



**REPORT  
OF THE  
INVESTIGATION COMMITTEE  
ON**

**THE CLINICAL TRIAL OF  
TROVAFLOXACIN (TROVAN)  
BY PFIZER, KANO, 1996**

**FEDERAL MINISTRY OF HEALTH**

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**MARCH 2001**

## ACKNOWLEDGEMENTS

The Committee on investigation of 1996 Trovan clinical trial in Kano appreciates the opportunity given to it by the Hon. Minister of Health to carry out this important assignment which touches on the health of the most vulnerable citizens of our country – children.

In the course of carrying out its assignment, the committee received immense encouragement and support from Dr. Tim Menakaya, the past Minister of Health. Prof. A.B.C. Nwosu, the Minister of Health has also been generous with his support.

To do a thorough job, the committee had to rely on the cooperation of all those it interviewed. They were all forthcoming and most cooperative, and in some cases provided unsolicited, but useful documents. Some even returned on their own volition to provide further evidence and clarifications.

The Kano state Ministry of Health was also cooperative, as all of its functionaries, (including the Commissioner), who were invited by the committee responded promptly.

The full cooperation of all interviewed and the financial assistance of some members towards the completion of the committee's work is gratefully acknowledged.

We hope that this report will contribute to the prevention of a recurrence of such an event in our country.

Members of the committee, and the secretariat in particular, with the exception of one who could not participate in the proceedings of the meetings due to unavoidable reasons, despite their tight schedule did not only participate in virtually all the meetings but made meaningful, detailed and valuable contributions.

**Dr. A. Nasidi**  
Chairman

## EXECUTIVE SUMMARY

In December, 2000 and early 2001, some foreign (Washington Post) and Nigerian Newspapers (Thisday, Guardian, and Vanguard) reported a trial by Pfizer in Kano in 1996 involving the use of Trovan. Following these publications, the Minister of Health constituted an Investigation Committee with specific terms of reference to investigate the reported incident. The committee's terms of reference required it to make recommendations on the basis of its findings. The committee conducted a series of meetings in Kano and Abuja during which most of the individuals involved directly or indirectly with the trial were interviewed to ascertain the roles of each individual and agency. Documents submitted by such individuals were reviewed and analyzed. All interviews were recorded on celluloid tape and confidentiality of all the interviews maintained.

On the whole, 26 people were interviewed and the committee received good cooperation from all those who responded. The few that could not appear before the committee did not send any apologies; as such the committee could not ascertain their reason for not appearing. However, any relevant document with the signature of such individuals was scrutinized and used where necessary.

Government documents and other statutory documents guiding the conduct of such trials both in Nigeria and Internationally were obtained and examined vis-à-vis our terms of reference. The committee was unable to interview any of the patients recruited into the trial nor their relations due to the absence of adequate records of such patients.

At the end of its deliberations, the committee established that Pfizer actually conducted a Phase III Clinical trial of its drug, Trovafloxacin (Trovan) cerebro-spinal meningitis (CSM) epidemic. Two hundred (200) critically ill children were involved in the trial with 100 and 98 receiving Ceftriaxone (Rochepin) (gold standard) and Trovan respectively. The case fatality rate were 6 (6%) for Rochepin and 5 (5%) for Trovan. While there was evidence of previous use of the drug in patients with infectious diseases in the literature, this seems to be the first time the oral preparation of this drug was used in children for meningoccal meningitis.

*The committee further established that the procedure as laid down in the NAFDAC Guidelines for clinical trials (1996) of which Pfizer was aware (as shown by their subsequent application for clinical trial of the same drug in 1997), were not followed. Although there were efforts to stop the trial after it had commenced, this seemed to have been frustrated by the apparent resentment of the activities of the Federal Task Force on epidemic control by some functionaries of the Federal and Kano State Ministries of Health. The NAFDAC's approval referred to by Pfizer remains controversial because of its ambiguity with even NAFDAC officials who wrote it misinterpreting its meaning. However, it was clear to the committee that the letter did not convey approval to conduct the trial, but for the importation of the drug in Nigeria for investigational purposes only.*

The Principal Investigator recruited by Pfizer was inexperienced in the conduct of clinical trials and appeared to have been used with the main objective of involving a local medical practitioner. He did not have a deep knowledge of both the scientific and administrative activities taking place. He also allowed the visiting Pfizer team to take away all patient data and records as well as the scientific analysis of the trial. Publications using the data generated by the trial where he was the first author did not sufficiently reflect his role.

