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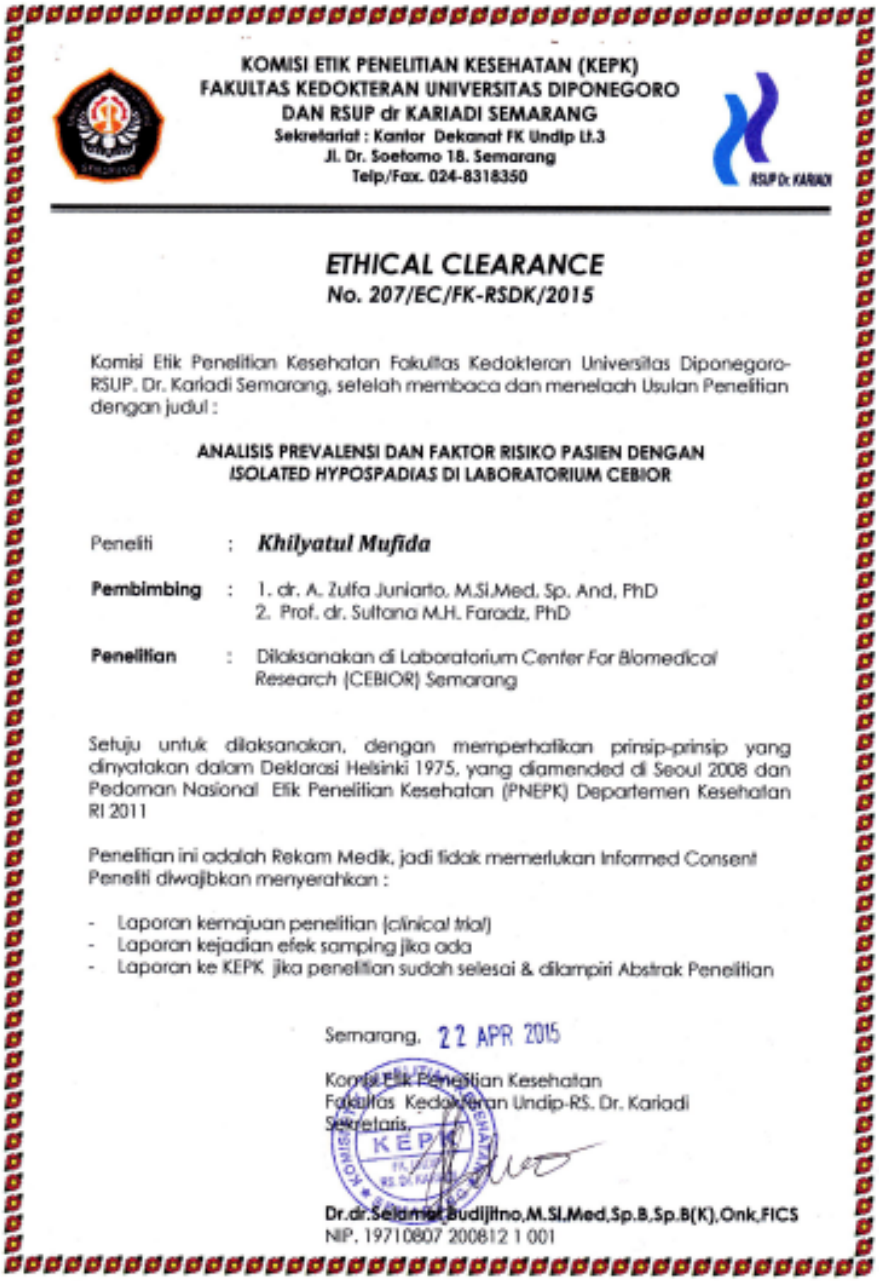
Lampiran 1. ***Ethical Clearance***



