus failing in any of these components shall be considered failed in that course.
10. The admission to PGD-VI program offered by Central Research Institute, Kasauli (affiliated to Himachal Pradesh University, Shimla) will be strictly on merit basis or as decided by Himachal Pradesh University, Shimla from time to time.
11. Eligibility criteria for the admission of a candidate to PGD-VI program will be: Master's Degree in any discipline of life sciences including Microbiology, Medical Microbiology, Biochemistry, Biotechnology, Immunology, Botany, Zoology etc. or MD/ M.V.Sc from any Institute/ University recognized by the Himachal Pradesh University, Shimla with at least 55% aggregate marks for General Category, and 50% marks for the SC/ ST Category students..
12. The tuition fee and other annual charges will be as follows:

S.No.	Item	Amount (Rs)
1.	Course Fee	48000/-
2.	Institutional Security*	10000/-
3.	Library Security*	2000/-

* The institutional and library security will be refunded after completion of the course.

OUTLINES OF COURSES FOR POST GRADUATE DIPLOMA ON VACCINOLOGY & IMMUNOBIOLOGICALS

Course No.	Title of Course	Marks			Total Marks
		Theory	Practical	Internal Assessment	
<i>Semester I</i>					
PGDVI-101	Vaccine Production	80	40	30	150
PGDVI-102	Antisera Production	80	40	30	150
PGDVI-103	Diagnostic Reagent Production	80	40	30	150
PGDVI-104	Project report and Viva-Voce	-	-	50	50
Total Marks in Semester I		240	120	140	500
<i>Semester II</i>					
PGDVI-201	Quality Control	80	40	30	150
PGDVI-202	Quality Assurance and cGMP	80	40	30	150
PGDVI-203	Animal Care and Management	80	40	30	150
PGDVI-204	Project Report and Viva-Voce*	-	-	50	50
Total marks in Semester II		240	120	140	500
Grand Total (Semester I-II)		480	240	280	1000

*The External Examiner may evaluate the Project report submitted by the candidate(s), and will conduct seminar and viva-voce examination of the students.

FIRST SEMESTER COURSES

COURSE PGDVI-101: VACCINE PRODUCTION

Maximum Marks – 80

Teaching Hours – 45

Note:The Examiner will set a total of nine (9) questions covering all topics/units of the prescribed course by setting at least two questions from each unit. Out of the nine questions, one question containing eight (8) short-answer type questions that will cover entire course will be compulsory. The candidate will attempt a total of five questions (one from each unit) including the compulsory question. All questions will carry equal marks.

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UNIT-I **12**

Historical background of vaccination, vaccine preventable infectious diseases, human vaccine manufacturers and licensed vaccines. Over view of bacterial and viral vaccines and their importance to public health. Epidemiology and pathophysiology of vaccine preventable diseases with special emphasis on Diphtheria, Tetanus and Pertussis.

UNIT-II **11**

Conventional and modern methodologies to bacterial seed strain characterization. Overview of the immune system and basic aspects of immune response(s) to vaccines. Adjuvants: history, types, mechanisms and current achievements. Immunization strategies for disease control and eradication. New vaccines under development and prominent vaccine delivery systems. Production life cycle of inactivated bacterial vaccine: DTwP, Adsorbed.

UNIT-III **11**

Overview of national and international regulatory requirements/ guidance for production, quality control and Current Good Manufacturing Practices (cGMP) implementation. Importance and implementation of cGMP in the production of safe and efficacious biological products/ vaccines, and clean-in-place (CIP) cycle development for process equipment. Equipment cleaning and validation. Validation of sterilization equipment's.

UNIT-IV **11**

Consistency approach for vaccine quality improvement. Toxicity and potency evaluation of bacterial and viral vaccines: overview of currently approved methods and alternative methods under development.

Suggested books [Latest edition]

1. Vaccines. 6th Edition, Stanley Plotkin Walter Orenstein Paul Offit.
2. New Generation Vaccines. Fourth Edition, Myrone M. Levine , Myron M. Levine, Gordon Dougan , Michael F. Good , Margaret A. Liu , Gary J. Nabel , James P. Nataro, Rino Rappuoli.
3. Vaccine Development and Manufacturing. Emily P. Wen (Editor), Ronald Ellis (Editor), Narahari S. Pujar (Editor).
4. Vaccines & Vaccine Technologies. Jose Ronnie Vasconcelos.
5. Indian Pharmacopeia.
6. Schedule M, Drugs and Cosmetics Act.
7. Kuby Immunology. Thomas J. Kindt, Richard A. Goldsby, Barbara A. Osborne, Janis Kuby.
8. Immunology. 8th Edition, David Male Jonathan Brostoff David Roth Ivan Roitt.