The Chairman of the Task Force for the Epidemic Disease Control who first raised the alarm was not only ignored by the Federal and States Ministries of Health, but also was maligned for trying to do so. The Task Force was also not funded and most expenses incurred for the control of such trials remained unsettled. The Ministries clearly shied away from their responsibilities and allowed the conduct of an illegal trial of an unregistered drug.

In general, the committee is of the opinion that the drug trial violated the Drugs and Related Products (Registration, ETC) Decree Number 19 of 1993, the Declaration of Helsinki on Ethical Principles of Medical Research involving human subjects and the Convention on the Right of the Child adopted by the General Assembly of the UN on the 20<sup>th</sup> November, 1989.

The committee also made appropriate recommendations on all the individuals and organizations involved as well as on ways of forestalling a recurrence.

## **CHAPTER 1**

### **1.1. INTRODUCTION**

The American Washington Post of 17th December 2000 reported the death of eleven Nigerian children and deformation of many others arising from clinical trials on Trovafloxacin (Trovan) a new antibiotic drug involving 200 critically ill children. It was reported that Pfizer Inc. conducted the clinical trials in Kano, Nigeria in April 1996 during a triple epidemic of measles, cholera and cerebro-spinal meningitis (**Appendix I**).

The former Honorable Minister of Health, Dr. Tim Menakaya consequent upon this report issued a press statement (**Appendix II**) and set up a Committee to investigate this trial with a view to finding out what really happened (see **Appendix III**).

### **1.2. TERMS OF REFERENCE.**

The terms of reference of the committee were as follows:

- (i) Collect and review all documentations related to the said trial;
- (ii) Examine the procedure adopted by Pfizer for the trial and the roles played by government functionaries in granting approval for the trial;
- (iii) Identify and interview all those involved in the trials;
- (iv) Advise the Honorable Minister on appropriate actions to be taken to ensure equity and justice;
- (v) Make any other recommendations that the committee may deem necessary for conducting future clinical trials of drugs and biologicals in Nigeria.

## **CHAPTER 2**

### **KANO MEETING AND THE INTERVIEWS – 10<sup>th</sup> and 11<sup>th</sup> January, 2001**

#### **2.1. Review of Terms of Reference and Preparation of Questionnaires**

The committee reviewed the terms of reference and agreed on the modalities for carrying out its assignments. Questions were then prepared for each of the individuals to be interviewed.

#### **2.2. Interviews:**

##### **2.2.1 Pfizer Representatives.**

Pfizer was represented by the following:

1. Mr. Robert A. Tade,- Managing Director Pfizer Nigeria & Country Manager Anglophone West Africa (Leader),
2. Mr. 'Lere Baale –Pharmaceutical Director for Anglophone West Africa
3. Dr. Segun Dogunro –Medical Director for Anglophone West Africa

The chairman welcomed the Pfizer delegation and introduced members of the Investigation Committee, which he said was mainly for fact finding. The Pfizer team leader introduced himself and members of his team. He (Pfizer) then submitted a 39-page document made up of:

1. 1-page public statement of the company's position titled "Facts on Pfizer's Humanitarian Intervention in the 1996 CSM/Cholera Outbreaks" with supporting documents (see Appendix IV).

In their opening statement the company stated the following: "the CSM/Cholera outbreak started in November 1995 and was spreading like wild fire ravaging most states in the north with devastating consequences. Pfizer's intervention was therefore strictly a humanitarian gesture aimed at saving lives at that material time. It was totally devoid of any commercial undertone. It is unimaginable that a company like ours would be involved in a clinical study without the approval of the appropriate agencies."