KOMISI ETIK PENELITIAN KESEHATAN (KEPK)
FAKULTAS KEDOKTERAN UNIVERSITAS DIPONEGORO
DAN RSUP dr KARIADI SEMARANG
Sekretariat : Kantor Dekanat FK Undip Lt.3
Jl. Dr. Soetomo 18. Semarang
Telp/Fax. 024-8318350

RSUP Dr. KARIADI

ETHICAL CLEARANCE
No. 207/EC/FK-RSDK/2015

Komisi Etik Penelitian Kesehatan Fakultas Kedokteran Universitas Diponegoro-RSUP. Dr. Kariadi Semarang, setelah membaca dan menelaah Usulan Penelitian dengan judul :

ANALISIS PREVALENSI DAN FAKTOR RISIKO PASIEN DENGAN *ISOLATED HYPOSPADIAS* DI LABORATORIUM CEBIOR

Peneliti : ***Khilyatul Mufida***

Pembimbing : 1. dr. A. Zulfa Juniarto, M.Si.Med, Sp. And, PhD
2. Prof. dr. Sultana M.H. Faradz, PhD

Penelitian : Dilaksanakan di Laboratorium *Center For Biomedical Research* (CEBIOR) Semarang

Setuju untuk dilaksanakan, dengan memperhatikan prinsip-prinsip yang dinyatakan dalam Deklarasi Helsinki 1975, yang diamended di Seoul 2008 dan Pedoman Nasional Etik Penelitian Kesehatan (PNEPK) Departemen Kesehatan RI 2011

Penelitian ini adalah Rekam Medik, jadi tidak memerlukan Informed Consent
Peneliti diwajibkan menyerahkan :

- Laporan kemajuan penelitian (*clinical trial*)
- Laporan kejadian efek samping jika ada
- Laporan ke KEPK jika penelitian sudah selesai & dilampiri Abstrak Penelitian

Semarang, 22 APR 2015

Komisi Etik Penelitian Kesehatan
Fakultas Kedokteran Undip-RS. Dr. Kariadi
Sekretaris,

KEPK

Dr.dr.Seldinar Budijitno,M.Si,Med,Sp.B,Sp.B(K),Onk,FICS
NIP. 19710807 200812 1 001

Lampiran 2. Prosedur Analisis Sitogenetika

1. **Alat**

- Spuit 3cc untuk mengambil sampel darah pasien
- Gelas ukur
- Tabung steril 15 ml
- Tabung vacuum 3cc
- *Tube* eppendrofe 1,5 ml
- *Blue tip, yellow tip*
- Pipet pastur steril
- Sentrifuse
- Inkubator
- *Waterbath*
- Almari es
- Almari asam
- *Object glass*
- Rak tabung reaksi
- Botol semprot untuk KCl
- *Tissue*
- *Laminar flow*
- Mikroskop cahaya, mikroskop fotografi

2. **Bahan**

Bahan yang diperiksa adalah darah vena dengan antikoagulan heparin.

3. Reagen yang dibutuhkan

- Media kultur kromosom

  Media yang digunakan adalah MEM dan RPMI 1640
- Bahan pemicu mitosis yaitu *Phytohaemaglutinin-mixture* (PHA-M)
- *Fetal bovine Serum* (FBS) 10% dari kadar medium sebagai nutrisi
- Colcemid untuk menghentikan mitosis (*spindle inhibitor*)
- KCl 0,075 M sebagai larutan hipotonik untuk memecah sel
- Larutan Carnoy's (3 metanol : 1 asam asetat glacial) sebagai larutan fiksasi sel
- Giemsa
- Buffer fosfat
- *Phosphat Buffer Saline* (PBS) pH 6,8
- Larutan Tripsin 1% stok dalam PBS
- Aquabides
- *Immersion Oil*

1. Prosedur Pengambilan Bahan

Sebelum mengambil darah pasien, dicatat identitas pasien, diberi *informed consent,* dan pemeriksaan fisik terlebih dahulu. Sampel darah diambil dari pembuluh darah vena cubiti dengan menggunakan antikoagulan heparin.

