インドネシア共和国
ワクチンプロジェクト
予備調査団報告書

1986年6月

国際協力事業団 医療協力部

インドネシア共和国
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序　　文

当事業団は、昭和６１年４月８日から１５日まで８日間にわたり、(財)日本ポリオ研究所常務理事　吉岡勇雄氏を団長とするインドネシア共和国ワクチンプロジェクト予備調査団をインドネシア共和国へ派遣した。

ポリオ・麻疹両ワクチンの製造に係る技術協力プロジェクト実施可能性の有無を調査するのがその目的であった。本報告書はその調査結果をとりまとめたものである。

本プロジェクトの去就は、今後の検討に待つところであるが、本調査結果がその資料として大いに活用されることを期待する次第である。

調査団員各位、関係者の皆様のご尽力に対し心より謝意を表したい。

昭和６１年６月２日

国　際　協　力　事　業　団

医療協力部長　　長谷川　　豊

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Bio Farma にて　（中央が Nasution 総裁）

保健省

Bio Farma 中庭

Bio Farma 玄関前

I 調 査 団 派 遣

1. 調査団派遣の経緯と目的

昭和５９年７月３日付いおいて、インドネシア側との間で本プロジェクト予備調査団派遣につき合意がなされている。インドネシア側の本プロジェクト協力要請Ｔ／Ｒは、概要以下のとおり。

「 １億5,５００万の人口に対して組織的な予防接種プログラムを実施するため大量のポリオ・麻疹ワクチンが必要である。これを自国にて低コストで原液から一貫大量生産し、外国へも輸出することも計画中。このために技術協力としてワクチン製造・品質管理の専門家派遣、及び研修員の受入れ、機材の供与を要請する。」

要請のとおり原液からの一貫製造には、

①原液　　②施設、機器　　③人材

が必要であり、たとえ、これらが揃っても、外国から輸入するより低コストになるかは疑問である。まして、麻疹・ポリオ両ワクチンについて同時進行的に製造へ向けて協力することは不可能と予想された。

以上の状況から、技術協力の範囲・可能性を調査することが本調査団の主目的であった。

また、在インドネシア大使館からの情報としてインドネシア国における今年度開発予算の大幅削減、新規プロジェクト開始禁止が伝わっており、実際同国における他プロジェクトにおいてもインドネシア側によるローカルコスト負担の縮少化が多々見られていた。その他、供与機材や携行機材の通関遅延はかなり以前から続いていた。これによるプロジェクト日本チームへの圧迫は甚だしく、プロジェクト運営にも大きな支障を来たしている状況であった。

このようなことが本プロジェクトにおいても繰返された場合、プロジェクト自体、中途半端な形で終了しかねない。日本人専門家個人に対しても業務、生活面で大きな支障が生ずる。

よって、このような行政面においてのインドネシア側の取組み姿勢を確認しておくことも本調査団の目的であった。

2. 団 員 構 成

団長　吉岡勇雄
(財)日本ポリオ研究所
常務理事

団員　橋爪壮
千葉大学看護学部
教授

団員　高久慶典
(財)阪大微生物病研究会
観音寺研究所長

団員　山崎弘美
ＪＩＣＡ研修第二課

日順	月日	曜日	行程	交通手段	宿泊地	時刻	調査内容
1	4/8	火	(吉岡、山崎) 東京 —CX501→ 香港 —CX711→ ジャカルタ (高久) 東京 —CX503→ 香港 —CX711→ ジャカルタ 大阪 —CX711→ ジャカルタ	航空機	ジャカルタ	11:15発 / 11:20発 → 21:20着	出発(吉岡団長、高久・山崎団員)
2	9	水	(橋爪) 東京 —JL721→ ジャカルタ	〃	〃		〃 (橋爪団員)
			(吉岡、高久、山崎)				
			(午前) ホテル ～ JICA事務所 ～ 保健省			8:40 10:00	JICA事務所表敬及び打合わせ 保健省表敬、協議及びNQCL見学
			(午後) ジャカルタ ——→ バンドン	汽車	バンドン	14:00	移動(吉岡団長、高久・山崎団員)
3	10	木	(橋爪) ジャカルタ ——→ バンドン	汽車	〃		移動(橋爪団員) 午後15:30 BIO FARMAへ
			(吉岡、高久、山崎)				
			ホテル ～ BIO FARMA	車		8:30	BIO FARMAと協議及び所内見学
4	11	金	(全員) ホテル ～ BIO FARMA	〃	〃	8:30	BIO FARMAと協議
5	12	土	(全員) バンドン ——→ ジャカルタ	〃	ジャカルタ	9:30	移動
6	13	日			〃		資料整理等
7	14	月	(橋爪・高久)				帰国(橋爪・高久団員)
			ジャカルタ —CX710→ 香港 —CX500→ 東京 香港 —CX502→ 大阪	航空機		7:45発 → 21:15着 20:20着	
			(吉岡・山崎)				
			ホテル ～ JICA事務所 ～ 大使館		吉岡団長のみジャカルタ	9:30 10:30	JICA事務所へ調査報告及び在「イ」日本大使館表敬及び調査報告等
			(山崎)				
			ジャカルタ —JL722→ 東京	航空機	機中	18:45発 → 6:05着	
8	15	火	(吉岡)		吉岡団長		帰国(山崎)
			ジャカルタ —GA966→ シンガポール —SQD48→ デリー	航空機	デリー	15:00発 23:00着	吉岡団長引き続きインドへ

4. 面会者リスト

Organization

Ministry of Health

Dr. MIDIAN SIRAIT

Director General of Food and Drug, DEPKES

Dr. CHARLES J.P. SIREGAR MIC

Head of National Quality Control

Laboratory of Drug and Food

Drs. SANTOSO ATMOJO

Head of Narcotics and Hazardous

Substances Div.

Drs. SUJAS WADI

Head of Traditional Drug Div.

Dr. PUJO PRAYITNO

Head of Cosmetic and Medical Devices Div.

Drs. TJARTUN HASAN

Head of Administration Div.

Drs. MA'ROEF

Acting Head of Food and Beverages Div.

Dr. EMELIO LOGAWA

Head of Drugs Division

Bio Farma

Dr. NASUTION

President Director

Mrs. S. SUHARTO

Commercial Director

Dr. J. SUTARYO DVM. (Mr.)

Production Director

Mrs. K. WENAS

Head of Quality Control

Dr. INA MADIA DIPURA (Mrs.)

Head of Viral Vaccine Prod.

Dr. BENNY KALIGIS (Mr.)

Head of Viral Vaccine Control

Dr. AMYRETNO SUPRAPTO (Ms.)

Head of Measles Vaccine Prod.

日本大使館

大　　使　　武藤利昭

一等書記官　　平山一男

ＪＩＣＡインドネシア事務所

所　　長　　遠藤英夫

所　　員　　西尾久光

ＪＩＣＡ医療専門家（薬品品質管理プロジェクト）

① Dr. JIRO KAWAMURA

リーダー（川村次良）

② Dr. HIROTAKA KONUMA

（小沼博隆）

Ⅱ 調 査 結 果

1. 業 務 面

吉 岡 勇 雄 団長

1－1. Bio Farma

Bio Farmaは公社的性格をもつ、インドネシア唯一の人体用ワクチン製造所であり、インドネシア全土に必要な人体用のワクチン類を製造し、２７の州（省）に供給している。本製造所で製造したワクチン類を、保健省に有償で買上げてもらい、得た代金を再生産用の資金として運営されている。

本製造所はジャカルタの南方約１８０kmのバンドン市内にあり、９０,０００平方米の敷地と、延面積２０,０００平方米の製造施設・教育施設等を現在保有している。動物飼育施設は本所構内にあるものとは別に、バンドン市外にも保有している。

現存の製造設備は良く整備されて居り、機械・器具類も一応のものが設置されている。ワクチン製造に不可欠の基本的要素である電気、水、蒸気の供給については、現在の全製造に必要とされる量をまかなうに足るよう、自家発電装置４基、地下水汲上装置４ケ所、ボイラー４基を備え、集中管理方式で製造に支障をきたさないよう配慮されている。また、各種作業用機械を備えた工作機室があり、製造用機械、設備等の維持、整備がはかられている。

教育施設も同所構内にあり、primary high schoolを卒業して入所した従業員等を、３ケ年の教育期間で、微生物学および化学の領域の専門職員を養成せんとする訓練校で、将来laboratory technicianとしてワクチン製造あるいは保健衛生に従事するよう教育している。

現在、本製造所の従業員総数は４００人で、この内scientistは４０人、laboratory technician７５人を擁し、ＢＣＧ、ＤＰＴ、コレラ、腸チフス、狂犬病等のワクチンおよび各種抗血清を製造している。しかしながら、ＷＨＯの提唱するExpanded Programme on Immunizationの目標を充たすまでには未だ到っていない。すなわち、１９８５年８月のWHO Weekly Epidemiological Recordによれば、同国の１才以下の幼児へのＢＣＧ接種率は５６％、ＤＰＴの接種率は６％となって居り、本製造所の上記ワクチン製造能力がまだまだ不充分であることを物語っている。なお、ポリオ、マシンに関しては、接種率は共に７％と前記Recordに報告されているが、これは主に最終製品として輸入されたもの、あるいは輸入したbulkを小分けした製品による接種である。因みに、現在単価

bulkを輸入し、本製造所で混合、希釈、分注して作られたポリオワクチンは２０万ドースとのことであった。

以上、Bio Farmaの現状について述べたが、ＥＰＩに必要とするＢＣＧ、ＤＰＴワクチンの充足率よりみて、Bio Farmaの現在の活動状況はまだ充分とは言い難く、施設の拡充、必要人員の確保等でより一層の努力が要求されよう。

他方、今回の訪問の対象となったポリオおよびハシカワクチン製造プロジェクトについてBio Farmaは、かって馬小屋のあった跡地2,１００平方米（７０×３０米）の所に、両ワクチンの製造及び品質管理のための建物（延面積2,０００平方米）の建設を計画している。この建物の建設費と電気・ガス・空調等の付帯設備費として、１３億６千万ルピア（約２億３千万円）をBio Farmaが保有する自己資金より拠出の用意をしている。そして、製造に必要とする無菌空気供給設備、機械器具購入費及びその他の費用を、外部からの援助に期待している。その総額は５３０万ＵＳドルとなっている。その積算根拠となる個々の項目についての設備、機械費をみると、過少と考えられるものが散見されるので、実際の総額は上記の額の1.5倍以上となるのではないかと想像される。

今回の訪問時、所長Dr. Nasution以下７名の人々と会談する機会をもった。その内の４名が本プロジェクトの遂行の責任者・担当者－２名が製造関係、２名が品質管理関係－となると想定されるが、その人々のウィルス病の研究、ワクチン製造等の経験不足が見受けられた。また、本プロジェクトに必要とされる員数のScientistを充足するために、大学の研究員、新規大学卒業者等の採用を予定しているがウイルスワクチン製造の戦力となるには、かなりの日時を要するものと思う。ワクチン製造の中でも難しいとされるポリオとハシカのワクチン製造に従事する人々が、限られた期間内で養成され得るか否かが、本プロジェクトの成否を左右することとなろう。更に、本プロジェクトは長期に亘るものであり、周到な準備と綿密な計画を必要とするものである故、もし実施の場合には、インドネシア側に熱意のある推進者を期待したい。

1－2. National Quality Control Laboratory of Drug and Food

インドネシア当局者は、Bio Farmaで製造されたワクチン類の安全性、有効性を国家検定により再確認したいという意図をもっている。

現在、一般医薬品等の品質管理のために、ジャカルタ市内に当Laboratoryが設置、強化されつつある。すなわち、ＪＩＣＡプロジェクトの一つとして、日本の国立衛生試験所の協力の下、１９８３年より５年計画で、３階建の新棟の建設、機材の供与、研修員受入、専門家派遣を実施しつつある。しかしながら、当Laboratoryでワクチン類の国家検定を実施しようと企図するようになったのは最近のことであり、現在このために当Laboratoryの組織の中に試験室として新たに設置することが提案されているのが実状である。したがって、すでに建設された新棟の中に、ワクチン類の国家検定を実施するための充分なスペ

ースがない。本 Laboratory の所長 Dr. Siregar によれば、ポリオ・マシンワクチンの国家検定のために必要とされる試験室は、同所構内に設立されるであろうとのことであった。ポリオ・マシンの神経毒力試験を含めて、国家検定のための諸試験を当 Laboratory で実施するには、動物収容施設、病理試験室等のために計４００平方米余の建物が必要となろう。

また、諸試験を実施するに必要な Scientist、Laboratory Technician、Animal attendant 等の確保・養成をしなければならない。

2. ポリオ生ワクチン製造プロジェクトについて

橋爪　壮　団員

2－1. 本プロジェクトを推進しようとする背景

インドネシアにおける乳幼児死亡の原因として、下痢疾患、急性呼吸器疾患、破傷風の3つが重要な要因となっているにもかかわらず、あえてポリオワクチンの予防接種を普及させるため本プロジェクトを推進しようとする理由として、次の点があげられる。

(1) 1974年にだされたWHOのExpanded Program on Immunizationに協力するためにも、インドネシア政府は第四次5ケ年計画（1985－1989）の終りには現在の約7%の予防接種率を最低65%、できれば平均95%にしたいと考えている。

(2) ポリオは1976－1977年に各地で発生がみられ、その罹患率は0－4才台で10万対90、麻痺患者は0－14才で10万対4－7と推定されている。ちなみに昭和35年の北海道の大流行時の罹患率が10万対6.0であったことから考えても、かなりの流行があったものと思われる。