The highlights of the presentation by the Pfizer Executives included:

- a. Pfizer Nigeria was established 1957, and it is the present headquarters of Pfizer Anglophone West Africa which comprises Nigeria, Ghana, Gambia, Sierra-Leone, Liberia.
- b. Pfizer WA reports to Pfizer South Africa and accounts for only 0.15% of the total Pfizer turnover worldwide. The company has a strong Medical Division having medical doctors who are specialists in their own fields in its employ.
- c. The company has marketed the following types of drugs in Nigeria from inception to date:
  - i) Anti-hypertensives,
  - ii) Antibiotics,
  - iii) Anti-Diabetics,
  - iv) Anti-Depressants,
  - v) Anti-Rheumatics,
  - vi) Anti-Fungals,
  - vii) Over-The-Counter Drugs – Vitamins Etc.

In Nigeria as at 1996, Pfizer had offices at Ikeja, Aba, Benin, Kaduna, Kano, and Maiduguri. It had in the past conducted clinical trials of all of the company's products in Nigeria to meet NAFDAC requirements. The company was requested to submit a list and reports of clinical trials conducted by it in the past in Nigeria.

d. The Trovan Clinical Trial.

- i) The Representatives of the company confirmed that the clinical trial of Pfizer's Trovan oral antibiotic did take place during the 1996 epidemic at the Infectious Diseases Hospital, Kano.
- ii) The clinical trial was a Phase III Open Label Randomized Study
- iii) 200 patients whose average age was ten years were recruited for the trial.
- iv) The study was a comparative trial of Trovafloxacin (Trovan,) (a Pfizer product) and Ceftriaxone (Rocephin) (a Roche product) which is regarded as the gold standard for treatment of cases of cerebrospinal meningitis.
- v) Trovan was administered to 99 children while 101 received Rocephin.



- vi) The fatality for the Trovan and Rocephin groups was 5 and 6, respectively.
- vii) This was the first time Pfizer was conducting a Phase III trial in Nigeria
- viii) That the motive of the Trovan trial was purely philanthropic.
- ix) That Trovan had been tried in the US, South Africa, and Egypt.
- x) That Trovan is known to have a high CSF penetration rate and needs to be administered once daily as against Unasyn, which must be administered 2-3 times daily with the attendant disadvantages in an epidemic situation.

e. More on the trial:

- i) Pfizer Nigeria Plc learnt of the epidemic from print and electronic media.
- ii) Their discussions about the trials with Pfizer Inc. started sometimes in early 1996.
- iii) Alatrofloxacin for intravenous administration was registered for twelve (12) indications in adults excluding meningococcal meningitis in the United States in 1997 and in one EU country in 1998. Trovan was registered in the US only in 1997 and that the trial, which took place before then in Nigeria (1996) *was granted the go ahead by the US FDA so as to save many lives.*
- iv) On the basis of above NAFDAC was contacted for clearance on March 18, 1996
- v) Alatrofloxacin had been used in South Africa, Egypt and Morocco before the trial in Nigeria.
- vi) In 1998 there were reports of liver problems with 12 individuals who had been administered the drug. The EU had consequently banned it and Pfizer Inc, placed it on restricted marketing following this
- vii) The trial was authorized by NAFDAC and that the company contacted NAFDAC, Federal Ministry of Health, DG NAFDAC, the Federal Minister of Health in 1996 and his Special Assistant – Dr. A. E. Ike before the trial.
- viii) A fax copy of NAFDAC's letter with reference number NAFDAC/DG/555/I of 20<sup>th</sup> March 1996 was tendered. (see Appendix V)
- viii) Contact with Kano Ministry of Health (D-G and the Commissioner) was made by the company's former Chairman/Managing Director, Mr. Sam Ohuabunwa

