UNIVERSITI SAINS MALAYSIA

Second Semester Examination
2012/2013 Academic Session

June 2013

EKC 376 – Downstream Processing of Biochemical and Pharmaceutical Products
[Proses Hiliran untuk Produk Biokimia dan Farmaseutikal]

Duration : 3 hours
[Masa : 3 jam]

Please ensure that this examination paper contains SIX printed pages and THREE printed pages of Appendix before you begin the examination.

[Sila pastikan bahawa kertas peperiksaan ini mengandungi ENAM muka surat yang bercetak dan TIGA muka surat Lampiran sebelum anda memulakan peperiksaan ini.]

Instructions: Answer **ALL** questions.

*[**Arahan:** Jawab **SEMUA** soalan.]*

In the event of any discrepancies, the English version shall be used.

[Sekiranya terdapat sebarang percanggahan pada soalan peperiksaan, versi Bahasa Inggeris hendaklah digunapakai].

Answer ALL questions.
Jawab SEMUA soalan.

1. Under Good Manufacturing Practice, Facilities Conceptual Design is concerning the segregation of process and building utilities to avoid contamination. Figure Q.1. is the facility layout of a bioprocessing industry.

Di bawah Amalan Pengilangan Baik, Rekabentuk Kemudahan Konseptual adalah mengenai proses pengasingan dan utiliti bangunan untuk mengelakkan pencemaran. Rajah S.1. adalah susun atur kemudahan industri biopemprosesan.

[a] Proposed the material and personnel traffic (show directly on the sketch sheet)

Cadangkan trafik bagi bahan dan kakitangan tersebut (tunjukkan secara langsung pada lembaran lakaran). *[6 marks/markah]*

[b] Suggest on how to prevent contamination between the corridor and the work zone.

Cadangkan bagaimana untuk mengelakkan pencemaran antara koridor dan zon kerja. *[4 marks/markah]*

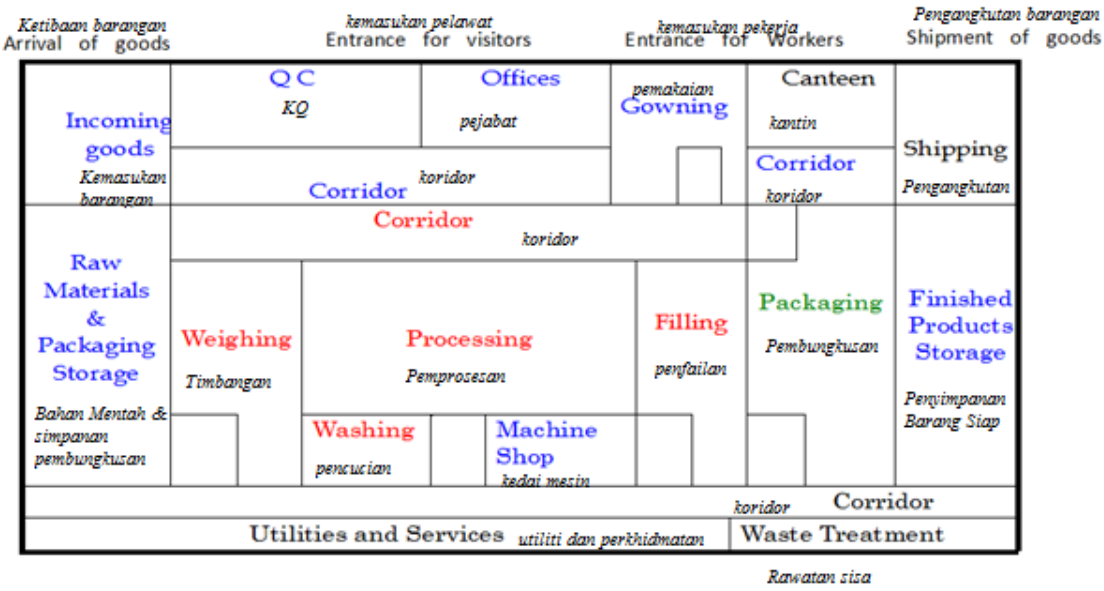


Figure Q.1.
Rajah S.1.