(3) 自国生産により、ワクチン輸入のための外貨節約ができるだけでなく、より安い価格が期待でき、広範な予防接種が可能となる。

2－2. 人口とワクチン製造目標

推定人口は160,000,000で、出産率は3.3～3.5%、年間の新生児は5,200,000～5,600,000と推定されている。

従って一年齢層だけ毎年予防接種を行うものとすれば、年間の最低必要量は、1、2、3型混合ワクチンを2回投与方式として10,400,000～11,200,000 doses、3回投与方式を採用すれば、15,600,000～16,800,000 dosesとなる。これにロス分とおそらく緊急事態用をみこした量と考えられるが、一応20,000,000 dosesを最終製造目標量としている。

2－3. Bio Farmaの計画

(1) 麻疹ワクチンとポリオワクチンの製造施設の建設

土地のスペース（1,200㎡）の関係から、2階もしくは3階の同一の建物内に麻疹とポリオの製造室、検定室、培地調整室、洗浄滅菌室を建設する計画で、下記表のように、設計に9ケ月、建設工事期間10ケ月、最終引き渡し迄22ケ月を予定しており、この間に、すべての大型機器の設置も完了する。

(2) 研修員の派遣

この２２ケ月間に研修員を派遣し技術を修得させる計画となっており、ポリオ関係の研修員の派遣計画は次のようになっている。

〔（　　）内の数字は計画がスタートした時点を０ケ月とする〕

イ．製造責任者（Production manager）

１名　　２ケ月間（１～２）

ロ．神経毒力試験のための病理学者

Bio Farma およびＦＤＡから各１名ずつ　　１年間（２～１３）

ハ．製造担当高級技術者（scientist）　　２名

製造品質管理担当高級技術者　　１名

計３名　　３ケ月間（９～１１）

ニ．製造技術者（technician）

２名　　２ケ月間（１９～２０）

ホ．品質管理技術者（technician）

Bio Farma およびＦＤＡより各１名ずつ　　３ケ月間（２４～２６）

(3) 製造指導者の現地指導要請

この件は受入希望時期など、まだあまり具体的でないが、一応次の４名を考えている。

イ．製造の expert　　１名　　１０週間

ロ．品質管理の expert　　２名　　各２ケ月ずつ

おそらく１名は bulk からの製造を始める時期（第１８ケ月頃か）と、他の１名は原液製造時期（第２４ケ月以降）を考えているのではなかろうか。

ハ．機器の設置、試運転、などに１名６週間を予定しているが、おそらく分注器関係のためではないかと考えられる。

(4) ワクチンの供給体制

イ．建設工事がほぼ完了し、製造関係の技術者の研修がある程度完了する第１８ケ月迄は最終製品を輸入する。

ロ．第１８ケ月以降は bulk 輸入をはじめ、３価混合ワクチンの試作製造を開始する。

ハ．計画開始２年後、即ち第２４ケ月よりポリオワクチンの試験製造を開始し、１年ないし２年後から通常の本格的製造に入る。

(5) 機材の供与

ポリオ関係に必要とされる機材と、麻疹との共通機材に分けられる。

イ．ポリオ関係

動物舎関係	$150,000
製造室	350,000
分注関係	275,000
計	775,000

ロ．共通機材設備

包装関係	225,000
無菌室関係	600,000
培養液調整室関係	75,000
原液貯蔵室関係	50,000
検定室関係	430,000
病理検査関係	40,000
最終製品保管室関係	160,000
計	1,580,000

イ． ＋ ロ． ＝ 2,355,000

2－4. 本プロジェクトの実現性と問題点

昭和61年4月10、11日の両日にわたりBio Farmaを視察し、Dr. Nasution所長以下本プロジェクトに関係のある6名の責任者の方々と討議を通じて得た私見を以下述べてみたい。

(1) Bio Farmaの生産能力：

Bio Farmaは立地条件が良く、かなりゆったりした敷地を持ち、環境条件はきわめて良い。日本の衛生検査技師学校に似た学校を併設しており、technicianクラスの技術員の確保は比較的容易にできるものと思われる。

施設はこれまで全て平家建で、ゆとりのある配置をしており、建物の維持管理もゆきとどき非常に清潔である。ボイラーも1t程度の容量のものを2基備え、電気も大容量の自家発電装置を備え、一般の電灯以外は自家発電によりまかなっているほどで、製造施設としてしっかりしている。

百日咳菌、破傷風菌などもワクチン培養をしており、細菌関係のワクチン製造には高度の技術水準を持っているものと見受けられた。多品目のワクチンを製造しているにしては、従業員が少ないようで、かなり効率良く運営されているものとの強い印象をうけた。

(2) 本プロジェクトに対する準備状況：

本プロジェクトは前述のように１９８５年度からの第４次５ケ年計画の一つとして取上げられた関係と考えられるが、既に本プロジェクトの可能性に関するWHO／UNICEF／USAIDの調査報告書が１９８４年９月にだされている。この報告書はこのプロジェクトの進めかた、年次計画、これにかかる経費、必要な人員などを極めて具体的、詳細に述べており、Bio Farmaあるいはインドネシア政府はこの報告書に基き計画案を作成したと考えられる。さらにDr. Nasutionらは世界各国のおもだった殆ど全ての製造所、研究所を視察し、検討を加えたもようである。

ポリオに関しては、彼らはＷＨＯの製造施設、製造用種ウイルス、品質管理に対する考え方を十分理解しており、この点ではブラジルよりも、むしろよく事前調査が行なわれているように思われる。

WHO／UNICEF／USAIDの報告書に示された勧告よりもポリオの施設の建設、ならびに一貫製造（試験製造）開始の時期が早くなっているのは、建設用地および建設に要する費用の関係でやむをえないかも知れないが、試験製造開始の時期、あるいはその内容については、さらに検討を要すると考える。できれば麻疹ワクチン製造を行いながら、細胞培養ワクチン、とくに生ワクチン製造を身につけた技術者層を養成し、その内から逐次ポリオ要員に振り替えて行くほうが無理がないのではないかと思われる。細胞培養を用いてウイルスを扱った経験者の少ないBio Farmaではポリオと麻疹に勢力を分散させることは危険で、この点ＷＨＯの勧告は適切と考えられる。

このプロジェクトを達成させるのに、技術者の養成が最も重要なポイントになるであろう。

Bio Farmaの必要人員予定では前記表のようにscientist ５、technician １２、補助者２となっているが、ＷＨＯの勧告案では、scientist ３、高級技術者８、技術者１８、補助者５としている。ちなみに日本ポリオ研究所の要員はscientist １２、高級技術者４、技術者７、補助者８の計３１名で構成されていることから考えてもBio Farma案はやや手薄な感じがする。ただし、輸入bulkから最終製品を作る当面の人員、および小規模の試験製造だけを考え、将来本格製造を始めるまでに逐次補充してゆく考えであれば、この案でもよいであろう。

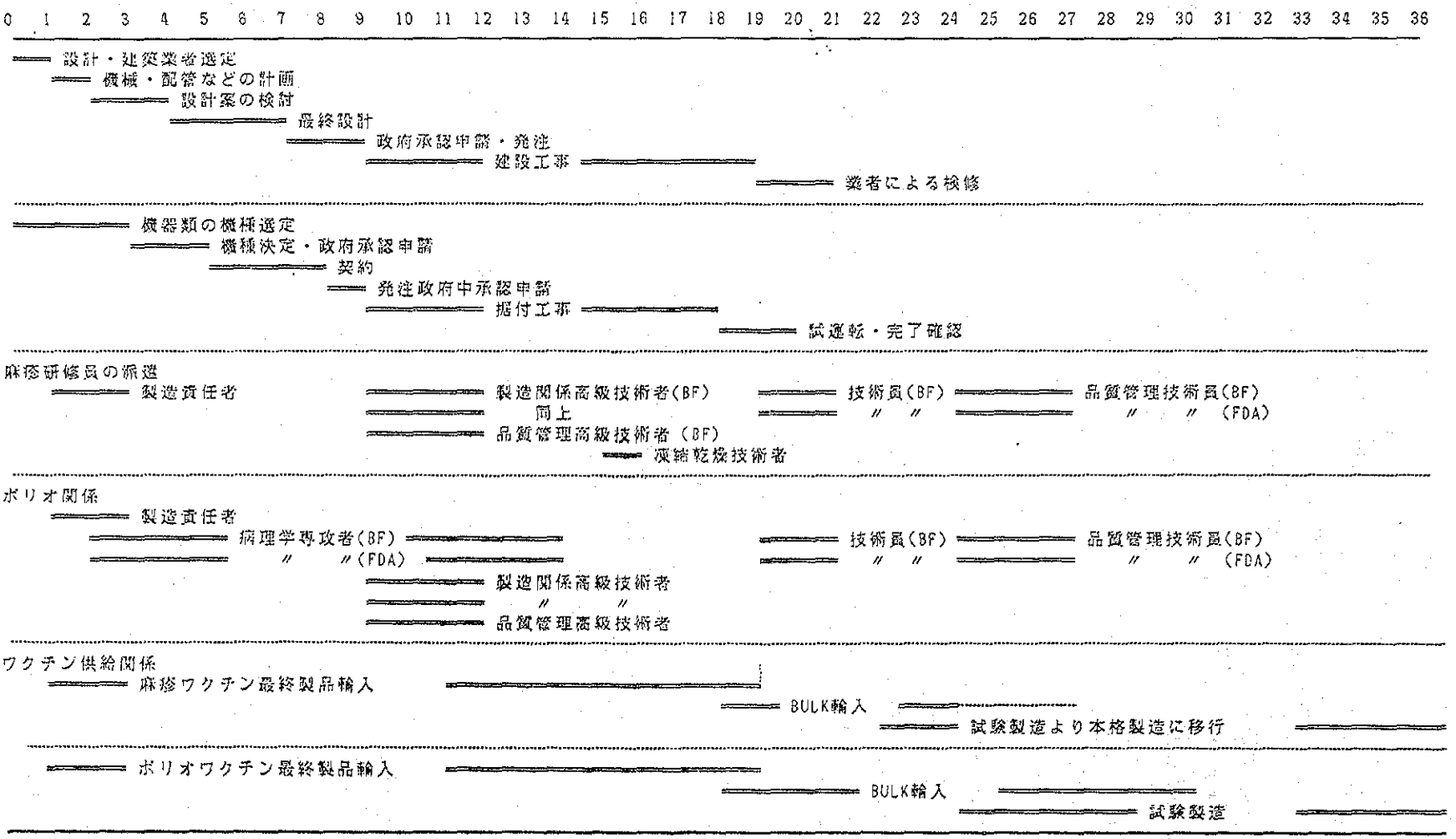
おわりに：　このプロジェクトの実行母体であるBio Farmaは内容の充実した施設で、われわれが出発する前に得ていた情報よりはるかによく事前調査もされ、検討された計画を持っており、この種のプロジェクトを進めるにはふさわしい施設と考えられた。しかし何分にも細胞培養を用いたウイルスの研究ないしは製造経験者の層の薄い点が心配で、これらの要員の養成がこのプロジェクト達成への鍵となるであろう。

別表 2

人員配置比較表

	Sr.Scientist	Sr. Technician	Technician	Attendant	Total
WHO	2	6	18	5	31
Bio Farma	5		12	2	19
JPRI	12	4	7	8	31

別表 1　　Time schedule Plan of the Project



3. 麻疹ワクチン

高　久　慶　典　団員

3－1. 麻疹ワクチン製造計画量

年間の新生児は約５００万人あるので、ロス分を考え、７００万doses（１０doses／vial）を製造目標量として、計画されている。

3－2. Bio Farmaでの製造計画

(1) 製造施設

ポリオと麻疹ワクチン製造施設は、新しく建設する計画で、設計・建設工事などを経て、最終引き渡しまで、２２カ月を予定しております。凍結乾燥機・分注機などの大型機械の設置は、建設工事中完了する必要があろう。

(2) 研修員の派遣

ポリオ・麻疹ワクチン製造施設が完了するまでに、製造に関する研修員を派遣して、技術を修得する計画になっております。麻疹ワクチン関係の研修員の派遣計画は、次のようになっている。〔（　）内の数字は、計画がスタートした時点を０カ月とする。〕

① 製造責任者（Production Manager）

１名　　１カ月（１～２）

② 製造関係高級技術者（Scientist）

２名　　３カ月（９～１１）

③ 品質管理高級技術者（Scientist）

１名　　３カ月（９～１１）

④ 凍結乾燥技術者

１名　　１カ月（１５～１６）

⑤ 製造技術者（Technician）

２名　　２カ月（１９～２１）

⑥ 品質管理技術員（Technician）

Bio FarmaおよびＦＤＡより各１名

２名　　３カ月（２４～２６）

(3) 製造指導者の現地指導要請

この件は、ポリオ関係と同様に受入れ希望時期など、あまり具体的でないが、３名を考えている。

① 製造のExpert　　１名　　１０週間

② 品質管理のExpert　　１名　　１０週間

③　機器の設置・試運転などに１名　　６週間

３－３.　ワクチンの供給体制

ポリオワクチン同様に、プロジェクト開始第１８カ月までは、最終製品を輸入する。第１８カ月以降は、Bulkを輸入し、試作製造し、第２３カ月目からは一貫製造の試作から、本格製造に入る。