List of Practicals

1. Aseptic handling and manipulation of bacterial cultures.
2. Lyophilisation of aerobic and anaerobic live bacterial cultures.
3. CIP (clean-in-place) and SIP (sterilization-in-place) of process equipment's
4. Cultivation of aerobic bacteria (*C. diphtheria* and *Bordetella pertussis*): conventional methods and bioreactor technology.
5. Cultivation of anaerobic bacteria (*Clostridium tetani*): conventional methods and bioreactor technology.
6. Aseptic harvest of bacterial mass: micro filtration and batch centrifugation.
7. Concentration, purification and sterile filtration of diphtheria and tetanus toxoids.
8. Toxicity and potency evaluation (*Corynebacteriumdiphtheria*, *B. pertussis* and *Clostridium tetani*).

COURSE PGDVI-102: ANTISERA PRODUCTION

Maximum Marks – 80

Teaching Hours – 45

Note:The Examiner will set a total of nine (9) questions covering all topics/units of the prescribed course by setting at least two questions from each unit. Out of the nine questions, one question containing eight (8) short-answer type questions that will cover entire course will be compulsory. The candidate will attempt a total of five questions (one from each unit) including the compulsory question. All questions will carry equal marks.

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UNIT-I 11

Introduction to therapeutic antisera and its importance. Antigens used for immunizations of Equines and storage of antigens. Adjuvants used in immunization of Equines. Storage of adjuvants. Washing of laboratory/production material. Sterilization of laboratory and production material. Cleaning of production and testing area. Fumigation of production and testing area. Environmental monitoring of production and testing area.

UNIT-II 12

Dose preparation for immunization of equines and immunization of equines for production of antisera. Manufacturing bleeding of equines for production of therapeutic antisera, collection and separation of plasma. Reinfusion of RBC's in equines.

UNIT-III 11

Processing of plasma for the production of therapeutic antisera: Pepsin treatment, precipitation with ammonium sulphate, dialysis of antisera, preparation of sub-lots, 0.45 μ M filtration of sub-lots, and preparation of final bulks of therapeutic antisera. Aseptic filtration of serum (0.22 μ M)

UNIT-IV 11

Testing of venoms (*in vivo* & *in vitro*). Testing of toxoid (*in vivo* & *in vitro*). Sterility testing, Abnormal toxicity testing, Test for pH, and Potency testing.

Suggested books [Latest edition]

1. WHO guidelines for the production control and regulations of snake antivenom immunoglobulin's.
2. Proteins. Walker, John M. (Ed.).
3. Immunochemical Protocols. Margaret M. Manson, Springer.

4. Current protocols in molecular biology, Wiley Interscience.
5. Indian Pharmacopeia.
6. Schedule M, Drugs and Cosmetics Act.

List of Practicals

1. Storage of antigens and adjuvants.
2. Preparation of laboratory for production of therapeutic antisera.
3. Environmental monitoring of production and testing area.
4. Dose preparation and immunization of equines.
5. Manufacturing bleeding, collection, separation of plasma, and reinfusion of RBC's in Equines for production of therapeutic antisera.
6. Processing of plasma: Pepsin treatment, Precipitation with ammonium sulphate, Dialysis of antisera, Preparation of sub lots, 0.45 μ filtration of sub lots.
7. Preparation of final bulk of antisera and its filtration.
8. Testing of venoms and toxoid (*in vivo* & *in vitro*).
9. Testing of antigen and product (pH, Sterility, Abnormal toxicity and Potency testing).

COURSE PGDVI-103: DIAGNOSTIC REAGENT PRODUCTION

Maximum Marks – 80

Teaching Hours – 45

Note: The Examiner will set a total of nine (9) questions covering all topics/units of the prescribed course by setting at least two questions from each unit. Out of the nine questions, one question containing eight (8) short-answer type questions that will cover entire course will be compulsory. The candidate will attempt a total of five questions (one from each unit) including the compulsory question. All questions will carry equal marks.