2. Benzylpenicillin is an antibiotic effective against anthrax disease. As part of a purification process, 200 mg of benzylpenicillin is mixed with 25 mL of n-octanol and 25 mL of water. After equilibrium is established, there is a water rich phase that contains essentially no n-octanol and an octanol-rich phase that contains 74 mol% n-octanol and 26 mol% water.

Benzilpenisilin adalah antibiotik yang berkesan terhadap penyakit antraks. Sebagai sebahagian daripada proses penulenan, 200 mg benzilpenisilin dicampur dengan 25 mL n-oktanol dan 25 mL air. Selepas mencapai keseimbangan, fasa yang kaya dengan air tidak mengandungi n-oktanol, dan fasa yang kaya dengan n-oktanol mengandungi 74 mol% n-oktanol dan 26 mol % air.

[a] Assuming infinite dilution, determine the concentrations of benzylpenicillin in each of these phases.

Andaikan pencairan tak terhingga, tentukan kepekatan benzilpenisilin dalam setiap fasa. *[12 marks/markah]*

[b] For the real solution, if the ratio of $\frac{\gamma_{BP}^{W}}{\gamma_{BP}^{O}}$ is <1, comment on the concentration changes of benzylpenicillin in the n-octanol phase.

Untuk larutan sebenar, jika nisbah $\frac{\gamma_{BP}^{W}}{\gamma_{BP}^{O}}$ *<1, ulaskan perubahan kepekatan benzilpenisilin dalam fasa n-oktanol.* *[3 marks/markah]*

Data: The molecular weight of benzylpenicillin is 334.5, that of n-octanol is 130.23, the liquid density of n-octanol is 0.826 g/cm^3, and partition coefficient of benzylpenicillin in n-octanol/water is 65.5.

Data: Berat molekul benzyilpenisilin adalah 334.5, n-oktanol adalah 130.23, ketumpatan cecair n-oktanol adalah 0.826 g/sm^3 dan pekali petakan benzilpenisilin n-oktanol/air adalah 65.5.

3. A 400 L solution of a protein at 0.05 g/L needs to be concentrated to 1.5 g/L using an ultrafiltration membrane of surface area 500 cm^2 at a flux of 12 x 10^{-5} cm/s. The protein has a diffusion coefficient of 1.8 x 10^{-6} cm^2/s at 15^{o}C.

Satu larutan 400 L protein pada 0.05 g/L perlu dipekatkan kepada 1.5 g/L menggunakan membran penurasan ultra dengan keluasan permukaan 500 sm^2 pada fluks 12 x *10^{-5} sm/s. Protein mempunyai pekali resapan sebanyak 1.8* x *10^{-6} sm^2/s pada 15 ^{o}C.*

[a] Determine whether concentration polarization is an important external factor affecting the membrane's performance. Assume that the boundary layer thickness is 0.015 cm.

Tentukan sama ada polarisasi kepekatan adalah faktor penting luaran yang mempengaruhi prestasi membran. Anggapkan bahawa ketebalan lapisan sempadan ialah 0.015 sm. *[6 marks/markah]*

…4/-

[b] What is the concentration of protein on the surface of the ultrafiltration membrane for the bulk concentration of 1.5 g/L?

Apakah kepekatan protein pada permukaan membran penurasan ultra untuk kepekatan pukal 1.5 g/L? *[3 marks/markah]*

[c] Calculate the time needed to complete the filtration and achieved the desired final concentration.

Kirakan masa yang perlu untuk melengkapkan penapisan dan mencapai kepekatan akhir yang dikehendaki. *[6 marks/markah]*

4. [a] Discuss the significance of *G* value and Σ factor in the scaling up of centrifuges.

Bincangkan kepentingan nilai G *dan faktor* Σ *dalam pengskalaan besar pengempar.* *[8 marks/markah]*

[b] A rotary vacuum filter is to be used to filter a suspension of *Bacillus subtilis* cells for recovery of protease. The filter area is 350 m^2 and the vacuum pressure is 100 kPa. In a laboratory experiment, filter leaf tests have been performed on a cell broth with a viscosity of 0.05 g/cm.s. The tests gave a specific cake resistance of 1 x 10^{11} cm/g and a medium resistance of 1 x 10^8 cm^{-1}. The cell suspension deposits 15 g cake solids (dry basis) per liter of filtrate. It is desired to operate the large filter with a cycle time of 60 s and a cake formation time of 15 s. What is the filtration rate (in L/h) expected for the rotary vacuum filter? How significant is the medium resistance? Give comment to your answer.