３－４.　機材の供与

麻疹関係に必要とされる機材と、ポリオとの共通機材に分けられる。

麻疹機材として

製造室	$３５０,０００.－
分注・凍結乾燥機	$４２５,０００.－
計	$７７５,０００.－

３－５.　本プロジェクトの実現性と問題点

(1)　Bio Farmaについて

Bio Farmaは、９０,０００㎡の敷地内に延２０,０００㎡の製造施設で、細胞培養を用いたワクチン以外の、ＤＰＴ・ＢＣＧ・コレラ・腸チフス・狂犬病などのワクチン、および各種抗毒素が製造されておる。

製造施設は整備されており、ワクチン製造には、かなりの技術水準をもっている。

しかし、Bio Farma独自で、新しいワクチンの開発をする、研究施設にはなっていないようだ。

さて、インドネシア政府による、本プロジェクトの計画案が作成されておるが、建物の設計、そして凍結乾燥機・分注機などは、製造量を考慮して、訂正する必要があるようだ。

(2)　ＳＰＦ鶏卵について

麻疹ワクチン製造にはＳＰＦ鶏卵を必要とし、ＳＰＦ鶏卵を生産するPoultry Farmを確立するには、６カ月を要する。

インドネシアでは、日本の協力でＳＰＦ鶏卵が生産されるといわれているが、麻疹ワクチンに使用する量が、確保できるかも、調査する必要がある。

4. 行　政　面

山　崎　弘　美　団員

4－1. 開発予算の削減状況

前年度に比して２２％の削減、さらに繰越ができない、といった措置がとられている。

4－2. プロジェクト実施に係る支援体制等

本件については日本政府の協力可否が不明な現況においては、予算措置等につき具体的に講ずることはできないが、もし、本件実施が確定されれば、それに生ずるローカルコストの負担等は当然請け負うものとする。ついては機材引取り、通関手続に関しても同様。

4－3. カウンターパート

本件プロジェクトの実施が明らかになった時点で必要なスタッフを調達する。また大学等からのリクルートも考えているが、現時点で具体的に示すことは困難である。

4－4. 保健省とBIO FARMAとの関係等

保健省はBIO FARMAの主管官庁として位置づけられており、事業実施、運営等について管理・監督を行なう。従って、本件実施に際しては保健省に予算措置、プロジェクトの運営等につき協議する必要があると思われる。

但し本件プロジェクトが実施される場合、プロジェクトマネージャーはBIO FARMA側になると思われる。

予算についてはBIO FARMAで得た収入については保健省経由で大蔵省に納付され、改めて予算としてBIO FARMAに交付される仕組みとなっている。

なお、人的交流については上級の管理者で往来が多少あるようであり、BIO FARMAの総裁であるDr. NASUTIONも以前保健省に属していたとのことである。

4－5. インドネシア側要望について

BIO FARMAは本件の早期実施を強く要望していると思われた。

資　　料　　1

T／R, LIVE ATTENUATED ORAL POLIMYELITIS AND MEASLES VACCINE PROJECT

(Project Aid Proposal) Code Number :

1. Project Title	:	Live attenuated oral poliomyelitis and measles vaccine production.
2. Location	:	Perum Bio Farma, 28 Jalan Pasteur, Bandung, West-Java, Indonesia.
3. Executing Agency	:	Directorate General of Food and Drug Administration, Ministry of Health.
4. Objectives	:	To improve the Health Services by the provision of viral vaccines, particularly live attenuated oral poliomyelitis and measles vaccines in sufficient amounts and at a reasonable price to be within financial reach of the people.
5. Project Description	:	The project is planned to build a complete manufacturing plant for live attenuated oral poliomyelitis and measles vaccines. The plant will consist of facilities for production, quality control, washing, and for animal holding. When finished, the plant will be able to produce 20 million doses of live attenuated oral poliomyelitis vaccine and 7 million doses of measles vaccine per annum. The scope of work consists of : - Construction of a completely new production facility. - Provision of production- and laboratory equipment including its spare parts. - Provision of equipment for quality control-, washing-, and animal holding facilities.

6. Implementation time	: 3 (three) years after approval of the proposal.		
7. Project Cost	: Total cost	: US $ 5.312.500,- and Rp. 1.360.000.000,-	
	Local cost	: Rp. 1.360.000.000,-	
	Foreign Exchange Cost	: US $ 5.312.500,-	
8. Amount Proposed for Commitment	: US $ 5.312.500,-		
9. Related to Technical Assistance	:		
10. Stage of Project Preparation	: - A feasibility study by a joint with WHO/Unicef/Usaid consulting team has been carried out on September 1984. - Building space available at this moment.		

(Technical Assistance Proposal) Code Number :

1. Project Title : Live attenuated oral poliomyelitis and measles vaccines production.

2. Location : Perum Bio Farma,
28, Jalan Pasteur,
Bandung, West-Java, Indonesia.

3. Executing Agency : Directorate General of Food and Drug Administration, Ministry of Health.

4. Objective : To improve the Health Services by the provision of viral vaccines, particularly live attenuated oral poliomyelitis and measles vaccines in sufficient amounts and at a reasonable price to be within financial reach of the people.

5. Project Description : To provide expert services, fellowships and transfer of technology for a complete manufacturing plant for live attenuated oral poliomyelitis and measles vaccines.
The plant will consist of facilities of production, quality control, washing, and for animal holding.
When finished the plant will be able to produce 20 million doses of poliomyelitis and 7 million doses of measles vaccines per annum.

6. Scope of assistance required :

6.1. Equipment including packaging, freight, insurance and incidental expenses	US $	3.912.500,-
6.2. Transfer of technology fee	US $	500.000,-
6.3. Expert Services	US $	275.000,-
6.4. Training of Bio Farma personnel	US $	325.000,-
6.5. Other expenses	US $	300.000,-
T o t a l	US $	5.312.500,-

7. Related to Project Aid :

TERMS OF REFERENCE

LIVE ATTENUATED ORAL POLIOMYELITIS-
AND MEASLES VACCINE PRODUCTION

I. BACKGROUND AND SUPPORTING INFORMATION

1. Justification of the project

1.1. WHO initiated the Expanded Programme on Immunization in 1974 and it has become an essential element of the strategy to achieve "health for all by the year 2000" (WHO Resolution no. 30.53, adopted in May 1977) with the goal of reducing morbidity and mortality from diphtheria, pertussis, tetanus, measles, polio and tuberculosis by providing immunization against these diseases for every child in the world by the year 1990.

While the reported numbers of cases and death may underestimate the extend of the consequence of those 6 disease, they are thought to cause some 5 million deaths among children under 5 years, while an additional 5 million are permanently desabled worldwide (6th Report on the World Health Situation, part I: 1980). The importance of EPI as an essential component of maternal and child health and primary health was emphasized at various forums.

The demand for vaccines in Indonesia is expected to increase sharply because the present coverage of the target population will increase to 100% at the end of the Fourth Five-year Development Plan (Repelita IV).

It is therefore essential to increase the production of vaccines required in the Expanded Programme on Immunization accordingly.

1.2. This project proposal is submitted with the objective of improving the health services by the provision of viral vaccines, particularly live attenuated oral poliomyelitis and measles vaccines in sufficient amounts and at a reasonable price to be within financial reach of the people.

One of the targets of the 4th Five Years Development Plan (REPELITA IV) is to strengthen the general public health status of the population through prevention of communicable diseases by immunization. By improving the health services, it is expected that the mortality rate of the population which stands now at 11.9 per 1.000 will drop to 10.3 per 1.000 at the end of 1989, the infant mortality rate

from 90.1 to 70 per 1.000 live births and the mortality rate for children younger than 5 years (the so-called "Balita" group) from 17.8 to 14 per 1.000.

Many childhood diseases, in this particular case poliomyelitis and measles could be prevented by active immunization only.

Poliomyelitis, a viral and communicable disease is recognized as a disease entity with epidemic potentials, occurring throughout the year in tropical regions.

A great majority of cases occur in the younger age group; over 90% in infants under 5 years of age, almost 80% under 2 years, and about 50% in children younger than 1 year.

1.3. In Indonesia during polio outbreaks in several regencies in 1976 - 1977, attack rates in the 0 - 4 year age group was 90 per 100.000 population with estimated paralytic poliomyelitis incidence rates between 4 - 7 per 10.000 in the 0 - 14 year age group.

During that period, surveys by house to house visits revealed that 80% were paralytic at the age of 3 years and 50% after receiving either therapeutic or preventive injections.

All three types of poliomyelitis viruses have been encountered in the outbreaks. Cases among adults were also detected and clinically diagnosed either as polyneuritis and/or encephalitis; the youngest was 17 years old and the oldest over 60 years of age, also accompanied by paralysis.

This means that the disease is highly endemic.

1.4. Measles is an acute and highly contagious viral disease in childhood, and in developing countries half the children become infected during their first year of life with mortality rates reaching as high as 60%.

Measles is usually contracted during childhood with bronchopneumonia, encephalitis and otitis media as its chief complications, with some of these complications resulting in lifelong handicaps and sequellae.

Secondary bacterial and viral complications are mainly responsible for the high fatality rates of measles in certain developing countries.

Besides, a direct correlation was also found between mortality and malnutrition which alters the host response to the virus.

Socio-economic and public health factors play also an important role in the outcome of the disease.

1.5. Measles is endemic throughout most countries of the world, having a characteristic tendency to become epidemic every 2 - 3 years. The highest incidence is usually in the 1 - 5 years age group, and by the age of 20 years about 90% of persons have had an infection with measles virus.

1.6. Serious outbreaks of measles with significantly high mortality rates have been reported in some developing countries.
In Chile for instance, measles was responsible for 2 to 3.5% of all deaths in the country and for 50% of all deaths due to acute communicable diseases.
In West Africa, measles was one of the leading causes of death and disability in children with an overall mortality rate of 5 - 10%.

A large outbreak of measles occurred on the islands of Lombok in 1977 affecting 12.508 children with a case fatality rate of 2 - 9%.
In 1983 - 1984, outbreaks of measles also occurred in West Java with case fatality rates between 15% and 24%.
Smaller outbreaks have subsequently occurred in several regions of the country with case fatality rates ranging between 2.9 to 25 %.
It was also evident that during these outbreaks most of the victims were at age 1 to 4 years, and that nutritional status plays an important role on the outcome of the disease as proved by the fatal cases.
Secondary bacteriological and viral complications are most probable responsible for the relativey high case fatality rates.

1.7. Hospital surveys carried out in Indonesia during 1969 - 1971 proved that the case fatality rates for measles was still as high as 8,8%.
Although data concerning complications of measles in Indonesia are not available yet, but as can be seen from the figures in the German Democratic Republic, complications occur in 6 - 7% of all measles cases.
After introduction of mass immunization, only sporadic cases were recorded in that country during the following years.

1.8. The excistance of well-organized immunization programmes and public health services in developed countries reduced the complications due to measles to 0.2 - 1.0 per 1.000 cases.

1.9. After the eradication of smallpox globally, and knowing the achievement reached by developed countries in controlling infectious diseases, WHO has launched an Expanded Programme on Immunization in 1974 and it has become an essential element of the strategy to achieve "health for all by the year 2.000" (WHO resolution no. 30.53 adapted in May 1977) with the goal of reducing morbidity and mortality from diphtheria, pertussis, tetanus, tuberculosis, poliomyelitis and measles for every child in the world by the year 1990.

1.10. Indonesia also commits to this Expanded Programme on Immunization and is active conducting it; therefore the demand of poliomyelitis and measles vaccines in Indonesia is expected to increase sharply because the present coverage of the target population will increase to about 100% at the end of the Fourth Five-year Development Plan.
Hence, it is therefore essential to increase the production of poliomyelitis- and measles vaccines required for the Expanded Programme on Immunization.

1.11. In order to protect these susceptible children, preventing measures by active immunization as has been carried out in developed countries should be initiated.

1.12. In the frame of efforts to be self-reliant on the production and supply of poliomyelitis- and measles vaccines needed for the immunization programme, strengthening of Perum Bio Farma as a state enterprise assigned by the Government to produce vaccines, in this case poliomyelitis- and measles vaccines in essential.
When the vaccines are produced locally, a large amount of foreign currency could be saved annually, while the price of the vaccines could be expected lower and within the financial reach of a larger part of the population.

1.13. Tis project proposal is submitted with the objective of improving the health services by the provision of live attenuated poliomyelitis- and measles vaccines in sufficient amounts and at a reasonable price to be within financial reach of the population.
One of the targets of the 4th Five-year Development Plan (REPELITA IV) is to strengthen the general public health status of the population through prevention of communicable diseases by immunization.

By improving the health services, it is expected that the mortality rate of the population which stands now at 11.9 per 1.000 will drop to 10.3 per 1.000 at the end of 1989, the infant mortality rate from 90.1 to 70 per 1.000 live births and the mortality rate for children younger than 5 years (the so-called "Balita" group) from 17.8 to 14 per 1.000.

Many childhood diseases, in this particular case measles, could be prevented by active immunization only.

2. Name of the project and its activities

2.1. Name of the project : Live attenuated oral Poliomyelitis and Measles Vaccine production.

2.2. Purpose and significance of the project :

a. Criteria have been used by countries to determine whether poliomyelitis is a health problem requiring regular immunization such as, if paralytic cases in the age group of 0-4 years are higher than 10 per 100.000, and also if the number of new poliomyelitis cases is at least 1 per 100.000 per year.

b. In Indonesia poliomyelitis is endemic and occurs throughout yhe year, occasionally in epidemics.
Although the infection may be inapparent or subclinical, paralysis may result for which the patient may be handicapped for life.

c. Considering the data accumulated during poliomyelitis outbreaks, the above mentioned criteria have been fulfilled, even exceeded such as for instance in North Sulawesi and on the island of Bali. Paralysis prevalence rates were respectively 34 and 37 per 10.000 during 1977 and 1978 and in Palembang it was 21 per 10.000 in 1977.

d. As far as measles is concerned, this pediatric diseases has been previously always considered as a mild disease with occasionally secondary bacterial infection of the lungs as a complication. However, since 1976-1977, outbreaks have occurred particularly in the age group of 1-4 years, with a case fatality rate ranging between 2.9% to 25%, a majority of these patients suffering also from malnutrition.