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UNIT-I

11

Introduction to diagnostic reagents. Production of *Salmonella* agglutinating suspension for Widal test: Introduction, Strains used, media used for morphological, biochemical and serological characterization of *Salmonella*. Harvesting and inactivation of bacterial culture, Opacity determination, Identity test (slide/tube agglutination test, titre determination by tube agglutination test), Preservation, filling, physical checking, labelling and storage of Widal antigens.

UNIT-II

11

Production of *Proteus* agglutinating suspension for Weil Felix Test: Introduction, Strains used, Media used for morphological, biochemical and serological characterization of *Proteus*, Harvesting and inactivation of culture, Opacity determination, Identity test (slide/tube agglutination test, titre determination by tube agglutination test), Preservation, filling, physical checking, labelling and storage of *Proteus* sp. antigens.

UNIT-III

12

Production of *Vibrio cholera* antisera: Introduction, Strains used, Media used for morphological, biochemical and serological characterization of *Vibrio cholera*, Harvesting and inactivation of culture, Opacity determination, Identity test (slide/tube agglutination test, titre determination by tube agglutination test), Immunization of rabbits, Bleeding of rabbits, Preparation of absorbing suspension of *V. Cholera*, Absorption of antiserum with absorbing suspension of *Vibrio cholera*, Filtration, preservation, labelling and storage of antisera.

UNIT-IV

11

Production of *Salmonella* antisera: Introduction, Strains used, Media used for morphological, biochemical and serological characterization of *Vibrio cholera*, Harvesting and inactivation of culture, Opacity determination, Identity test (slide/tube agglutination test, titre

determination by tube agglutination test), Immunization of rabbits, Bleeding of rabbits, Preparation of absorbing suspension of *Salmonella*, Absorption of antiserum with absorbing suspension of *Salmonella*, Filtration, preservation, labelling and storage of antisera.

Suggested books [Latest edition]

1. Proteins. Walker, John M. (Ed.).
2. Immunochemical Protocols. Margaret M. Manson, Springer.
3. Current protocols in molecular biology, Wiley Interscience.
4. Guidelines on Quality of Diagnostic Reagents for Health Laboratories.
5. Schedule M, Drugs and Cosmetics Act.

List of Practicals

1. Revival of freeze dried culture.
2. Morphological, biochemical and serological characterization of bacterial culture.
3. Inoculation of media containing bottles.
4. Harvesting of growth and inactivation of culture.
5. Opacity determination by Brown's opacity method.
6. Identity test by slide agglutination and titre determination by tube agglutination method.
7. Immunization of rabbits.
8. Test bleeding and titration of antiserum.
9. Final bleeding and titration of antiserum.
10. Preparations of absorbing suspension of cross reacting antigen.
11. Absorption of antiserum with absorbing suspension of antigen.
12. Purification of antibody by affinity chromatography.
13. Conjugation of antibody and purification.

COURSE PGDVI-104: PROJECT REPORT

Maximum Marks – 50

Each of the candidates will carry out the project work assigned to him/her. The candidate will submit three copies of project report performed by him/her duly certified by the supervisor. The report should cover the abstract, introduction, literature review, materials and methods, results and discussion, conclusion and references. The references will be arranged alphabetically under the format given below:

Bibliography style to be followed:

Referred journal

Bhalla TC, Sharma NN and Sharma M (2006). Expression of alkaline protease in *Rhodococcus* sp. J Appl Biotechnol 32: 225-230.

Books

Demartino GN (1996). Purification of proteolytic enzyme. In: Proteolytic enzyme: a practical approach. Berjnon RJ and Bond JS (Ed. Or Eds.), IRL Press, New York, pp 120-180.

Thesis

Verma ML (2006). Production, purification and characterization of thermotolerant *P. Aeruginosa* lipase. Ph.D. Thesis, Himachal Pradesh University, Shimla, India.

Website

www.elsevier.com

- * The candidate will present a seminar and his/ her performance shall be evaluated by a viva-voce examination. The dissertation and viva-voce will carry 50 marks.

SECOND SEMESTER COURSES

COURSE PGDVI-201: QUALITY CONTROL

Maximum Marks – 80

Teaching Hours – 45

Note: The Examiner will set a total of nine (9) questions covering all topics/units of the prescribed course by setting at least two questions from each unit. Out of the nine questions, one question containing eight (8) short-answer type questions that will cover entire course will be compulsory. The candidate will attempt a total of five questions (one from each unit) including the compulsory question. All questions will carry equal marks.