2. Prosedur Pemeriksaan Bahan

- Penanaman

1. Mengeluarkan medium, PHA-M, dan FBS dari almari es dan dihangatkan dalam *waterbath* 37ºC selama 15 menit.
2. Meneteskan FBS sebanyak 10% dari jumlah medium kedalam masing-masing tabung berisi media MEM dan RPMI 1640, lalu dicampur secara perlahan.
3. Menambahkan 100µl PHA-M kedalam tabung dan dicampur kembali secara perlahan.
4. Jika sampel darah baru diambil, proses penanaman dilanjutkan dengan meneteskan 4 tetes *buffy coat* dan 6 tetes *whole blood* kedalam tabung. Namun, jika sampel darah sudah lama (sampel darah sudah didiamkan pada suhu 4ºC) penanaman dilanjutkan dengan meneteskan 10 tetes *whole blood* kedalam tabung. Selanjutnya, tabung dikocok lagi secara perlahan-lahan.
5. Melakukan inkubasi sampel pada suhu 37º C selama 72-96 jam dengan sudut kemiringan tabung 45º agar memberi peluang tumbuhnya sel di permukaan, dalam inkubator.
6. Setiap 1x24 jam, masing-masing tabung dikocok secara perlahan-lahan.

*Langkah 2, 3, dan 4 dilakukan dalam *laminar flow*.

- Pemanenan

1. Meneteskan 100 µl Colcemid pada setiap tabung, dan diinkubasi dalam inkubator pada suhu 37º selama 30 menit.
2. Setelah dilakukan inkubasi, lalu dipusingkan selama 10 menit dengan kecepatan 1000 RPM .
3. Membuang supernatan yang terbentuk, kemudian meresuspensikan endapan (pelet) dengan menambahkan larutan hipotonik hangat KCl 0,075 M, lalu dikocok secara kuat, diresuspensikan homogen dan diinkubasi pada suhu 37º C dalam *waterbath* selama 15-30 menit.
4. Melakukan pemusingan kembali pada 1000 RPM selama 10 menit, lalu membuang supernatan yang terbentuk, dan menambahkan 5ml larutan fiksasi Carnoy's pelan-pelan melalui dinding tabung, kemudian dikocok.
5. Melakukan pemusingan kembali pada 1000 RPM selama 10 menit, mengulangi pemberian larutan fiksasi Carnoy's sampai didapatkan presipitat jernih.
6. Melakukan suspensi residu dengan larutan Carnoy's secukupnya sesuai dengan banyaknya pelet yang terbentuk.
7. Meneteskan dan menyebarkan 2 tetes suspensi pada gelas objek pada lokasi yang berbeda.
8. Mengeringkan gelas objek, lalu mengamati dibawah mikroskop cahaya.

9. Menghitung jumlah kromosom pada 1 metafase sebagai skrining awal, lalu penghitungan jumlah kromosom dilakukan sampai 20 metafase.
10. Jika terdapat kesulitan dalam mengamati adanya metafase di bawah mikroskop cahaya, dilakukan pengecatan dengan giemsa : buffer phosphate (1:9). Lalu slide dikeringkan lagi, dan diamati kembali dibawah mikroskop cahaya.

- Pengecatan Trypsin tanpa penghangatan (GTG banding)
  1. Mencelupkan slide yang berumur lebih dari 3 hari kedalam larutan Trypsin 0,1% yang dilarutkan dengan 100 ml PBS pH 6,8 selama 10-15 detik.
  2. Mencuci slide dengan larutan PBS, selanjutnya slide dimasukkan ke larutan giemsa 10% dalam buffer fosfat (1:9) selama 10-15 menit.
  3. Mencuci slide dibawah air mengalir, lalu dikeringkan.
  4. Mengamati slide dibawah mikroskop cahaya.