In 1983-1984, outbreaks of measles also occurred in West Java with case fatality rates between 15% and 24%.
Encephalitis as a complication of this disease have been detected during these outbreaks, leaving permanent sequellae on its victims.

e. Since measles mainly encounter children, prevention should be conducted of which immunization is the only way reduce morbidity, mortality and consequences of complication among these youngsters.

f. Immunization are usually given as basic immunization in the first year of life.

g. Since poliomyelitis and measles mainly encounter children, prevention should be conducted of which immunization is the only way to reduce morbidity, mortality and consequences of complications among these youngsters.

h. Immunizations are usually given as basic immunization in the first year of life.

3. Institutional framework

3.1. Similar to the production of other bacterial and viral vaccines in Indonesia, Perum Bio Farma will be the only institute responsible for the production of poliomyelitis-and measles vaccines.

3.2. Perum Bio Farma is a state enterprise under the auspices of the Ministry of Health and was assigned by the Government to produce vaccines and sera.
Perum Bio Farma is responsible for the production of biologicals especially vaccines, antisera, diagnostics etc. which are urgently needed for the improvement of the Social Health Services as outlined by the 4th Five Years Development Plant (REPELITA IV).

3.3. By submitting this project Perum Bio Farma intends to develop its production to provide for live attenuated oral poliomyelitis-and measles vaccines for the country.

3.4. Besides Perum Bio Farma's intention to develop its production capacity, this project will also strengthen the capabilities of the National Control Authority, resulting in the development and production of vaccines of high quality.

4. Government follow up

4.1. Whenever this project is completed, the need for poliomyelitis may be fulfilled since this project will be able to produce 2.000.000 vials @ 10 doses of live attenuated oral poliomyelitis vaccine per annum at a reasonable price to conduct the Expanded Programme on Immunization of the Government.

The need for measles live vaccine may also be fulfilled since this project will be able to produce 700.000 vials @ 10 doses of measles live vaccine per annum.

4.2. As a further development at the completion of this project, the production of poliomyelitis-and measles vaccines may be increased continually, while improving its quality in compliance with the development of the latest technology and increasing its capacity in accordance with the increasing needs in the future.

4.3. Through this project, Perum Bio Farma will gain technical knowhow about the manufacturing process and quality control of poliomyelitis- and measles live vaccines.

II. OBJECTIVES OF THE PROJECT

As its immediate objective, whenever this project has been completed, the provision of poliomyelitis- and measles vaccines will be fulfilled in accordance with Government's program for the supply of biologicals as outlined by the 4th Five Year Development Plan (REPELITA IV).

The long term objective of this project is to continually improve the products quality as well as its quantity and to manufacture with the latest technology of production so that it may become more commonly available and within the financial reach of the people.

III. PLAN OF OPERATION

This project is to be carried out in three years as follows :

A. Designing of buildings, approval of design, and erection of buildings.

B. Purchasing, procurement, installation and testing of equipment.

C. Training of Bio Farma personnel.

D. Production starts after finishing of building and installation of equipment.

IV. EXTERNAL AND BIO FARMA INPUTS

1. External Inputs :

1.1. Equipment for the production and quality control of live attenuated poliomyelitis-and measles vaccine.

1.2. Transfer of technology for poliomyelitis-and measles vaccine.

1.3. Expert Services

Expert on production and quality controle and expert for installation, testrun and troubleshooting of equipment.

1.4. Training of Bio Farma personnel;

trainees for production manager, production processing, production control, animal care and for quality control;

training of technicians and machine operator.

1.5. Other expenses.

2. Bio Farma Inputs :

2.1. Building for production and quality control of poliomyelitis-and measles vaccine including warehouse, restrooms, shower rooms etc.

2.2. Building space for above buildings.

2.3. Services

Consisting of installation of electricity, piping for gas, pressured air, vacuum, distilled water, household water etc., including installation of complete air conditioning system.

V. ESTIMATED COST OF THE PROJECT

A. External Inputs :

1. Equipment for :

1.1. Animal house	US $	150.000,-	280 rb
1.2. Polio Production Laboratory	US $	350.000,-	650
1.3. Measles Production Laboratory . . .	US $	350.000,-	
1.4. Sterile Filling	US $	275.000,-	510
1.5. Sterile Filling and freeze-drying Measles vaccine	US $	425.000,-	790

1.6. Packaging Department	US $	225.000,-
1.7. Sterile Zone	US $	600.000,-
1.8. Medium Preparation	US $	75.000,-
1.9. Bulk Storage of Polio and Measles vaccines	US $	50.000,-
1.10. Controle Laboratory	US $	350.000,-
1.11. In Vitro Controle Laboratory . . .	US $	80.000,-
1.12. Histology Laboratory	US $	40.000,-
1.13. Warehouse; storage of finished products	US $	160.000,-
	US $	3.130.000,-

- Costs for packaging, freight and insurance of equipment :
  15% x US $ 3.130.000,- = US $ 469.500,-

- Incidental expenses :
  10% x US $ 3.130.000,- = US $ 313.000,-

. . . . .	US $	782.500,-
T o t a l	US $	3.912.500,-

2. Transfer of Technology fee for Poliomyelitis- and Measles vaccines . . US $ 500.000,-

3. Expert Services :
   For Poliomyelitis vaccine
   3.1. 1 expert for production (10 weeks)
   3.2. 2 experts for quality control (2 months each)
   3.3. 1 expert for installation, testrun and troubleshooting of equipment (6 weeks)
   3.4. Travel expenses
   3.5. Hotel and meals for experts during 32 m. weeks

   Estimated expenses ..... US $ 150.000,-

   For Measles Vaccine
   3.6. 1 expert for production (10 weeks)
   3.7. 1 expert for quality control (10 weeks)
   3.8. 1 expert for installation, testrun and troubleshooting of equipment (6 weeks)

3.9. Travel expenses

3.10. Hotel and meals for experts during 26 m. weeks

Estimated expenses ..... US $ 125.000,-

4. Training of Bio Farma Personnel :

For Poliomyelitis Vaccine

4.1. 1 production manager (1 month)

4.2. 1 for production processing (3 months)

4.3. 2 for production controle (3 months each)

4.4. 2 for neurovirulence testing (12 months each)

4.5. 1 for animal care

4.6. 2 technicians (3 months each)

4.7. 2 for quality control (1½ months each) National quality Control NCL. atau

4.8. Travel expenses

4.9. Lodging and meals for trainees during 46 m. months

Estimated expenses ..... US $ 200.000,-

For Measles Vaccine

4.10. 1 production manager (1 month)

4.11. 1 production processing (3 months)

4.12. 1 for animal care (3 months)

4.13. 1 for production control (3 months)

4.14. 2 technicians (3 months each)

4.15. 2 for quality control (1½ months each)

4.16. 1 machine operator (1 month)

4.17. Travel expenses

4.18. Lodging, meals and other expenses during 20 m. months

Estimated expenses ..... US $ 125.000,-

5. Other expenses ..... US $ 300.000,-

6. Total :

6.1. Equipment, including packaging, freight, insurance and incidental espenses ..... US $ 3.912.500,-

6.2. Transfer of technology fee for Poliomyelitis and Measles vaccines ..... US $ 500.000,-

6.3.	Expert Services :		
	for Poliomyelitis and Measles vaccines	US $	275.000,-
6.4.	Training of Bio Farma Personnel,		
	for Poliomyelitis and Measles vaccines	US $	325.000,-
6.5.	Other expenses	US $	300.000,-
		US $	5.312.500,-

B. Bio Farma Inputs :

1. Buildings

1.1. Shared facilities for Poliomyelitis and Measles vaccines

- medium preparation room	36	sqm
- storage room	46	sqm
- toilets	12	sqm
- freezer rooms for storage of bulk vaccine and finished products	144	sqm
- washing and sterilizing rooms	124	sqm
- corridors	20	sqm
	382	sqm

1.2. Building for Poliomyelitis vaccine

- production facilities	170	sqm
- quality control facilities	170	sqm
- laboratory for virulent polio-virus strains . . .	36	sqm
- laboratorium for neurovirulence test	36	sqm
- filling and dispensing room	70	sqm
- offices, meeting rooms, rooms for personnel . . .	55	sqm
- corridors	110	sqm
- animal room	285	sqm
	932	sqm

1.3. Building for Measles vaccine

- production facilities	169	sqm
- quality control facilities	169	sqm
- laboratory/reading room	36	sqm
- offices, meeting rooms, rooms for personnel . .	55	sqm

- toilets	36	sqm
- filling and dispensing room	70	sqm
- freeze drying room	32	sqm
- corridors	110	sqm
	677	sqm

Estimated cost : 2.000 sqm x Rp. 400.000,- = Rp. 800.000.000,-

2. Building space

   1.200 sqm x Rp. 175.000,- . . . . . Rp. 210.000.000,-

3. Services, consisting of :

   3.1. Installation of electricity wiring

   3.2. Installation of piping for gas, pressured air, vacuum, distilled and household water, etc.

   3.3. Air conditioning . . . . . Rp. 350.000,000,-

   Rp.1.360.000.000,-

Grand total :

- External Inputs : US $ 5.312.500,-
- Bio Farma Inputs : ~~US $~~ 1.360.000.000,-