- ix) No report was submitted to NAFDAC because there was no intention to apply for registration. And also no report of the study was submitted to any Nigerian authority. The company was directed to submit copies of the report and the trial protocol to the committee.
- x) No written informed consent, however nurses involved in the treatment of the patients obtained verbal informed consent from the parents or guardians of the patients in the local language - Hausa.
- xi) A special ward was allocated at the Infectious Disease Hospital, Kano for the trial
- xii) The patients came through the normal hospital channel and were thereafter sent either to the MSF camp or Pfizer camp.
- xiii) There were no hospital case files at the Infectious Diseases Hospital, Kano but Pfizer had its own patient report forms, which were sent to the parent company after the trial and none of such forms were left behind in Nigeria with any organization.
- xiv) The Principal Investigator (PI) for the Trovan trial was Dr Isa Dutse, a Kano based medical practitioner who participated as a sub-investigator in a previous Pfizer clinical study conducted by Prof. Fakunle. The PI was assisted by two other Nigerian doctors recruited by him, had the patient care responsibilities whilst the Americans only offered laboratory services.
- xv) Pfizer Inc. designed the protocol of the trial in the US.
- xvi) Apart from the Principal Investigator and his team, honoraria were paid to certain individuals who participated in the trials.
- xvii) The known adverse effects of the drug that the company confirmed are: dizziness in the up-right position in all categories of patients whilst others are nausea, headache, vomiting and vaginitis while the company believed that atralgia and arthritis could have been caused by the disease.
- xviii) Chairman of the Federal Task Force on the epidemic, Prof. Idris Mohammed was not initially informed of the trial but got to know after they had started. When he was given their protocol, he commended it as being well written and said that they should go ahead with the trial. He requested that samples of cerebrospinal fluid should be collected for him for his research work.
- xix) When asked whether Prof. Idris Mohammed made any demands on the company, the Pfizer representatives declined to comment.
- xx) Parts of the CSF samples collected were sent to Central Laboratory, Converse, Indianapolis, USA.
- xxi) The trial actually commenced on 3rd April 1996.
- xxii) The Kano State Ministry of Health gave a written permission to Pfizer staff to treat patients in Kano state government hospitals in response to a request from Pfizer.

- xxiii) The trial of Trovan saved lives as the case fatality rate in the epidemic population of 30% came down to 6% in the group treated with Trovan.
- xxiv) Unlike Nigeria, in Africa, Ghana and South Africa had benefited more from Pfizer's development programs and therefore Pfizer (Nigeria) wanted the country also to benefit and so did all that was done with good intentions to conduct the "the humanitarian trial".
- xxv) Pfizer thanked the committee for their attention and promised that he and his team will be available whenever needed.

At the end of the interview, the company was requested to submit the list of Nigerian and American personnel involved in the trial, copies of the list of those who were paid honoraria including other relevant documents.

## **2.2.2 THE PRINCIPAL INVESTIGATOR OF THE CLINICAL TRIAL**

Dr. Isa Dutse was Pfizer's Principal Investigator for the Trovan clinical trials in Kano in 1996. He is a Chief Consultant Physician and Ag. Dean of Medicine at the Bayero University, Kano. In his presentation, he confirmed the following:

- i) that he was contacted on the 30<sup>th</sup> March 1996 by Dr. Segun Dogunro, the Medical Director of Pfizer because of a previous study for Pfizer in which he participated along with Prof. Fakunle of Ahmadu Bello University, Zaria.
- ii) that he met with Drs. Dogunro and Scott Hopkins of Pfizer Inc. who gave him the Investigator's Brochure (**Appendix VI**) before the trial.
- iii) That After going through the brochure on Trovan, he was satisfied that the drug had great potentials.
- iv) That the Pfizer representatives informed him that they had clearance from NAFDAC to carry out the trials and that the Federal Ministry of Health had assisted them to obtain a duty exemption waiver from the Federal Ministry of Finance.
- v) That Pfizer also informed him that Kano State Ministry of Health had approved the trial.
- vi) That the Infectious Diseases Hospital at Kano was chosen as the site of the trial.
- vii) That at the time of the trial time there was no Ethics Committee at the Aminu Kano Teaching Hospital and that he (Dr Dutse), who was the Chairman of the Medical