- Analisis
  - Analisis dikerjakan oleh dokter ahli sitogenetika dengan menyiapkan format analisis untuk mencatat koordinat dan jumlah metafase yang dihitung dan dianalisis.
  - Analisis untuk seluruh kasus harus dengan pengecatan G-Banding, paling sedikit 8 metafase dan penghitungan 20 metafase. Apabila didapatkan kelainan mosaik, analisis dilakukan pada 100 metafase.

- Prosedur Laporan/Diagnosis

Cara melaporkan bentuk atau konsitusi kromosom adalah mengikuti cara yang diharuskan oleh *International System for Human Cytogenetic Nomenclature* (ICSN). Standar penulisan konsitusi kromosom adalah pertama kali tulis jumlah kromosom kemudian diikuti koma dan jenis kromosom seks, diikuti koma lagi dan selanjutnya kelainan struktural (bila terdapat kelainan struktural). Apabila melibatkan kelainan kromosom pada 2 kromosom maka ditulis jenis kromosom secara urut nomor yang kecil. Seluruh metafase yang telah dianalisis, kemudian difoto hitam putih, tiap-tiap kromosom digunting dan ditempel pada kertas yang sudah disediakan sesuai dengan urut-urutanan nomernya. Dokter ahli sitogenetika menetukan jenis kariotip serta memberikan kesimpulan dari hasil pemeriksaan.

Lampiran 3. Hasil Analisis Program Statistik

Case Processing Summary

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
Obat Nyamuk * *Isolated hypospadias*	233	93.6%	16	6.4%	249	100.0%
Ayah Perokok * *Isolated hypospadias*	233	93.6%	16	6.4%	249	100.0%
Kontrasepsi hormonal * *Isolated hypospadias*	233	93.6%	16	6.4%	249	100.0%
Pestisida * *Isolated hypospadias*	233	93.6%	16	6.4%	249	100.0%
Penggunaan obat * *Isolated hypospadias*	233	93.6%	16	6.4%	249	100.0%
Paritas * *Isolated hypospadias*	227	91.2%	22	8.8%	249	100.0%
Usia ibu * *Isolated hypospadias*	220	88.4%	29	11.6%	249	100.0%
Berat badan lahir* *Isolated hypospadias*	146	58.6%	103	41.4%	249	100.0%

Statistics

		Paritas	Usia Ibu	Berat Badan Lahir
N	Valid	235	229	191
	Missing	14	20	58
Mean		1.58	28.00	2848.99
Median		1.00	27.00	2900.00
Std. Deviation		1.182	6.740	697.358
Minimum		1	16	1000
Maximum		12	50	4500

Penggunaan Obat Nyamuk * *Isolated Hypospadias*

Crosstab

			Isolated hypospadias		Total
			Berat	Ringan	
Penggunaan Obat Nyamuk	Ya	Count	9	43	52
		% within *Isolated hypospadias*	22.5%	22.3%	22.3%
	Tidak	Count	31	150	181
		% within *Isolated hypospadias*	77.5%	77.7%	77.7%
Total		Count	40	193	233
		% within *Isolated hypospadias*	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.001[a]	1	.976		
Continuity Correction[b]	.000	1	1.000		
Likelihood Ratio	.001	1	.976		
Fisher's Exact Test				1.000	.561
Linear-by-Linear Association	.001	1	.976		
N of Valid Cases	233				

a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 8.93.

b. Computed only for a 2x2 table

Risk Estimate

	Value	95% Confidence Interval	
		Lower	Upper
Odds Ratio for penggunaan obat nyamuk (Ya/ Tidak)	1.013	.448	2.290
For cohort *Isolated hypospadias* = Berat	1.011	.515	1.985
For cohort *Isolated hypospadias* = Ringan	.998	.867	1.149
N of Valid Cases	233		