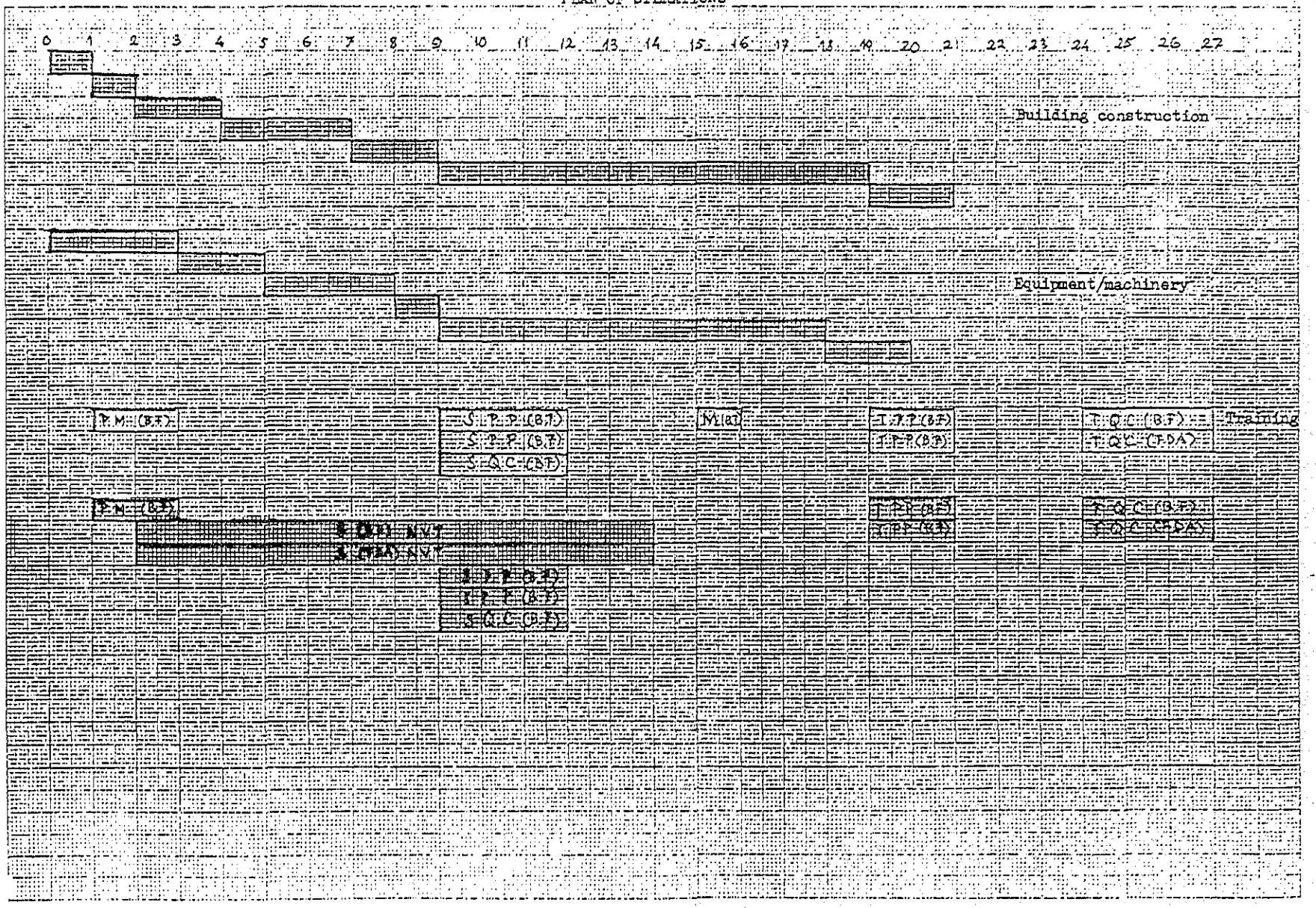
Bandung, 19 Februari 1986

P L A N O F O P E R A T I O N S

Building Construction		Equipment/Machinery		Training				Production Activities	
Month	Specification	Month	Specification	Month	Number	Specification	Duration (month)	Month	Specification
1	Selection and nomination of Engineering Company for preparing design and drawing of the building to be constructed. Prequalification of contractor for construction of building.	1	Input of specification of equipment/machinery, Process Flow and Piping installation (Masterlist preparation)	2	1	Production Manager for Measles Vaccine production.	2	1-18	Importation of MV in final containers.
2	Input of building, equipment/ machinery and Process Flow and Piping installation specification for preparation of predesign by the Engineering Company.	4	Specification finished and approval of Masterlist by the government.		1	Production Manager for OPV production	2	18	Validation of filling and freezedrying for MV.
3	Consultation and approval of predesign and drawing	6	Quotations requested from suppliers and expected quotations received within 3 months time.	3	2	Scientist for neurovirulence test (OPV)	12		Importation of bulk MV.
5	Preparation of the specification of material used for building construction and complete drawing of the building finished. Preparation of tender document.	9	Approval of the government for issuing order.		2	Scientist for production processing (MV)	3	22	Start basic production MV.
8	Tender for construction of the building and nomination of contractor after approval of the government.	10	Order issued and delivery time estimated 9 month included shipment and custom clearance.	10	2	Scientist for production processing (OPV)	3	24	Complete production cycles on routine basis for MV.
10	Building construction started and estimated finished within 10 month and ready for usage.	19	Installation of Equipment/ Machinery. Validation and trial run.		1	Scientist for Quality Control (MV)	3	1-18	Importation of OPV in final containers.
20	Maintenance phase of the building by the contractor.				1	Scientist for Quality Control (OPV)	3	18	Validation of filling for OPV. Importation of bulk OPV.
				16	1	Mechanician for freeze drier (MV)	1	24	Start basic production of OPV
				20	2	Technicians for Production processing (MV)	2	36-48	Complete production cycles on routine basis for OPV.
					2	Technicians for Production processing OPV)	2		
				24	2	Technicians for Quality Control (MV)	3		
					2	Technicians for Quality Control (OPV)	3		

Note : MV = Measles Vaccine
OPV = Oral Polio Vaccine

PLAN OF OPERATIONS



人　員　計　画

		Required	Present	To be recruited
I. Polio Vaccine Production				
A. Production				
1. Scientist	:	1	1	-
2. Technician	:	4	1	3
B. Production Control				
1. Scientist	:	2	2	-
2. Technician	:	4	1	3
C. Animal house/neurovirulence Test				
1. Scientist	:	1	-	1
2. Technician	:	2	-	2
3. Animal lab. assistant	:	2	-	2
D. Quality Control				
1. Scientist	:	1	1	-
2. Technician	:	2	1	1
Total :				
Scientist	:	5	4	1
Technician	:	12	3	9
Animal lab. assistant	:	2	-	2

		Required	Present	To be recruited
I. Measles Vaccine Production				
A. Production				
1. Scientist	:	1	1	-
2. Technician	:	4	1	3
B. Production Control				
1. Scientist	:	2	1	-
2. Technician	:	4	-	4
C. Freeze-drying				
Technician	:	4	1	3
D. Quality Control				
1. Scientist	:	1	1	-
2. Technician	:	2	1	1
Total :				
Scientist	:	4	3	-
Technician	:	14	3	11
Grand Total for Polio and Measles Vaccine Production				
Scientist	:	9	7	1
Technician	:	26	6	20
Animal Lab assistant	:	2	-	2

資　　料　　2

A Feasibility Study by a Joint

WHO／UNICEF／USAID Consulting

Team

APPENDIX B

PRODUCTION OF MEASLES VACCINE AND POLIO VACCINE IN INDONESIA

A FEASIBILITY STUDY BY A JOINT WHO/UNICEF/USAID CONSULTING TEAM

Jakarta, September 20, 1984

INTRODUCTION

- Under the auspices of WHO, UNICEF and USAID a team of international experts was gathered to undertake a "Feasibility Study regarding the Production in Indonesia of Polio Vaccine and Measles Vaccine". (Names of the members of the Team are stated in Appendix I).

- The Team visited Jakarta and Bandung from September 10 to 20, 1984.

- This Report gives the Team's findings and recommendations

Jakarta, September 20, 1984

EXECUTIVE SUMMARY

We studied the technical and economic feasibility of Biofarma producing Measles and Polio Vaccines in Indonesia.

We recommend a step-wise approach to basic production of these two vaccines, as follows:

1) Increase the processing of Polio Vaccine from imported bulk concentrates from the current 30% of the amount used to 100%;

2) Process Measles Vaccine from imported bulk concentrate;

3) Introduce basic production of Measles Vaccine; and

4) Move to basic production of Polio Vaccine.

This step-wise approach allows for gradual transfer and assimilation of production skills, moving from less to more difficult types of vaccine technologies. It also allows for re-appraisal of the recommended programme on actual performance.

We estimate that the total capital investment to achieve basic production of both vaccines would be approximately $5.3 million, excluding the cost of technology transfer.

Our estimate of the cost per dose is $0.12 for Measles Vaccine and $0.04 for Polio Vaccine. These estimated domestic production costs appear to be of the same order as those of vaccines imported into Indonesia.

Concurrent with the development of production capabilities at Biofarma, the capability of the national control laboratory must be strengthened to assure that vaccines will meet WHO specifications.

Subject to the acquisition of production technology from an outside source, coupled with the provision of new facilities and considering the present level of expertise at Biofarma, we are confident that the basic production of Measles Vaccine and Polio Vaccine in Indonesia has an excellent chance of success.

TERMS OF REFERENCE FOR THE STUDY

- The Team spent approximately five days acquainting itself with the prevailing local conditions and obtaining definitions of the Terms of Reference for the Study.

- Following discussion with the Secretary - General of the Kementerian Kesehatan, the Director - General of Communicable Disease Control and other members of the Ministry of Health (see Appendix II) the following parameters were established:

  . the products to be considered are:
  Measles Vaccine (Live) and
  Poliomyelitis Vaccine (Oral);

  . the maximum annual production capacities are to be:
  Measles Vaccine - 7 million doses
  Polio Vaccine - 20 million doses.

  . the options available to Indonesia are to be indicated;

  . general recommendations are to be made concerning the choice of options, methodologies and technologies to be employed;

- estimates are to be prepared of the approximate costings of the various options (wherever practical) broken down into individual components (such as buildings, equipment etc);

- approximate production costings/dose are to be calculated;

- estimated manpower requirements are to be indicated.

ASSESSMENT OF CURRENT SITUATION

1. Demographics of Indonesia

- Estimated total population: 160,000,000
- Birth-rate: 3.3 to 3.5%
- Number of New Borns Annually: 5.2 to 5.6 million infants.

2. Major Causes of Infant Deaths

- Diarrheal diseases
- Acute respiratory infections
- Tetanus

3. Estimated Immunization Coverage

- For diphtheria, tetanus and whooping cough - using DPT Vaccine 40%

- For tuberculosis-using BCG Vaccine 80%

- For poliomyelitis-using Polio Vaccine less than 10%

- For Measles-using
  Measles Vaccine — less than 10%

4. Vaccine Demand

- Current demand for vaccines is determined largely by Government purchases; the private market demand is small.

- REPELITA IV, the Indonesian five-year plan that began in 1984/85 states as one of its aim a minimum of 65% overall immunization coverage.

- Eventually the Government intends to achieve 95% average.

5. Infra-Structure for Vaccine Distribution

- Biofarma - Bandung is responsible for all imports and production of biologicals, both for Government and private market use.

- Biofarma distributes to the Propinsis, which in turn send it to the Kabupatens ,from which it goes to the Kecamatans.

- Actual immunization is effected through the Puskesmas (Community Health Center).

6. Biofarma - Bandung

- Biofarma is the organization in Indonesia manufacturing and importing biologicals.

- Biofarma is a Government entity, responsible directly to the Minister of Health. However it operates as a private concern and pays taxes applicable to a private Indonesian concern.

- Currently Biofarma manufactures the following:
  - Cholera Vaccine
  - Typhoid Vaccine
  - TAB Vaccine
  - Cholera - TAB Vacine
  - Pertussis Vaccine
  - Plague Vaccine
  - Polyvalent Staphylococcal Vaccine
  - Polyvalent Streptococcal Vaccine
  - BCG Vaccine
  - Diphtheria Toxoid
  - Tetanus Toxoid
  - DT Toxoid
  - DPT Vaccine
  - DP Vaccine
  - Rabies Vaccine
  - Oral Polio Vaccine (from imported concentrates)

- Diphtheria Antitoxin
- Tetanus Antitoxin
- Rabies Antitoxin
- Infusion Fluids (6)
- Diagnostics (8)

- The Team visited Biofarma and was extremely impressed with the level of expertise, facilities and housekeeping as applied to products currently being manufactured.

- Biofarma has essentially no expertise nor facilities for the large-scale production of Measles and Polio Vaccines and limited expertise and facilities for the control of these two products.

STUDY ASSUMPTIONS

The following major assumptions have been made:

- Biofarma will continue to be the sole source in Indonesia of all human vaccines.

- Technology for basic production of Measles and Polio Vaccines will have to be obtained in one form or another from source(s) outside Indonesia.

- The annual consumption of Polio Vaccine will eventually reach 20,000,000 doses and that of Measles Vaccine 7,000,000 doses.

- The Polio Vaccine required will be the Oral Live Vaccine type rather than the Injectable Killed Vaccine type.

- Production and quality control (Q.C.) facilities will conform to the pertinent WHO specifications. The final products will also conform to the appropriate WHO product specifications.

- Indonesia will have a adequate supply of cynomolgus monkeys.

- All estimates have been made on maximum capacity of 20 million doses Polio Vaccine and 7 million doses Measles Vaccine.

- All figures stated in this Report are estimates only, based on 1984 price. Before proceeding with implementation of any of the options, a detailed, up-to-date costing should be undertaken.

- The price of technology transfer has not been included in the Report as the possible configurations and components of technology transfer arrangements are highly variable. This cost will have to be determined by negotiations between Biofarma and potential sources it such technology.

- It is noted that in order to comply with the requirements of WHO the establishment of a comprehensive, independent national control facility must precede the manufacture of biological products. It is therefore assumed that if a decision is taken to initiate the production of Measles and/or Polio Vaccines in Indonesia, the Q.C. capability of the Food and Drug Directorate will be increased appropriately.

- As instructed by the Director - General of CDC the cost of money has not been included.

MAJOR OPTIONS

Summary of Option

Option I - Import Polio Vaccine bulk concentrate and import Measles Vaccine in final containers.

Option II - Import both Polio and Measles Vaccine bulk concentrates

Option III - Import Polio Vaccine bulk concentrate and basic production of Measles Vaccine

Option IV - Basic production of both Measles and Polio Vaccines sequentially

Option V - Basic production of both Measles and Polio Vaccine simultaneously

- All of these Options can be pursued and with the exception of Option V none are exclusive of one another.

- In arriving at our final recommendation we considered a large number of factors such as cost, technical expertise, chances for success (or failure) and the often started objective of almost all of the Indonesian officials to make Indonesia independent of outside sources to Polio and Measles Vaccines.

- Our analyses, although only estimates, indicate that the cost of Vaccine produced in Indonesia could be competitive with currently purchased vaccine once facilities and technologies are in place.

- On the other hand opportunities may exist for reductions in the purchase price of vaccines from outside sources.

RECOMMENDATIONS CONCERNING THE OPTIONS

Step 1:

- Currently Biofarma purchases 30% of Polio Vaccine as bulk concentrate for dilution and filling and 70% as final filled containers.

- As the initial step we recommend that all Polio Vaccine be purchased as bulk concentrate for finishing at Biofarma (Option I).

- We also recommend that improvements in long-range planning coupled with increased purchase volumes might be used as factors in negotiating lower prices for both vaccines.

Step 2

- Measles Vaccine currently is purchased in final containers.

- It is recommended that Measles Vaccine be bought as bulk concentrate for filling, freeze-drying and finishing (Option II).

- Although this may not be any savings, this would provide Biofarma with valuable additional technical experience in freeze-drying and final container Q.C.

- Financial outlay for processing of Measles Vaccine bulk concentrate represents a very significant portion of the total outlay required for basic production, so that the additional outlay required for Step 3 is greatly reduced.

Step 3

- We recommend that Biofarma introduce the basic production of Measles Vaccine while continuing to finish Polio Vaccine from bulk concentrates. (Option III).

- Having already introduced the processing of Measles Vaccine from bulk concentrate in Step 2, the major outlays for equipment and facilities will have already been made.

- Basic production of Measles Vaccine requires simpler production and control methods than that of Polio Vaccine, and thus would lead to greater possibility of initial success.

Step 4

- Once the Measles Vaccine basic production programme has been successfully completed, Polio Vaccine basic production should be introduced. (Option IV).

- We strongly recommend that Measles and Polio Vaccines basic production not be undertaken simultaneously (Option V). The resources and facilities at Biofarma or likely to be available to Biofarma are in our view, inadequate to handle both vaccine programmes simultaneously.

- Step 1 could be initiated immediately only requiring additional filling equipment.

- Initiation of Step 2 will need the provision of suitable space and services, and purchase and installation of filling and freeze-drying equipment for Measles Vaccine.