Sebuah penuras vakum berputar digunakan untuk menuras ampaian sel Bacilius subtilis *untuk perolehan protease. Keluasan penuras ialah 350* m^2 *dan tekanan vakum ialah 100 kPa. Dalam eksperimen makmal, ujian penuras-daun telah dijalankan ke atas kaldu sel dengan kelikatan 0.05 g/sm.s. Ujian tersebut memberikan rintangan kek spesifik 1* x 10^{11} *sm/g dan rintangan bahantara ialah 1* x 10^8 sm^{-1}. *Ampaian sel mengendapkan 15 g pepejal kek (asas kering) bagi setiap liter cecair turasan. Penuras besar perlu beroperasi dengan masa kitaran 60 s dan masa pembentukan kek ialah 15 s. Apakah kadar penurasan (L/jam) yang dijangkakan untuk penuras vakum berputar? Bagaimanakah rintangan bahantara ini bererti? Berikan komen kepada jawapan anda.*

[17 marks/markah]

5. [a] Paclitaxel is an anticancer drug that can be produced by plant cell cultures of *Taxus baccata*. However, most of the product is entrapped in the cells and require cell disruption to release the product into the suspension broth. Explain two techniques that can be used to disrupt the cells.

Paclitaxel ialah sejenis ubat anti-barah yang boleh dihasilkan oleh kultur sel tumbuhan Taxus baccata. *Bagaimanapun, hampir kesemua produk terperangkap di dalam sel dan memerlukan pemecahan sel untuk melepaskan produk ke dalam kaldu ampaian. Terangkan dua teknik yang boleh digunakan untuk memecahkan sel.* *[8 marks/markah]*

[b] An antibiotic is to be recovered from 25 liters of feed solution by adsorption using activated carbon. The concentration of the antibiotic in the feed is 2.5×10^{-6} g/g of water. Adsorption data obtained is shown below in Table Q.5.[b].:

Suatu antibiotik diperolehi daripada 25 liter larutan suapan melalui penjerapan menggunakan karbon teraktif. Kepekatan antibiotik dalam suapan ialah 2.5×10^{-6} *g/g air. Data penjerapan yang diperolehi ditunjukkan dalam Jadual S.5.[b].*

Table Q.5.[b].
Jadual S.5.[b].

y (g solute/g water) y *(g bahan larut/g air)*	*q* (g solute/g carbon) q *(g bahan larut/g karbon)*
0.1	1.3
0.3	1.7
0.6	2.3
0.9	2.4
1.2	2.6

If the data fits the Freundlich isotherm, how much adsorbent is required for 97% recovery of the antibiotic?

Jika data mengikuti garis sesuhu Freundlich, berapa banyakkah penjerap yang diperlukan untuk 97% perolehan antibiotik?

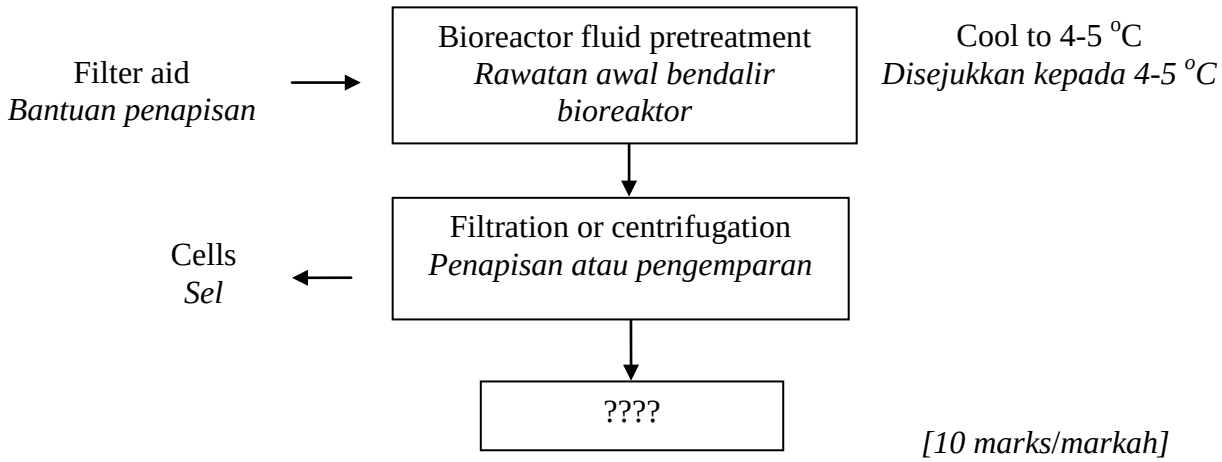
[12 marks/markah]