Ayah Perokok * *Isolated Hypospadias*

Crosstab

			Isolated hypospadias		*Total*
			Berat	Ringan	
Ayah perokok	Ya	Count	7	25	32
		% within *Isolated hypospadias*	17.5%	13.0%	13.7%
	Tidak	Count	33	168	201
		% within *Isolated hypospadias*	82.5%	87.0%	86.3%
Total		Count	40	193	233
		% within *Isolated hypospadias*	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.578[a]	1	.447		
Continuity Correction[b]	.258	1	.611		
Likelihood Ratio	.547	1	.459		
Fisher's Exact Test				.452	.296
Linear-by-Linear Association	.576	1	.448		
N of Valid Cases	233				

a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 5.49.

b. Computed only for a 2x2 table

Risk Estimate

	Value	95% Confidence Interval	
		Lower	Upper
Odds Ratio for ayah perokok(Ya/ Tidak)	1.425	.570	3.568
For cohort *Isolated hypospadias* = Berat	1.332	.645	2.752
For cohort *Isolated hypospadias* = Ringan	.935	.770	1.134
N of Valid Cases	233		

Penggunaan kontrasepsi hormonal* *Isolated Hypospadias*

Crosstab

			Isolated hypospadias		Total
			Berat	Ringan	
Penggunaan Kontrasepsi Hormonal	Ya	Count	3	23	26
		% within *Isolated hypospadias*	7.5%	11.9%	11.2%
	Tidak	Count	37	170	207
		% within *Isolated hypospadias*	92.5%	88.1%	88.8%
Total		Count	40	193	233
		% within *Isolated hypospadias*	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.652[a]	1	.419		
Continuity Correction[b]	.283	1	.595		
Likelihood Ratio	.712	1	.399		
Fisher's Exact Test				.584	.311
Linear-by-Linear Association	.649	1	.420		
N of Valid Cases	233				

a. 1 cells (25.0%) have expected count less than 5. The minimum expected count is 4.46.

b. Computed only for a 2x2 table

Risk Estimate

	Value	95% Confidence Interval	
		Lower	Upper
Odds Ratio for penggunaan kontrasepsi hormonal(Ya/ Tidak)	.599	.171	2.101
For cohort *Isolated hypospadias* = Berat	.646	.214	1.946
For cohort *Isolated hypospadias* = Ringan	1.077	.925	1.255
N of Valid Cases	233		

Paparan Pestisida* *Isolated Hypospadias*

Crosstab

			Isolated hypospadias		Total
			Berat	Ringan	
Paparan Pestisida	Ya	Count	8	32	40
		% within I*solated hypospadias*	20.0%	16.6%	17.2%
	Tidak	Count	32	161	193
		% within I*solated hypospadias*	80.0%	83.4%	82.8%
Total		Count	40	193	233
		% within I*solated hypospadias*	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.272[a]	1	.602		
Continuity Correction[b]	.085	1	.771		
Likelihood Ratio	.264	1	.607		
Fisher's Exact Test				.646	.374
Linear-by-Linear Association	.271	1	.602		
N of Valid Cases	233				

a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 6.87.

b. Computed only for a 2x2 table

Risk Estimate

	Value	95% Confidence Interval	
		Lower	Upper
Odds Ratio for paparan pestisida(Ya / Tidak)	1.258	.531	2.980
For cohort *Isolated hypospadias* = Berat	1.206	.601	2.419
For cohort *Isolated hypospadias* = Ringan	.959	.811	1.134
N of Valid Cases	233		

Konsumsi Obat * *Isolated Hypospadias*

Crosstab

			Isolated hypospadias		Total
			Berat	Ringan	
Konsumsi Obat	Ya	Count	11	52	63
		% within I*solated hypospadias*	27.5%	26.9%	27.0%
	Tidak	Count	29	141	170
		% within I*solated hypospadias*	72.5%	73.1%	73.0%
Total		Count	40	193	233
		% within I*solated hypospadias*	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.005[a]	1	.942		
Continuity Correction[b]	.000	1	1.000		
Likelihood Ratio	.005	1	.943		
Fisher's Exact Test				1.000	.541
Linear-by-Linear Association	.005	1	.943		
N of Valid Cases	233				

a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 10.82.