- We caution Biofarma to obtain outside expertise preferably from the transferor of Measles Vaccine technology prior to purchase and installation of the equipment.

- It is important to assure the compatibility of the equipment with the final facility design and production process.
- A proposed time-table for Steps 3 and 4 can be found later in this Report.

RECOMMENDED PRODUCTION TECHNOLOGY

Introduction

- It should be emphasized that the undermentioned recommendations are those of the Team but that final choice of technology has to be made by Biofarma and the transferor of technology.

- It is anticipated that the technology adopted will be similar or identical to that used in many major production laboratories. The technology will have been proven in past experience and it is anticipated that this technology will not be displaced by an improved technology in the forseeable future.

- Stress is laid on the absolute need for the transferor of technology to supply Biofarma not only with expertise (see "Recommended Methodology of Project Execution") but also most importantly, with seed strains, cell substrates and continuing technical support.

Measles Vaccine Technology

- Chick embryo fibroblasts should to be used to grow a strain of measles approved by WHO.

Oral Polio Vaccine Technology

- Primary monkey kidney cells should be used, with the Sabin seed strains approved by WHO.

RECOMMENDED METHODOLOGY OF PROJECT EXECUTION

- It is essential for Biopharma to first make arrangements with a current, large volume producer of Measles Vaccine for the transfer of the necessary technology and know-how, and for Polio Vaccine at some later date.

- For technical reasons and as a matter of practicality the purchase of technology should go hand in hand with the purchase of bulk concentrates from the same source. This is essential as production technology of one manufacturer may not be appropriate to process bulk concentrates from another producer.

- Transfer of technology to Biofarma should as a minimum, cover the undermentioned major items. It is of course understood that for all of these the transferor of technology will work in close collaboration with Biofarma.

  a. General Consulting.

  . scheduling of all major tasks and the monitoring thereof;
  . lay-out design of the facilities and collaboration with local architect/contractor;
  . regular inspection of the building of the facilities;

- selection of the required equipment and production components and potential sources thereof;
  purchase of the equipment and pre-shipment inspection thereof (if so desired);
- shipment and insurance of equipment and production components (if so desired);
- supervision of the installation of all static equipment;
- validation of buildings and equipment;
- trial production runs;
- monitoring of the manufacture of the "consistency" production runs;
- supply of all essential manuals;
- assistance in obtaining product "registration" from the appropriate local authorities;
- "trouble-shooting".

b) Training

- training of selected Biofarma personnel in premises of the transferor of technology in all required aspects of production, Q.C., maintenance, record-keeping etc;
- assistance in the training of other Biofarma personnel in Bandung.

c) Duplicate Q.C.

. Duplicate testing by the transferor of technology during certain stages of production until both parties are satisfied that production and Q.C. are running satisfactorily.

MAJOR REQUIREMENTS AND ESTIMATED COSTS FOR PROJECT EXECUTION

1. Site

- Sufficient ground is available at Biofarma to accommodate buildings for production and quality control of Measles Vaccine and Polio Vaccine and related requirements.

- No cost for land has been included in the calculations.

2. Buildings

- For production and quality control it is proposed that one building be erected consisting of the following:

  . quality control facilities for both Measles Vaccine and Oral Polio Vaccine (Space A);

  . production facility for Measles Vaccine (Space B);

  . central facility for washing and sterilizing, media preparation, water distillation, inspection, packaging, warehousing which can serve both Measles and Polio (Space C);

  . production facility for Oral Polio Vaccine (Space D).

- Such a building can be erected in two stages: Space A, B and C first with Space D later.
- In addition, before Polio Vaccine production can be commenced a separate Animal Holding Facility will have to be erected (Space E).

- The undermentioned figures for area and approximate building costs are approximations only and must be refined jointly by Biofarma and the transferor of technology.

-

Designated Space	Area in Sq. Meters	Cost/ Sq. M* (Rp.000's)	Estimated Total Total cost (Rp.000's)
A	230	250	57,500.0
B	450	250	112,500.0
C.	550	250	137,500.0
Sub total I	1.230		307,500.0
D	550	250	137,500.0
E	550	200	110,000.0
Sub total II	1.100		247,500.0
Grand Total	2,330		555,000

* The cost/sqm was estimated by Dr. Nasution of Biofarma and does not include airconditioning/ purification

3. Services

- No provisions have to be made for the generation of either steam or electricity as Biofarma have sufficient spare capacity.

- Water is also in abundance apparently, but provision will have to be made for deionization and distillation facilities.

- Gas will have to be purchased in bottles (LPG) and compressors will have to be installed for compressed air.

4. Estimated Equipment Costs

(includes airconditioning/purification)

4.1 Q.C, Measles production and Services	Rps. 000's	US$ 000's
Space A (Q.C. Facilities)		105.0
Space B and C (Measles Production and Central Services		1,600.0
Freight and Insurance		170.5
Duty, Sales Tax, VAT	600,160.0	
Installation and Validation		85.0
Sub Total I	600,160.0	1,960.5

4.2 Polio Vaccine

Space D (Polio Production)		1,300.0
Freight and Insurance		130.0
Space E (Animal House)		120.0
Freight and Insurance		12.0
Duty, Sales Tax and VAT	449,840.0	
Space E (Animal House locally made equipment)	30,000.0	
Installation and validation		71.0
Sub Total II	529,840.0	1,633.0
	(Rps.000's)	(US$000's)

4.3 Grand Totals	Rps.1,130,000.0	$3,593.5

5. Animals

- In this case "animals" refer only to the monkeys required for Polio Vaccine production and quality control.

- Other animal requirements are small and can be serviced by Biofarma's existing animal facilities.

- For full Polio Vaccine production/quality control it is estimated that the follbwing number of monkeys will be required annually:
  - production: 140 "clean" monkeys
  - quality control: 430 monkeys (not necessarily "clean")

  (The quantity for production may be over-stated)

- Assuming a 50% rejection rate of incoming monkeys the total estimated annual requirements are:

. production	280 animals
. quality control	430 animals
	710 animals

- It has been assumed that monkeys will be purchased from local sources at a laid-down price in Bandung of Rps. 30,000 each.

- Hence, total annual costs (in Rps. 000's):
  710 x Rp. 30 = Rps 21,300.0.
  (It has been taken that this figure will allow for feeding etc of the animals as well)

6. Production Components

- These comprise all chemicals, fetal calf serum, filters etc required for production and quality control.

- Estimated costs.

	Rps. 000's	US$000's
Measles Production		225.0
Quality control		50.0
Duty, Sales Tax, VAT	27,500.0	
Sub total I	27,500.0	275.0
Polio Production		225.0
Duty, Sales Tax, VAT	22,500.0	
Sub total II	22,500.0	225.0

7. Vials

7.1 Measles Vaccine

- It has been assumed that locally made vials will be used for the diluent and imported ones for the vaccine itself.

- It has further been assumed that approximately 15% breakage and discards will be experienced.

- Estimated costs:

	Rps.000's	US$000's
Diluent vials		
805,000 x Rps.49	39,445.0	
Vaccine vials		
805,000 x US$0.12		96.6
Duty, sales tax, VAT	20,500	
Total	59,945	96.6

7.2 Polio Vaccine

- It has been assumed that locally made vials will be used.

- Breakage and discards to be the same as for Measles Vaccine.

- Estimated costs	Rps.000's
2,300,000 x Rp. 32	73,600.0

8. Seals

- Locally made ones will be used

- Estimated cost -	Rps.000's	US$000's
Measles diluent		
805,000 pieces	3,220.0	-
Measles Vaccine -		
805,000 pieces	3,220.0	-
VAT	161.0	
Sub Total I	6,601.0	-
	=======	
Polio Vaccine - 2,300,000	9,200.0	-
VAT	230.0	
	9,430.0	
	=======	

9. Stoppers

- Imported stoppers will be employed

- Estimated costs	Rps.000's	US$000's
Measles Diluent 805,000		4.8
Measles Vaccine 805,000		4.8
Duty, Sales Tax, VAT	2,040.0	
Sub Total Measles	2,040.0	9.6
	=======	====

Polio Vaccine 2,300,000		13.8
Duty, Sales Tax, VAT	2,932.5	
Sub Total Polio	2,932.5	13.8

10. Dropper/Stoppers for Polio Vaccine

- Imported Dropper/Stoppers will be used, as is the case currently.

- Estimated costs	Rps.000's	US$000's
2,100,000 stoppers		42.0
Duty, Sales Tax, VAT	8,925.0	
	8,925.0	42.0

PERSONNEL

- It is considered that the following minimum staffing is required:

	Sr. Scientist	Engineer	Sr. Technician	Technician	Attendant
Quality Control*	1		1	5	1
Maintenance		1			
Measles production	1		5	14	3
Sub Total I	2	1	6	19	4
Polio production	1	–	5	14	3
Animal House	1		1	4	2
Sub Total II	2	–	6	18	5
Grand Totals	4	1	12	37	9

* For Polio Vaccine Q.C. a consultant histopathologist and two technicians will be required over and above the abovementioned staffing.

- Annual salary costs have been taken at the undermentioned figures which were supplied by Dr Nasution of Biopharma and are expressed in Rps. 000's:

  . Sr. Scientist 6,000.0 + 40% fringe = 8,400.0

  . Engineer (est) 4,000.0 + 40% fringe = 5,600.0

  . Sr. Technician 3,000.0 + 40% fringe = 4,200.0

  . Technician 2,100.0 + 40% fringe = 2,940.0

  . Attendant 1,800.0 + 40% fringe = 2,520.0

- Consequently the estimated annual salary costs calculate out as follows (in Rps. 000's):

  . Measles production and Q.C Rps. 113,540.0

  . Polio production and Animal house Rps. 107,520.0

FINANCIAL PROFILE

Notes:

- All figures stated are estimates only and must be refined jointly by Biofarma and the transferor of technology prior to proceeding with project execution.

- Estimated 1984 cost served as a basis.

- No allowance has been made for inflation.

- Cost of money has not been taken into account

- Direct production costs only have been calculated. None of Biofarma's overhead charges have been included.

- Depreciation has been calculated straight line 10 years for equipment and 50 years for buildings (as requested by Dr Nasution of Biofarma).

- Cost of technology transfer has not been included (see "Assumptions").

Estimated Direct Production Cost Measles Vaccine

	Rps.000's	US$000's
Depreciation Buildings	6,150.0	-
Depreciation Equipment	60,016.0	196.0
Production Components	27,500.0	275.0
Vials	59,945.0	96.6
Seals	6,601.0	-
Stoppers	2,040.0	9.6
Salaries	113,540.0	-
	275,792.0	577.2

No. of Doses produced: 7,000,000

Cost per Dose	Rps.39.40	US$0.0825

Total cost/dose	
(1 US$=Rps.1000)	Rps.121.90

Estimated Direct Production Costs - Oral Polio Vaccine

	Rps.000's	US$000's
Depreciation Buildings	4,950.0	-
Depreciation Equipment	52,984.0	163.3
Monkey Supply	21,300.0	-
Production Components	22,500.0	225.0
Vials	73,600.0	-
Seals	9,430.0	-
Stoppers	2,932.5	13.8
Droppers	8,925.0	42.0
Salaries	107,520.0	-
	424,841.5	444.1

No. of Doses produced: 20,000,000

Cost per Dose	Rps.15.21	US$0.0222
Total cost/dose (1 US$=Rps.1000)	Rps.37.41	

ANTICIPATED TIME FRAMES

Note:

- The undermentioned Time Table assumes that Option III will be executed with Option IV commencing in Year 4.

- Again it has to be stressed that Biofarma should redefine this Time Table with the transferor of technology.

Year 1

- Planning of Buildings for Measles Vaccine and Q.C;
- Erection of Buildings for Measles Vaccine and Q.C;
- Selection and Ordering of Equipment for Measles Vaccine and Q.C;
- Overseas training of Biofarma's Senior staff in "Intermediate" production and quality control of Measles Vaccine.

Year 2

- Training of staff in Bandung in "intermediate" production and final container quality control of Measles Vaccine;
- Installation and Validation of equipment;
- Validation of buildings;

- Production of Measles Vaccine from imported concentrates;
- Overseas training of Biofarma's senior staff in basic production and quality control of Measles Vaccine.

Year 3

- Training of staff in Bandung in basic production and quality control of Measles Vaccine;

- Production of Measles Vaccine from imported concentrate until basic production is running satisfactorily.

Year 4

- Planning of buildings for Oral Polio Vaccine;
- Erection of buildings for Oral Polio Vaccine;
- Selection and ordering of equipment for Polio Vaccine;
- Overseas training of Biofarma's senior staff in basic production of Oral Polio Vaccine;
- Basic production of Measles Vaccine continues.

Year 5

- Training of staff in Bandung in basic production and quality control of Oral Polio Vaccine;
- Installation and Validation of equipment;
- Validation of buildings;
- Biofarma's production of Oral Polio Vaccine from imported concentrates is moved from current facility to new building and continues until basic production of Oral Polio Vaccine runs smoothly;
- Basic production of Measles Vaccine continues.

Year 6

- End of Project.