[c] Describe a vacuum-shelf dryer and its application in industry.

Terangkan berkenaan pengering para-vakum dan aplikasinya dalam industri.
[5 marks/markah]

6. Protease, an enzyme that can degrade proteins, is used in products such as laundry detergent. Because it applications do not involve food products or injectable therapeutics, it need not be produced in a highly purified form. Protease can be produced in solid form. Develop and briefly explain the following steps that would improve the purity of the final product.

Protease, enzim yang boleh memecahkan protein, digunakan dalam produk seperti bahan pencuci dobi. Disebabkan aplikasinya tidak melibatkan produk makanan atau terapeutik suntikan, ia tidak perlu dihasilkan dalam bentuk yang sangat tulen. Protease boleh dihasilkan dalam bentuk pepejal. Bangunkan dan terang secara ringkas langkah-langkah seterusnya yang akan meningkatkan ketulenan produk akhir.



[10 marks/markah]

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Appendix

$$\frac{At}{V} = \frac{\mu\alpha\rho_0}{2\Delta P}\left(\frac{V}{A}\right) + \frac{\mu R_M}{\Delta P}$$

$$R_C = \alpha\rho_0\left(\frac{V}{A}\right) \qquad \alpha = \alpha'(\Delta P)^s$$

$$\upsilon_g = \frac{\rho_p - \rho_f}{18\mu} D_p{}^2 g$$

$$\upsilon_c = \frac{\rho_p - \rho_f}{18\mu} D_p{}^2 \omega^2 r$$

$$Q = \upsilon_g\left[\frac{2\pi d R^2\omega^2}{g}\right]$$

$$Q = \upsilon_g\left[\frac{2\pi m\omega^2}{3g}\left(R_0^3 - R_1^3\right)\cot\theta\right]$$

$$Q = \upsilon_g\left[\frac{\pi d(R_0^2 - R_1^2)\omega^2}{g\ln(R_0/R_1)}\right]$$