UNIT-I

12

Introduction of quality control aspects, functions and working. Details of various tests performed in quality control division. Sampling procedure for in-process, final bulk and final lot. Maintenance and use of national reference standards for testing of vaccines. Preparation of in-house reference standard(s) and their use(es). Procedure for retention and destruction of used samples. Role of animals in the quality control testing of vaccines. Maintenance and handling of small laboratory animals during quality control testing. Disposal of dead and diseased animals, and ethical issues.

UNIT-II

11

Environmental monitoring: Introduction, classification, entry/exit into classified areas, Media used and Different tests performed. Non-viable particles count (at rest and in operation). Active viable air sampling of classified areas by HI-AIR PETRI™ AIR SAMPLING SYSTEM. Passive viable air sampling of classified area by settle plate method. Viable sampling of operator by Finger Dab Plating. Viable surface monitoring by Contact Plate method; Total time of exposure of media plates, incubation period at different temperatures, Reading after different time intervals. Preparation of results, documentation, reporting and maintenance of records.

UNIT-III

11

General tests on vaccine/sera: Sterility test, abnormal toxicity test, pH, volume and biochemical analysis. Tests on vaccine: Specific toxicity test and, potency test. Quality control tests of antisera: Potency test.

UNIT-IV

11

Water plant monitoring: Introduction, classification, entry/exit into classified area, Media used and different tests performed. Preparation of bottles for collection of water sample for

microbiological and biochemical analysis, Sampling of water samples from main water storage tank, collection of water sample from water generation plant, transportation of portable and pharmaceutical grade water samples from collection site to quality control division. Preparation of water testing media for determining coliforms and plate count. Determination of colony forming unit (CFU) count in portable and pharmaceutical grade water sample. Presumptive coliform count by most probable number, pH, conductivity, endotoxin test and chemical analysis.

Suggested books [Latest edition]

1. Indian Pharmacopeia.
2. British Pharmacopeia.
3. United States Pharmacopeia.
4. European Pharmacopeia.
5. Manual for Quality Control of Diphtheria, Tetanus and Pertussis Vaccines.
6. Vaccines. 6th Edition, Stanley Plotkin Walter Orenstein Paul Offit.

List of Practicals

1. Sampling procedure for in process, final bulk and final lot sample.
2. Maintenance of reference standards.
3. Procedure for keeping retained samples and destruction of left over samples.
4. Care, management and handling of small laboratory animals for testing.
5. Environmental monitoring (Non-viable particle counts, physical examination of media plates, active and passive viable air sampling, viable sampling of operator by Finger Dab Plating, viable surface monitoring by Contact Plate method).
6. Documentation and maintenance of records in QC.
7. QC testing (sterility, abnormal toxicity, growth promotion, fumigation, specific toxicity, Potency).
8. Estimation of thiomersal, formalin, aluminium, aluminium phosphate, gel estimation, total protein, phenol, and protein nitrogen.
9. Preparation of bottles, sampling and collection of water sample from main water storage tank & water generation plant for microbiological and biochemical analysis.
10. pH, conductivity, endotoxin test and determination of colony forming unit (CFU) count in portable and pharmaceutical grade water samples.
11. Presumptive coliform count by most probable number.
12. Chemical analyses including hardness, total dissolved solids, chloride, magnesium, oxidizable substances, iron and aluminium content.

COURSE PGDVI-202: QUALITY ASSURANCE AND cGMP

Maximum Marks – 80

Teaching Hours – 45

Note: The Examiner will set a total of nine (9) questions covering all topics/units of the prescribed course by setting at least two questions from each unit. Out of the nine questions, one question containing eight (8) short-answer type questions that will cover entire course will be compulsory. The candidate will attempt a total of five questions (one from each unit) including the compulsory question. All questions will carry equal marks.

UNIT-I **12**

Introduction to good ware-house practices and good laboratory practices. Introduction to quality management system (QMS), change control, deviation handling, corrective and preventive action, compliant handling, self-inspections, AEFI, training systems, line clearance, annual product review, batch released system, preparation of master formula record, batch manufacturing record, summary protocols and IPQA activity.

UNIT-II **11**

Introduction to quality assurance systems and their functions. Introduction to regulatory guideline, good manufacturing practices (GMP), Good Documentation Practices (GDP), document preparation, document control, document numbering, document issuance & withdrawal, and document revisions. Introduction to standard operating procedures: preparation and control.

UNIT-III **11**

Introduction to qualification systems of facility, equipment's and utilities, basic risk assessment, user requirement specification, design qualification, installation qualification, operational qualification and performance qualification.