SUMMARY OF ESTIMATED CAPITAL COSTS BY YEAR

Year	Details	Rps000's	US$000's
1.	Building for Measles Production and quality control	307,500.0	
	Downpayment for Measles/Q.C. Equipment (33%)		568.0
		307,500.0	568.0
2.	Remaining Measles/Q.C Equipment Costs		1,137.0
	Freight/Insurance Equipment		170.5
	Duty, Sales Tax, VAT on Equipment	600,160.0	
	Installation and Validation Equipment		85.0
		600,160.0	1,392.5

4.	Buildings for Oral Polio Vaccine Production	247,500.0	
	Downpayment for Equipment for Oral Polio Vaccine Production and for Animal House		473.0
		247,500.0	473.0
5.	Remaining Polio/Animal House Equipment Costs	30,000.0	947.0
	Freight/Insurance Equipment		142.0
	Duty, Sales Tax, VAT on Equipment	499,840.0	
	Installation and Validation Equipment		71.0
		529,840.0	1,160.0
1 - 5	GRAND TOTAL	1,685,000.0	3,593.5

APPENDIX I

NAMES OF TEAM MEMBERS

Name	Country	Agency
Dr. Miroslav Beck (Chairman)	Yugoslavia	WHO
Mr. Robert E. Binnerts	Canada	USAID
Dr. Murray S. Cooper	U.S.	USAID
Dr. Alan Gray	U.S.	USAID
Dr. Stephen J. Lerman	U.S.	UNICEF
Dr. David Magrath	Britain	WHO

APPENDIX II

LIST OF PERSONS MET BY THE TEAM

1. Ministry of Health

- Dr. Soekaryo	-	Secretary General
- Dr. Brotowasisto	-	Head, Planning Bureau
- Prof. Dr. Loedin	-	Director, Research & Development.
- Dr. Median Siraid	-	Director General, Food and Drugs.
- Mr. Charles Siregar	-	Head Technical Implementation Unit, Food & Drugs
- Dr. M Adhyatma	-	Director General, CDC.
- Dr. Gandung Hartono	-	Secretary to Director-General
- Dr. Gunawan	-	Head Epidemiology and Immunization
- Dr. Karyadi	-	Chief, Epidemiology and Surveillance
- Dr. Titi Indijati Soewarso	-	Medical Officer, Epidemiology and Surveillance
- Dr. Guno Wiseso	-	Chief, Immunization
- Dr. Sorta Toruan	-	Medical Officer, Immunization

2 Perusahaan Umum Bio Farma

- Dr. M.S. Nasution	-	Director
- Mrs. S. Soeharto	-	Commercial Director
- Dr. Sutaryo	-	Production Director
- Dr. Ina Madiapura	-	Head, Virus Vaccine Production

3. Resident Agencies

-	Dr. David H. Calder	- Chief, Office of Population and Health, USAID
-	Mr. Warren Jones	- Administrative Officer, USAID
-	Dr. Richard S. Arnold	- Medical Epidemiologist, USAID
-	Mr. Daniel J. Brooks	- Representative to Indonesia UNICEF
-	Mr. Rodney Hatfield	- EPI Project Officer, UNICEF

APPENDIX C

AN INTRODUCTION TO CONNAUGHT LABORATORIES' TECHNOLOGY TRANSFER ACTIVITIES

Connaught Laboratories, Toronto, Canada has a long history in the transfer of technology for production and quality control of biological products.

This, coupled with Connaught being one of the world's major vaccine producers, caused the World Health Organization/Pan American Health Organization to appoint Connaught as its Consultant for Smallpox Vaccine by Latin American Governments.

A considerable amount of additional experience was gained through the technology transfer by Connaught to its joint ventures in Mexico and Brazil.

During the past three years, Connaught has acted as Consultant to the Government of Pakistan for the establishment in Islamabad of an Oral Polio Vaccine processing plant. This project, which was financed jointly by the Government of Pakistan and the Canadian International Development Agency was executed on time and under budget. Since then Connaught's services have been retained for this project in a "continuing support services" role.

In January 1983 Connaught won an international UNICEF tender to act as Consultants to the Pakistan Government for the setting up of a Measles Vaccine production unit. This project currently is being executed.

Negotiations with other foreign Governments for operations to manufacture Injectable Polio Vaccine, Rabies Vaccine (Human Diploid Cell origin), Measles Vaccine etc. are in advanced stages.

Connaught's philosophy of technology transfer is one of total commitment. It is for this reason that, in 1981, Connaught established a separate Division involved solely with technology transfer. To the best of our knowledge, Connaught is the only commercial biological producer to have such an entity.

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Connaught's production of a broad range of biologicals, coupled with its extensive research and development as well as its expertise in systematic technology transfer, enables Connaught to assist its clients in very many difference aspects of production and quality control.

In addition, Connaught always is interested in considering acquisition of incoming technology as well, thus potentially creating two-way technology transfer.

Last but not least, Connaught is acutely aware that its reputation is at stake in each and every project it undertakes. Consequently it tries to ensure at all times that commitments, time-frames, costings, etc. are strictly observed.

REB:rp

資　　料　　3

BIO　FARMA　in　brief

BIO FARMA

in brief

History

Bio Farma, which is also widely known as the Pasteur Institute is in fact an old establishment with a long and moving history, established in 1890 by decree of the Governor General.

It was then named the "Lands Koepok Inrichting", temporarily housed in the old military hospital in Jakarta, assigned to produce vacoinia virus vaccine ("lymph") particularly for the armed forces.

It was in particular the pioneering of scientists like SCHUCKINK KOOL and NIJLAND who caused this establishment to grow into a real institute which according to OTTEN's report in 1926 had even the greatest production capacity of lymph in the world.

In 1895 a rabies department was added, after which the institute was then popularly known as Pasteur Institute.

Significant results were obtained with the development and production of cholera-, plague- and typhoid fever vaccines which proved to be powerful tools to prevent the further spreading of these then rampant diseases.

Not long afterwards anti-tetanus, anti-diphtheria and anti-snake venom sera became available, followed by tetanus- and diphtheria toxoids for active immunization.

It is easy to contemplate that the vaccines produced by the institute was then a godsend tool to increase the health and welfare of the general population.

In 1923, when Pasteur Institute moved to its present location in Bandung, a routine diagnostic laboratory was set up widening the institute's role into disease diagnosis and public health. This laboratory has been and still is a great help for the medical practitioner and hospital doctor in making his diagnosis, and for health officials to make an epidemiological approach and evaluation of communicable diseases.

Since 1952, the management of Bio Farma has been entirely taken over by Indonesian personnel. Activities were increased and widened and this laboratory even developed into a National Reference Center for Enterobacteriaceae - including Vibrio cholerae and pathogenic E. coli - Leptospira, viral and rickettsial diseases.

In this way, we have not only a constant contact with current public health problems as far as the production of immunizing agents, but it can also solve and eludicate practical problems of public health and preventive medicine.

Because of its undeniable activities which were done with conscious responsibility, the institute was soon acknowledged by the Department of Health as a well-approved institution and was able to function as a Central Public Health Laboratory with its reference laboratories in many fields of microbiology.

Meanwhile, in 1955 the name "Pasteur Institute" was changed into "Perusahaan Negara Pasteur", and after another name change at long last it became "Perusahaan Umum Bio Farma", a state owned enterprise manufacturing biologicals.

Up till now, Bio Farma is the only facility in the country to produce vaccines and sera which are done under strict scientific control.

All products manufactured by the various production units are examined by the Quality Control Department before coming into the market. Bio Farma strives that all its products at least meet the minimal requirements of the W.H.O. or minimal requirements as stipulated by the Indonesian or by foreign pharmacopoeia, depending on the kind of test.

Activities and achievements

In its long history, Bio Farma has always played an important role in the field of production of biologicals, research, and public health as seen in the following list of achievements :

- One of the oldest vaccine developed and manufactured by Bio Farma was the plague vaccine when an outbreak of plague in East Java was reported in 1911.
  Afterwards, a new vaccine containing naturally dissociated live avirulent Pasteurella pestis strain Ciwidey organisms was developed, and several years later the avirulent Harbin strain was added.
  The isolation and discovery of this avirulent Ciwidey strain was done by this institute.

  The last serious outbreak of plague occured in the first quarter of 1968 in Boyolali (Central Java). No cases has been reported now due to the vigorous measures taken by the health services, and Bio Farma still maintains its skill to produce this vaccine as a precaution if the vaccine is needed again.

- Before the second world war, Indonesia was practically free of smallpox.
  This was due to a well-planned eradication programme managed and

conducted by this institute and the use of a potent vaccine. As a result of the detoriation of general public health conditions during and after the war, cases of smallpox reappeared endangering several parts of the country.

In 1946 the use of roomdried smallpox vaccine was introduced nationwide with great success. Smallpox epidemics which at that time threatened the country could be conquerred within a relatively short time. When the Government started an intensive eradication programme in cooperation with the W.H.O. in 1968, Bio Farma was ready with its new freezedried smallpox vacoine consisting of freezedried partially purified washed elementary bodies of the vacoinia virus, and as a direct result of the use of this vaccine, Indonesia was declared free of smallpox in 1974.

- In 1957 we were already using monkey kidney cells, chicken fibroblasts and HeLa cells for the diagnosis of viral diseases. The first isolation of the Dengue virus was achieved by Bio Farma in 1972 after its presence was proved previously by serological tests.

- To comply with the increasing needs for vaccines used in the expanded programme on immunization which is now being carried out by the government, Bio Farma is taking its first steps in the field of biotechnology five years ago by using automated fermentors in the large scale production of diphtheria, tetanus and pertussis vaccines. But we realize that we still have a long time to go. One of the targets of the fourth Five-year Development Plan is to lower the infant mortality rate by immunization of infants.
A large amount of vaccines will be needed for the expanded programme on immunization, and plans are allready drawn to order larger fermentors in order to fulfill the future needs for vaccines.

- Bio Farma is also moving into the production of plasma substitutes and sterile infuse solutions by transfer of technology from Behring Werke, Marburg.

Research and future plans

In order to improve the quality and ability of our technical and scientific personnel, the management of Bio Farma is stimulating them to carry out research and investigations in the fields of microbiology, public health, biochemistry etc. Young and promising scientists are send abroad to study and train in foreign universities, production facilities and research centers.

To keep up with recent improvements in vaccine production technology, new techniques including genetic engineering to produce vaccines cheaply and in sufficient amounts are being studied and explored for the possibilities of transfer of technology.

Because of it, Bio Farma is steadily developing into a combined production- and research facility, each working closely together in never ending efforts to produce better vaccines and sera and to develop new products.

Bio Farma also enjoys full cooperation from laboratories of foreign countries and from international organizations.

At this moment we are employing 400 people, consisting of 160 technical and 240 non-technical personnel. Of the technical personnel, 40 are scientists from different disciplines and 75 are laboratory technicians.

CURRICULUM VITAE OF BIO FARMA STAFFS

1. Name : Dr.(Mrs) Ina Madiadipura

   Date and Place of birth : 15 September, 1936, Padang, West Sumatra

   Education : Faculty of Medicine, Padjadjaran University - Bandung, 1965

   Experience and training :
   - 1965 Viral Vaccine Production Department, Bio Farma
   - 1969 Smallpox Vaccine Production and Control (6 months) :
     - Vaccine Institute Padwadangar, India - 2 months
     - National Institute for Communicable Diseases, New Delhi, India - 1 month
     - R.I.V, Bilthoven, Netherland - 3 months
   - 1978 Polio and Measles Vaccine Production and Control (6 1/2 months) :
     - Institute of Immunology, Zagreb, Yugoslavia - 6 weeks
     - Torlak Instiute, Beograd, Yugoslavia - 8 weeks
     - R.I.V., Bilthoven, Netherland - 3 weeks
     - Sclavo, Siena, Italy - 8 weeks
   - 1984 Short Course on Vaccine Production - EPI/ USAID :
     - Seminar, American Society of Microbiology St. Louis, Missouri, USA - 1 week
     - Bio-Technology, National Cancer Institute, Fort Detriech, Frederick, Maryland, USA - 1 week
     - Quality Control, National Institute of Health, Bethesda, Maryland, USA - 2 weeks
   - 1984 Workshop on Rabies Vaccine Production in Vero Cell, Pasteur Institute, Coonor, India 3 weeks
   - 1985 Measles Vaccine Control, Institute Merieux, Lyon, France - 3 weeks

2. Name : Dr.(Miss) Amy Retno Suprapto

   Date and Place of birth : 1 April 1941, Pasuruan, East Java

   Education : Faculty of Veterinary Medicine, Gajah Mada University, Yogyakarta, 1971

   Experience and training :
   - 1972 - 1980 Biomedical Research Centre, Ministry of Health, Jakarta
     - 1972 Intercountry Course in Laboratory Diagnosis on Smallpox, National Institute for Communicable Diseases, New Delhi, India - 3 weeks (WHO)
     - 1973 - 1974 Serological Study on Respiratory Virus Diseases (Influenza-Mumps-Measles-Rubella-Adenovirus), Department of Virology; Dengue Viruses, Department of PPreventive Medicine, The Research Institute for Microbial Diseases, Osaka University, Osaka, Japan (JICA)- 13 months
     - 1976 - 1977 Training Course on Tropical Epidemiology, Kobe University, School of Medicine Kobe, Japan :

- Dept. of Virology : Dengue viruses
  Dept.of Pathology Division I : Immunology
  Kobe Prefecture Institute of Health: Rubella virus

1980 : Bio Farma : Department of Virology

1983 : Bio Farma : Department of Quality Control III

1985 : Bio Farma : Department of Viral Vaccine Production

1984 : Short course on Vaccine Production -EPI/USAID

- Seminar, American Society of Microbiology, St.Louis,Missouri,USA- 1 week
- Biotechnology and Genetic Engineering,at National Cancer Institute, Frederick Cancer Research Facilities, Frederick,Maryland, USA- 1 week
- Quality Control, at National Institute of Health,Bethesda, Maryland, USA - 2 weeks