- Advisory Committee of the Hospital "did not succeed in constituting an Ethics Committee for the clinical drug trial."
- viii) That Prof. Idris Mohammed had discussions with Drs. Scott Hopkins and Dogunro and that he – Prof. Idris Mohammed endorsed the protocol.
  - ix) That on the first day of the trial only four patients were recruited and that lumbar punctures etc were carried out with two house officers assisting him.
  - x) That a couple of days after Prof. I. Mohammed was said to have stopped the trial.
  - ix) That later the trial continued as the problem was said to have been solved
  - x) That On the 11<sup>th</sup> April 1996 there was a letter from Prof. Mohammed specifically stopping the trial.
  - xi) That as far as he was concerned then he was convinced and sincerely believed that Trovan had great potential in the management of meningitis, particularly as it could be given orally
  - xii) He confirmed that even when Patient 0069 did not respond to oral Trovan, there was no change of therapy till the patient was lost.
  - xiii) That response to Trovan management was promising and the results were remarkable.
  - xiv) He confirmed he studied Medicine at Ahmadu Bello University, Zaria and was a prizewinner in Pediatrics.
  - xvi) He regretted not constituting an Ethical Committee before and at the time of the trial.
  - xv) That about 6 months after the test, Pfizer approached him for an Ethical Committee Clearance and he gave them one, albeit backdated.
  - xvi) That he deeply regretted this action, the implication of which he was just understanding

**2.2.2.1. 2<sup>nd</sup> Appearance of Dr. I. Dutse, (Principal Investigator)  
on 11<sup>th</sup> January 2001.**

On specific questions from the committee on some key issues, the P.I answered as follows:

- i) That there was no written letter from Dr. Dogunro of Pfizer officially commissioning him as the Principal Investigator for the Trovan drug trial.
- ii) Although his remuneration was not discussed before the trial, he was paid an honorarium after the trial.
- iii) That the brochure given to him indicated that about 5000 persons had been treated with "Trovan" at phase 3 in other parts of the world.
- iv) That the visiting American Doctors namely (Drs. Scott Hopkins, Debra Williams and Mike Dunne) participated in patient-care but that he did most of the lumbar punctures whilst Scott Hopkins and Mike Dunne did a few.
- v) He could not confirm if any of the visiting Pfizer Doctors were registered in Nigeria
- vi) He recruited two House officers namely Dr. Hassan Haroun (now at AKTH) and another Dr. Shehu Yusuf (now in the US) to assist him.
- vii) That he had no contact with the Kano State Ministry of Health but only Pfizer officials did.
- viii) That both the then Commissioner for Health and the Director-General of Kano State Ministry of Health visited the Pfizer study center whilst the trial was going on. Prof Idirs Mohammed, Chairman, Task Force on Epidemic Control also visited from time to time.
- ix) That members of the study group included himself (Dutse), Dr. S. Hopkins, Mike Dunne, Tunfafi, Hannatu (a Nurse from the Task Force)
- x) that he had read some literature on Trovan before accepting to participate in the trial.
- xi) That although *quinolones* are not used in children generally, the Pfizer group told him that Trovan is a fluoro-quinolone, a new generation quinolone that was safe for pediatric use.
- xii) That a ward was allocated to Pfizer specifically for the study.
- xiii) That he could not remember any conflict between his group and the Medicins Sans Frontiers (MSF).
- xiv) That 75% of the Trovan patients trial group took Oral Trovan
- xv) That the study group looked for adverse effects such as syncope, dizziness, abdominal pain, and moniliasis.
- xvi) That he was not sure that the mortalities were attributable to Trovan.