b. Computed only for a 2x2 table

Risk Estimate

	Value	95% Confidence Interval	
		Lower	Upper
Odds Ratio for konsumsi obat(Ya / Tidak)	1.029	.479	2.207
For cohort *Isolated hypospadias* = Berat	1.024	.545	1.924
For cohort *Isolated hypospadias* = Ringan	.995	.872	1.136
N of Valid Cases	233		

Paritas* *Isolated Hypospadias*

Crosstab

			Isolated hypospadias		Total
			Berat	Ringan	
Paritas	Primipara	Count	24	127	151
		% within I*solated hypospadias*	61.5%	67.6%	66.5%
	Multipara	Count	15	61	76
		% within I*solated hypospadias*	38.5%	32.4%	33.5%
Total		Count	39	188	227
		% within I*solated hypospadias*	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.525[a]	1	.469		
Continuity Correction[b]	.289	1	.591		
Likelihood Ratio	.516	1	.473		
Fisher's Exact Test				.463	.292
Linear-by-Linear Association	.522	1	.470		
N of Valid Cases	227				

a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 13.06.

b. Computed only for a 2x2 table

Risk Estimate

	Value	95% Confidence Interval	
		Lower	Upper
Odds Ratio for paritas(Primipara / Multipara)	.769	.376	1.569
For cohort *Isolated hypospadias* = Berat	.805	.449	1.443
For cohort *Isolated hypospadias* = Ringan	1.048	.919	1.195
N of Valid Cases	227		

Usia ibu * *Isolated Hypospadias*

Crosstab

			Isolated hypospadias		Total
			Berat	Ringan	
Usia ibu	>35 tahun	Count	9	20	29
		% within I*solated hypospadias*	23.1%	11.0%	13.2%
	≤35 tahun	Count	30	161	191
		% within I*solated hypospadias*	76.9%	89.0%	86.8%
Total		Count	39	181	220
		% within I*solated hypospadias*	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	4.056[a]	1	.044		
Continuity Correction[b]	3.073	1	.080		
Likelihood Ratio	3.574	1	.059		
Fisher's Exact Test				.064	.045
Linear-by-Linear Association	4.037	1	.045		
N of Valid Cases	220				

a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 5.14.

b. Computed only for a 2x2 table

Risk Estimate

	Value	95% Confidence Interval	
		Lower	Upper
Odds Ratio for usia ibu(>35 tahun / ≤35 tahun)	2.415	1.004	5.810
For cohort *Isolated hypospadias* = Berat	1.976	1.048	3.726
For cohort *Isolated hypospadias* = Ringan	.818	.636	1.052
N of Valid Cases	220		

Berat badan lahir * *Isolated Hypospadias*

Crosstab

			Isolated hypospadias		Total
			Berat	Ringan	
Berat Badan Lahir	<2500 gram	Count	9	33	42
		% within I*solated hypospadias*	33.3%	27.7%	28.8%
	≥2500 gram	Count	18	86	104
		% within I*solated hypospadias*	66.7%	72.3%	71.2%
Total		Count	27	119	146
		% within I*solated hypospadias*	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.337[a]	1	.562		
Continuity Correction[b]	.119	1	.730		
Likelihood Ratio	.330	1	.566		
Fisher's Exact Test				.639	.358
Linear-by-Linear Association	.335	1	.563		
N of Valid Cases	146				

a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 7.77.

b. Computed only for a 2x2 table

Risk Estimate

	Value	95% Confidence Interval	
		Lower	Upper
Odds Ratio for berat badan lahir(<2500 gram / ≥2500 gram)	1.303	.532	3.189
For cohort *Isolated hypospadias* = Berat	1.238	.605	2.532
For cohort *Isolated hypospadias* = Ringan	.950	.793	1.138
N of Valid Cases	146		