N a m e : H. Kartini Setyaningsih
Graduate : University of Padjadjaran, Bandung
Medical Faculty, 1981
Experience : 1982 : Virus Vaccine Production Department of Bio Farma

N a m e : Lia St. Halimah
Graduate : Bogor Agriculture Institute, Bogor
Faculty of Veterinary Medicine, 1982
Experience : 1982 : Virus Vaccine Production Department of Bio Farma

N a m e : Erman Boedisetianto
Graduate : University of Airlangga, Surabaya
Medical Faculty, 1981
Experience : 1982 : Public Health Center of West Java Province
1985 : Virus Vaccine Production Department of Bio Farma

N a m e : Benny Kaligis

Graduate : University of Padjadjaran, Bandung
Medical Faculty, 1976

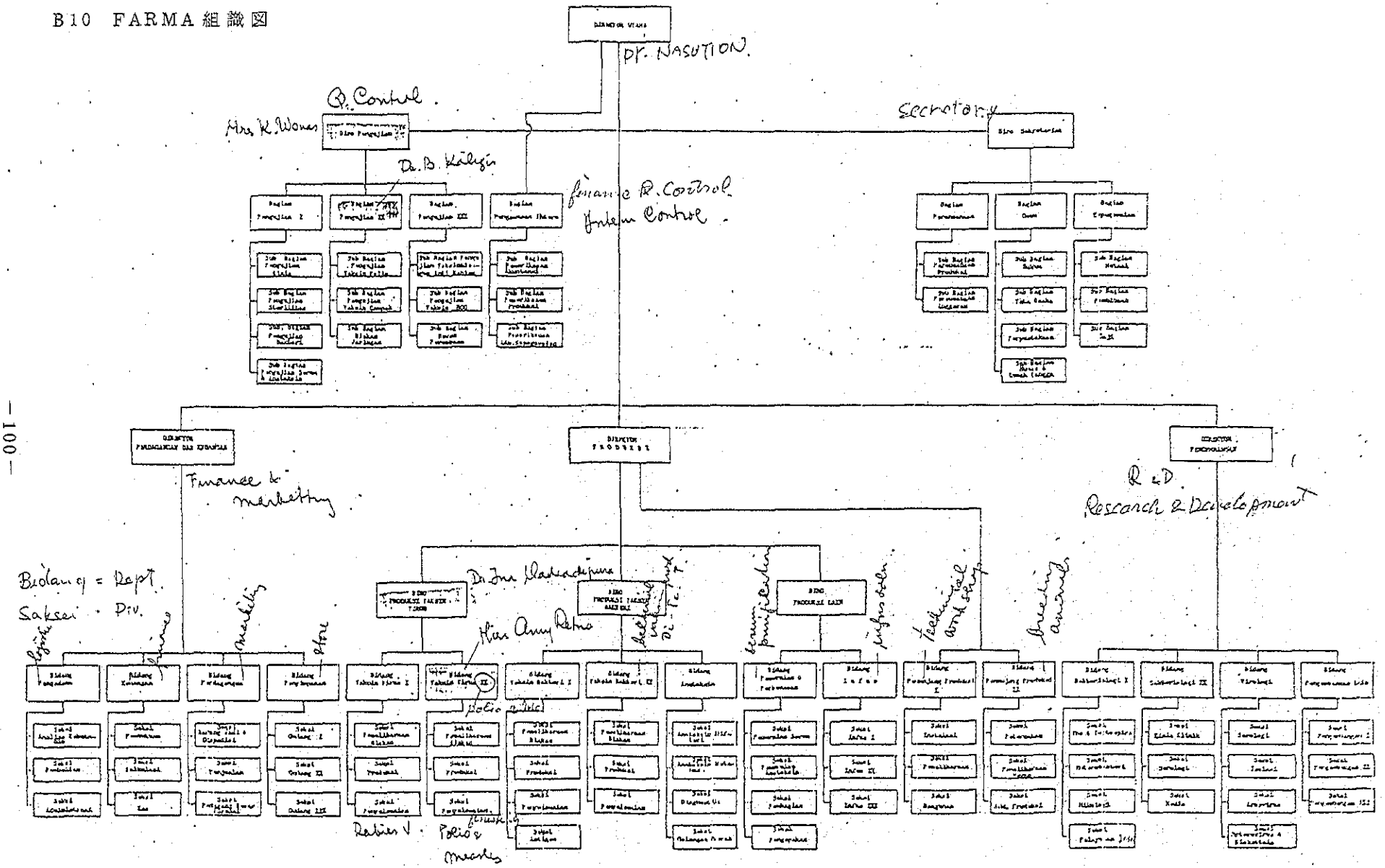
Experience,
training etc : - 1974 : Bio Farma Institute
- April, 1978 - March, 1979 : Microbial Disease Course at Research Institute For Microbial Diseases, Osaka University (Department of Virology)
- April, 1979 - December, 1979 : Viral Vaccine Training at N I H , Japan
- 1983 - 1985 : MPH Degree in Epidemiology from University of Michigan (USA)
- July, 1984 - August, 1984 : Quality Control Training Bureau of Biologics, FDA, Bethesda, USA
- 1980 - Now : Quality Control Department, Bio Farma

N a m e : Antik Tjantika Teguh

Graduate : Biologist, 1978 from
University of Padjadjaran, Bandung
Faculty of Matematics and Natural Sciences

Experience : - 1979 : Viral Vaccine Department of Bio Farma Institute
- 1983 - now : Quality Control Department of Bio Farma Inst.

B10 FARMA 組織図



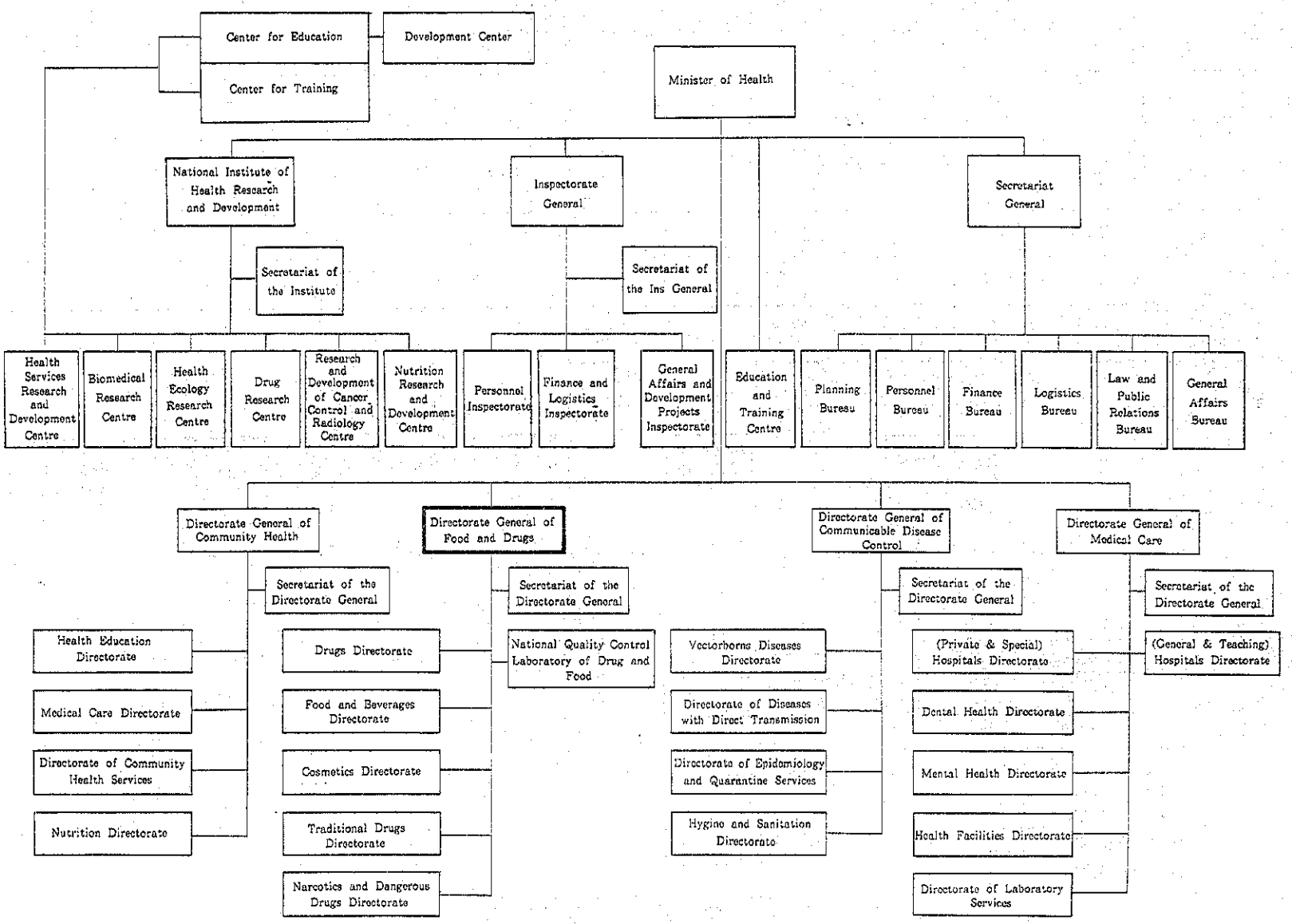
資　料　4

保健省組織図他

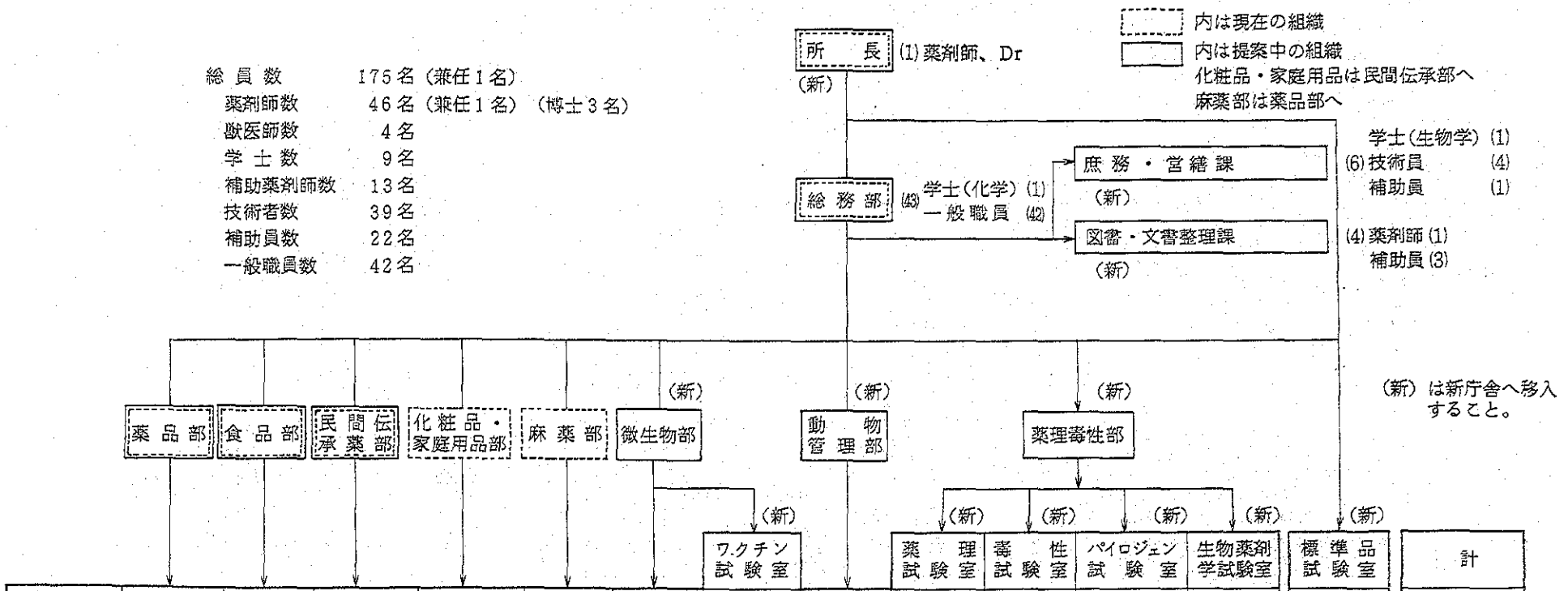
保健省組織図

THE ORGANIZATION OF THE MINISTRY OF HEALTH REPUBLIC OF INDONESIA

（１９８４年４月現在）



国立薬品食品品質管理試験所組織



	薬品部	食品部	民間伝承薬部	化粧品・家庭用品部	麻薬部	微生物部	ワクチン試験室	動物管理部	薬理試験室	毒性試験室	パイロジェン試験室	生物薬剤学試験室	標準品試験室	計
薬剤師	8 (Dr.1)	5	4	2	4	2	3	1	3 (兼任1)	5	2	2	3	44 (Dr.1 兼任1)
獣医師	0	0	0	0	0	0	0	3	0	1	0	0	0	4
学士	0	0	0	0	0	5 (Dr.1)	1	0	0	0	1	0	0	7 (Dr.1)
補助薬剤師	3	0	0	1	0	2	0	0	0	2	1	1	3	13
技術者	5	9	5	4	5	4	0	2	0	0	0	1	0	35
補助員	3	2	1	2	1	2	0	7	0	0	0	0	0	18
計	19	16	10	9	10	15	4	13	3 (兼任1)	8	4	4	6	121 (Dr.2 兼任1)