- xvii) That the sample size of 200 was determined by Pfizer.
- xviii) That they stated that the dose of Trovan - 3mg/kg body weight once daily was effective.
- xix) That the study findings were not made available to him nor to any health authority in Nigeria until he was invited to the U.S. to participate in an International Conference in Atlanta, Georgia, where he presented a paper.
- xx) That no patient case records were left with the IDH by the study group.
- xxi) That Pfizer Inc. had taken away all records, including patient records and so he had no records with him, except a list containing initials of the patients and not their full names. (see Appendix VII).
- xxii) That he had not published the result of the study in any scientific journal.
- xxiii) That he was not in possession of any document, such as patient records, informed consent or results of laboratory tests.
- xxiv) that though he got a copy of the laboratory results but could not trace them right now.
- xxv) That the laboratory tests were done in Geneva, however, in Kano one Eric Oout and Dr Tunfafi did cultures, gram stains and latex agglutination tests.
- xxvi) That he could not recommend the replacement of chloramphenicol Injection with oral Trovan for the treatment of Meningitis, as he believes more work needs to be done before making such recommendation. However, in private practice, he would offer Rocephin® - Ceftriaxone if the patient can afford it.
- xxvii) That there was no written informed consent but he and some nurses obtained oral informed consent.
- xxviii) That Dr Scott Hopkins took pictures of most of the patients and kept many records.
- xxix) That Drs Scott Hopkins and Mike Dunne returned six weeks later for follow-up of the patients during which only about 50% of the patients were seen the first day while two patients came the second day.
- xxx) That there was no financial assistance to the patients.
- xxxi) That although on hindsight he had regrets about the clinical trial, his motive was not negative. He added, "*I have trusted people and am disappointed*".
- xxxii) That although Pfizer might have had legitimate authorization to come in and do the trials, he believes that Pfizer's primary motive was far from philanthropic.

xxxiii) *In his closing comments he said, " I regret this whole exercise, I wonder why on earth I did this? I did not do it for any personal benefit. I did not go out to kill anyone or injure or put anyone's life at risk."*

xxxiv) That the Government of Kano State needs to be more serious on matters of Public Health to return Kano to its pre-eminent status of a clean city with good quality potable water instead of the headquarters/source of epidemics as in recent times

xxxv) That now that Kano populace is now rejecting oral polio and meningitis immunization on religious grounds he wondered what would happen in case of another meningitis outbreak or resistance of the infective organism to Chloramphenicol?

### **2.2.3 CHIEF MEDICAL DIRECTOR (CMD)– AMINU KANO TEACHING HOSPITAL, KANO.**

The CMD – Aminu Kano Teaching Hospital, Kano – Dr. Sadiq Suleiman Wali met with the Committee in the company of the hospital's Chairman – Medical Advisory Committee – Dr. Musa Borodo and the Ag. Director of Administration. Dr. Wali was a personal physician to the former Head of State at Abuja. He is a fellow of the Internal Medicine Society of London and West Africa. He is an Adviser to the World Health Organization in the development of a conjugate vaccine. He had conducted some research on gastro-enteritis, hepatitis C, HIV, haematology among others. He is currently over-seeing some drug trials on anti-hypertensives, anti-helicobacter for Glaxo-Wellcome in a multi-centre trial. He was appointed Honorary CMD of AKTH in 1992 and Chief Medical Director (CMD) April 1998.

While testifying, he informed the Committee thus:

- i) That an Ethical Committee was established in AKTH in October 1996 well after the trial took place.
- ii) That a list of the past and present members of the ethical committee would be made available to the committee (see **Appendix VIII**).
- iii) That the present Chairman, Medical Advisory Committee (MAC) is Dr. Musa Borodo.
- iv) That the current Chairman of the Ethical Committee is Dr. Isa Dutse.
- v) That the AKTH Ethical Committee is involved only in trials within the AKTH.