Lampiran 4. Biodata Mahasiswa

Identitas

Nama : Khilyatul Mufida

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TTL : Tuban, 14 April 1993

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Riwayat Pendidikan Formal

1. TK : Tunas Rimba, Tuban, Jawa Timur Lulus Tahun : 1999
2. SD : SDN 1 Sugihan, Tuban, Jawa Timur Lulus Tahun : 2005
3. SMP : SMPN 1 Jatirogo,Tuban, Jawa Timur Lulus Tahun : 2008
4. SMA : SMAN 1 Tuban, Jawa Timur Lulus Tahun : 2011
5. FK UNDIP, Masuk tahun 2011

Keanggotaan Organisasi :

1. Badan Analisis Pengembangan dan Penelitian Kedokteran Indonesia (BAPIN), ISMKI, Tahun 2014 s.d 2015
2. Asisten Mahasiswa Bagian Anatomi FK Undip Tahun 2013 s.d 2015
3. Kelompok Studi Mahasiswa FK Undip Tahun 2012 s.d 2014
4. Himpunan Mahasiswa FK Undip Tahun 2012 s.d 2014
5. Asisten Mahasiswa Bagian Kimia FK Undip Tahun 2012 s.d 2013
6. *Reproduction Health Education Unit* FK Undip Tahun 2012 s.d 2013
7. Jaringan Mahasiswa Kesehatan Indonesia Tahun 2012 s.d 2013
8. Rohani Islam FK Undip Tahun 2012 s.d 2013

Pengalaman Penelitian :

1. Prevalensi Infeksi Cacing Cambuk (*Trichuris trichiura*) dan Cacing Tambang (*Necator americanus* dan *Ancylostoma duodenale*) pada Ibu Hamil di Kota Semarang, 2013-2014.

Pengalaman Presentasi dan Mengikuti Lomba Karya Ilmiah

1. *Pengaruh kombinasi teh hijau dan kulit manggis terhadap profil lipid serum, foam cell, dan ketebalan aorta : Studi pada Tikus Wistar yang Diinduksi Aterosklerosis.* Departemen Riset BEM FK KM Undip. [Juara 2 Proposal Penelitian - Fakultas] 2014.
2. *Depression Among Indonesian Homosexual Men.* FK Universitas Indonesia. [Semifinalis Research Article - Internasional] 2014
3. Himpunan Mahasiswa Kedokteran Umum Undip. [Finalis 10 Besar Poster Ilmiah - Nasional]
4. *Kombinasi Dietilkarbamazin dan Naringenin dari Kulit Jeruk Purut (Citrus hystix) melalui Transdermal patch: A Novel Therapy for Filariasis.* Badan Analisis dan Pengembangan Ilmiah Nasional (BAPIN)-Ikatan Senat Mahasiswa Kedokteran Indonesia (ISMKI) beserta FK Universitas Padjajaran. [Juara 2 Gagasan Tertulis - Nasional] 2013.
5. *Potensi Vaksin Kombinasi Brugia Malayi Abundant Larval Transcript-2 (Bmalt-2) Dan Brugia Malayi Small Heat Shock Protein (Bmhsp) Melalui Microneedle Patch Terhadap Filariasis Limfatik.* Rohani Islam FK Undip. [Juara 1 Gagasan Tertulis - Nasional] 2013.
6. *Restorative Yoga For Breast Cancer Survivors: Physical And Psychological Benefits,* FK Universitas Indonesia. [Semifinalis Literature Review - Internasional] 2013
7. *Kombinasi Melatonin dan Vitamin D sebagai Terapi Target Lupus Eritematosus Sistemik melalui Modifikasi Sistem Imun.* FK Universitas Sumatera Utara.[Finalis 10 Besar- Nasional] 2012