g = 980 cm/s^2

$$t_E = \frac{}{\upsilon\varepsilon}(K + \varepsilon - K\varepsilon)$$

$$\upsilon y_F t^* = L\rho_b q_{sat}$$

$$\theta = 1 - \left(\frac{t_E - t_B}{2t_B}\right)$$

$q = Ky$ $\qquad$ $q = Ky^n$ $\qquad$ $q = \frac{q_0 y}{K + y}$

$$J(x) = \frac{D}{\delta(x)}\ln\frac{C_w}{C_b}$$

$$\left(\frac{C_{final}}{C_o}\right) = \left(\frac{V_o}{V_f}\right)^R$$

…2/-

Common Engineering Conversion Factors

Length	Volume
1 ft = 12 in = 0.3048 m, 1 yard = 3 ft 1 mi = 5280 ft = 1609.344 m 1 nautical mile (nmi) = 6076 ft	1 ft^3 = 0.028317 m^3 = 7.481 gal , 1 bbl = 42 U.S. gal 1 U.S. gal = 231 in^3 = 3.7853 L = 4qt = 0.833 lmp.gal. 1 L = 0.001 m^3 = 0.035315 ft^3 = 0.2642 U.S. gal
Mass	**Density**
1 slug = 32.174 lb_m = 14.594 kg 1 lb_m = 0.4536 kg = 7000 grains	1 slug/ft^3 = 515.38 kg/m^3 , 1 g/cm^3 = 1000 kg/m^3 1 lb_m/ft^3 = 16.0185 kg/m^3 , 1 lb_m/in^3 = 27.68 g/cm^3
Acceleration & Area	**Velocity**
1 ft/s^2 = 0.3048 m/s^2 1 ft^2 = 0.092903 m^2	1 ft/s = 0.3048 m/s , 1 knot = 1 min/h = 1.6878 ft/s 1 min/h = 1.4666666 ft/s (fps) = 0.44704 m/s
Mass Flow & Mass Flux	**Volume Flow**
1 slug/s = 14.594 kg/s. 1 lb_m/s = 0.4536 kg/s 1 kg/m^2s = 0.2046 lb_m/ft^2s = 0.00636 slug/ft^2s	1 gal/min = 0.00228 ft^3/s = 0.06309 L/s 1 million gal/day = 1.5472 ft^3/s = 0.04381 m^3/s
Pressure	**Force and Surface Tension**
1 lb_f/ft^3 = 47.88 Pa, 1 torr = 1 mm Hg 1 psi = 144 psf, 1 bar = 10^5 Pa 1 atm = 2116.2 psf = 14696 psi = 101,325 Pa = 29.9 in Hg = 33.9 ft H_2O	1 lb_f = 4.448222 N = 16 oz, 1 dyne = 1 g cm/s^2 = 10^{-5}N 1 kg_f = 2.2046 lb_f = 9.80665 N 1 U.S. (short) ton = 2000 lb_f , 1 N = 0.2248 lb_f 1 N/m = 0.0685 lb_f/ft
Power	**Energy and Specific Energy**
1 hp = 550 (ft.lb_f)/s = 745.7 W 1 (ft.lb_f)/s = 1.3558 W 1 Watt = 3.4123 Btu/h = 0.00134 hp	1 ft lb_f = 1.35582 J, 1 hp·h = 2544.5 Btu 1 Btu = 252 cal = 1055.056 J = 778.17 ft lb_f 1 cal = 4.1855 J, 1 ft.lb_f/lb_m = 2.9890 J/kg
Specific Weight	**Heat Flux**
1 lb_f/ft^3 = 157.09 N/m^3	1 W/m^2 = 0.3171 Btu/(h ft^2)
Viscosity	**Kinematic Viscosity**
1 slug/(ft.s) = 47.88 kg/(m.s) = 478.8 poise (p) 1 p=1 g/(cm.s) 0.1 kg/(m.s) = 0.002088 slug/(ft s)	1 ft^2/h = 2.506 .10^{-5} m^2/s, 1 ft^2/s = 0.092903 m^2/s 1 stoke (st) = 1 cm^2/s = 0.0001 m^2/s = 0.001076 ft^2/s
Temperature Scale Readings	
^oF = (9/5)^oC + 32 ^oC = (5/9) (^oF – 32) ^oR = ^oF + 459.69 ^oK = ^oC + 273.16	
Thermal Conductivity*	**Gas Constant***
1 cal/(s.cm.^{o}C) = 242 Btu/(h.ft.^{o}R) 1 Btu/(h.ft.^{o}R) = 1.7307 W/(m.K)	R = 82.057 atm.cm^3/(gmol.K) = 62.361 mm Hg.L/(gmol.K) = 1.134 atm.ft^3/(lbmol.K) = 0.083144 bar.L/(gmol.K) = 10.73 psi. ft^3/(lbmol. ^{o}R) = 555.0 mm Hg.ft^3/(lbmol. ^{o}R)

- Note that the intervals in absolute (Kelvin) and ^{o}C are equal. Also, 1 ^{o}R = 1 ^{o}F.

Latent heat: 1 J/kg = 4.2995 × 10^{-4} Btu/lb_m = 10.76 lb_f.ft/slug = 0.3345 lb_f.ft/lb_m , 1 Btu/lb_m = 2325.9 J/kg

Heat transfer coefficient: 1 Btu/(h.ft^2.^{o}F) = 5.6782 W/(m^2.^{o}C).

Heat generation rate: 1 W/m^3 = 0.09665 Btu/(h ft^3)

Heat transfer per unit length: 1 W/m = 1.0403 Btu/(h ft)

Mass transfer coefficient: 1 m/s = 11.811 ft/h, 1 lb_{mol}/(h.ft^2) = 0.013562 kgmol/(s.m^2)

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Sketch Sheet

Sketch the material and personnel flow onto this sketch sheet. Detach it from the question paper and submit together with your answer booklets.