- vi) That a list of the applications/approvals for clinical trials considered by the AKTH Ethical Committee would also be made available (see Appendix IX).
- vii) That the hospital management was not officially aware of any clinical trial on Trovafloxacin (Trovan) whether at AKTH or any hospital in Kano.
- viii) That the hospital became aware of Dr. Dutse's and Dr. Hussein Haroun's participation in the Trovan trial only after the Washington Post publication.
- ix) That no group or any Ethical Committee at the AKTH saw the protocol neither was the results/report of the trial submitted to the Hospital management.
- x) That the letter issued on the letterhead of AKTH was irregular." (see Appendix IX).
- xi) that Salisu Isah Adamu the signatory to the "irregular" letter of ethical clearance" was a confidential Secretary to Dr. Dutse (see Appendix IX).

On the role of the AKTH in controlling cerebrospinal-meningitis, cholera, measles etc, that have become endemic in Kano State, he said that AKTH would continue to provide tertiary care, diagnostic services and laboratory support services. He stated that a good water supply system should eliminate cholera. He also stated that the AKTH was prepared to assist the state whenever there is a need to do so and that the AKTH was prepared to participate in preventive care activities that would include patient management, disease surveillance studies for Kano so that epidemics could be predicted and prevented. The AKTH was also ready to provide adequate laboratory service, if need be.

He stated that sensitivity studies carried out at AKTH confirmed that the causative organisms of cerebrospinal meningitis are still sensitive to chloramphenicol and that chloramphenicol is still effective for the management of meningitis. The CMD stated that he knew little about Trovan save what he read from newspapers and the Internet. Concerning the Trovan trial, he wondered if the trial was really necessary and he wondered if the drug was cheaper or more efficacious than chloramphenicol. He also believes that the follow-up should be longer than six weeks and that in his hospital some money is given to patients to enable them transport themselves back for follow-up.

The CMD believes that if Pfizer's intention had been humanitarian, its activities should have been restricted to donation of vaccines and drugs of choice.



He said that although AKTH is yet to develop a written protocol for the treatment of meningitis, he will ensure that this was done as soon as possible. The CMD regretted that it was possible for foreign health workers not registered in Nigeria to come in and treat patients.

#### **2.2.4 COURTESY CALL ON THE KANO STATE COMMISSIONER OF HEALTH.**

The Committee took a break to pay a courtesy call on the Honourable Commissioner of Health Kano State, Dr. Mansur Kabir. After introduction of the members, Committee Chairman – Dr. A Nasidi informed the Hon. Commissioner of the mission of the Committee's visit to Kano State.

The Hon. Commissioner informed us that the State had set up a similar committee and that he will direct its Chairman as well as any other person the Committee may wish to interview to cooperate.

#### **2.2.5 ALHAJI ALIYU MUKTAR - DIRECTOR OF PHARMACEUTICAL SERVICES KANO STATE MINISTRY OF HEALTH.**

The Kano State Director of Pharmaceutical Services Alhaji Aliyu Muktar in his presentation stated as follows:

- i) That he was involved in the management of the 1996 epidemic in Kano State.
- ii) That the State received donations of drugs/equipment from various sources such as Pfizer, MSF, the German Red Cross, Niger Republic and members of the general public.
- iii) That the Pfizer donation was received by the State without the involvement of the Task Force.
- iv) That Dr. M. A. Kura – Chairman of the State's Epidemic Committee received the donations on behalf of the State.
- v) That the drugs were delivered to the IDH, Kano except those distributed to the 44 Local Government Areas.
- vi) That Pfizer donation consisted of 5 different drugs.
- vii) That clearance for any activity by a donor had to be given by Prof. Idris Mohammed – Chairman of the Federal Task Force for the Control of the epidemic.
- viii) That no Pfizer official informed him that a drug trial was to take place in Kano at the time of the epidemic.

- ix) That to the best of his knowledge, none of his officials participated and he did not know at that time that a drug trial took place.
- x) That about 3 months after the epidemic was over, a petition on the drug trial written by Prof. Idris Mohammed to the then Health Minister was endorsed to the then State Commissioner of Health for comment and that he was a member of a 3-man Committee that prepared the State Ministry of Health's comment on that petition.
- xi) That the State Health Ministry has no Ethical Committee for drug trials.