UNIT-IV **11**

Introduction to validation, Process validation, cleaning validation and analytical validation.

Suggested books [Latest edition]

1. Schedule M, Central Drugs Standard Control Organization
2. Quality assurance of pharmaceuticals, World Health Organization.
3. Vaccines. 6th Edition, Stanley Plotkin Walter Orenstein Paul Offit.

List of Practicals

1. SOP preparation.
2. Case studies.
3. Preparation of qualification protocols.
4. Performance Quality assessment.
5. Self inspection.
6. Line clearance.
7. Training and case studies.
8. Validation protocols.
9. Good ware house practices.
10. Good laboratory practices.

COURSE PGDVI-203: ANIMAL CARE AND MANAGEMENT

Maximum Marks – 80

Teaching Hours – 45

Note: The Examiner will set a total of nine (9) questions covering all topics/units of the prescribed course by setting at least two questions from each unit. Out of the nine questions, one question containing eight (8) short-answer type questions that will cover entire course will be compulsory. The candidate will attempt a total of five questions (one from each unit) including the compulsory question. All questions will carry equal marks.

UNIT-I **12**

Introduction, types of laboratory animals, uses of laboratory animals, basic of selection of laboratory animals for different experimentation and animal used for antisera production. CPCSEA: Purpose and scope of CPCSEA, IAEC and the guidelines, Laboratory animal facility: Basic design of laboratory animal facility. GMP facility, WHO guidelines for laboratory animal facility, maintenance of record and documentation in animal facility.

UNIT-II **11**

Housing and care of laboratory animals: Nutrition, animal housing, climate control, behaviour and environment, maintenance and hygiene, handling and basic procedures, health monitoring, transportation, euthanasia, common diseases of laboratory animals and their management. Methods of disposal of dead animals, personal hygiene of staff working in animal facility, introduction to SPF and genetically modified laboratory animals.

UNIT-III **11**

Basic of selection of equines for antisera production, screening procedure, transportation of equines, quarantine of new equines, housing and care of equines. Handling, housing and hygiene, Nutrition and feeding, prophylactic measures, grooming, hoof care, care of sick and injured equines, Common disorder in equines used in production of biologicals.

UNIT-IV **11**

Hyper-immunized sera production: Introduction, immunization programme(s) and roots of immunogenic inoculation. Plasmapheresis: Introduction, CPCSEA guidelines and procedure.

Suggested books [Latest edition]

1. Guide for the Care and Use of Laboratory Animals: Eighth Edition 8th Edition.
2. The UFAW Handbook on the Care and Management of Laboratory and Other Research Animals, 8th Edition. Robert C. Hubrecht and James Kirkwood.

3. Handbook of Laboratory Animal Management and Welfare, 4th Edition. Sarah Wolfensohn and Maggie Lloyd.

List of Practicals

1. Visit to laboratory animal facility.
2. Types of laboratory animals and their handling.
3. Activities in laboratory animal facilities.
4. Inoculation of laboratory animals through different routes.
5. Methods of collection of blood in laboratory animals.
6. Visit to equines stables.
7. Handling and restraining of equines.
8. Grooming of equines.
9. Routes of inoculation in equines.
10. Plasmapheresis in equines.

COURSE PGDVI-204: PROJECT REPORT

Maximum Marks – 50

Each of the candidates will carry out the project work assigned to him/her. The candidate will submit three copies of project report performed by him/her duly certified by the supervisor. The report should cover the abstract, introduction, literature review, materials and methods, results and discussion, conclusion and references. The references will be arranged alphabetically under the format given below:

Bibliography style to be followed:

Referred journal

Bhalla TC, Sharma NN and Sharma M (2006). Expression of alkaline protease in *Rhodococcus* sp. J Appl Biotechnol 32: 225-230.

Book

Demartino GN (1996). Purification of proteolytic enzyme. In: Proteolytic enzyme: a practical approach. Berjnon RJ and Bond JS (Ed. Or Eds.), IRL Press, New York, pp 120-180.

Thesis

Verma ML (2006). Production, purification and characterization of thermotolerant *P. Aeruginosa* lipase. Ph.D. Thesis, Himachal Pradesh University, Shimla, India.

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www.elsevier.com

- * The candidate will present a seminar and his/ her performance shall be evaluated by a viva-voce examination. The dissertation and viva-voce will carry 50 marks.