#### 2.2.6. DR. HUSSEIN HARUNA.

Dr. Hussein Haruna is currently a Registrar in Medicine at the Aminu Kano Teaching Hospital, Kano. He is a 1995 Medicine graduate of the University of Ilorin. In 1996 at the time of the drug trial, he was a house officer at the Murtala Mohammed Specialist Hospital, Kano.

He was an Assistant Investigator under Dr. Isah Dutse for the Trovan drug trial. He stated as follows:

- i) That he participated in the trial together with one Dr. Shehu Yusuf and one Abdulkadir who were staff of the Kano State Ministry of Health.
- ii) That his role during the drug trial was to set drip lines and assist generally in clinical management of the patients.
- iii) That the drug trial to him and his colleagues was a blind trial.
- iv) That he did not take part in patient screening or selection.
- v) That he observed that the drugs seemed to be beneficial to the patients.

#### 2.2.7 MEDECINS SANS FRONTIERE (MSF), REPRESENTATIVES KANO OFFICE

The MSF was represented by:

- i) Dr. Marie-Claire Mutanda – a 1994 Medical graduate from the Republic of Congo (Zaire) who is the present MSF Kano Project Coordinator.
- ii) Ms Helen Cox – a 1998 Australian graduate with a Master's Degree in Public Health, the MSF Epidemiologist in Kano.

- iii) They both informed the committee that the Kano Office was established in 1998. Their Lagos office is the administrative office with 4 expatriate staff and 18 national staff.

Neither of the two was involved in the 1996 epidemic. The MSF is currently engaged in sentinel surveillance of selected sites in Kano for meningitis, measles and cholera for emergency preparedness and intervention.

The MSF representatives could not respond to the prepared questions but promised to send their response later.

#### **2.2.8 DR. MOHAMMED SANI ADO – CHAIRMAN OF THE KANO STATE INFORMATION GATHERING COMMITTEE ON THE DRUG TRIAL.**

Dr. M.S. Ado, who is the Chairman of the Kano State committee was interviewed on the findings of his committee and presented as follows:

- i) That the committee had no written letter of appointment and had no terms of reference
- ii) That his Committee confirmed that there was a triple epidemic of cholera, meningitis and measles in 1996.
- iii) That the record of epidemic, in their opinion was not well handled
- iv) that there were 21,739 cases of Meningitis and about 1,000 deaths.
- v) That on the whole at the IDH, there was 6,133 cases and a mortality of 247
- vi) The epidemic started at the tail end of 1995 and lasted until 23<sup>rd</sup> May 1996, when the non-governmental organizations (NGOs) started winding up their operations in Kano.
- vii) That the figures at the IDH were obtained from February 1996 onwards.
- viii) That the situation overwhelmed the State Government making it necessary for assistance to be sought from the Federal Government and other International agencies
- ix) That the Federal Ministry of Health constituted a Task Force headed by Prof. Idris Mohammed.
- x) That it was the Federal Task Force which handled all control activities including donor support, except the Pfizer support.
- xi) That there was a request from Pfizer to the Kano State Government for permission to bring relief material and participate in the treatment of patients.
- xii) That it was 2-3 months after the control of the epidemic that the State Ministry of Health learnt that a clinical trial was conducted through a request from the FMH for the comment of the Hon.

Commissioner of Health, Kano State on a petition written by Prof. Idris Mohammed protesting the drug trial by Pfizer.

- xiii) That following the petition, the Kano State Ministry of Health set up a Committee led by Dr. Kura to look into the petition.
- xiv) That the Committee found evidence that the trial did take place and that the Federal Ministry of Health and NAFDAC approved it.
- xv) That on the whole about 200 patients were involved in the trial (100 were treated with Trovan and 100 with Rocephin).
- xvi) That the mortality of 5 for the Trovan group and 6 for the Rocephin group was established whilst 3 from each group had complications related to meningitis
- xvii) That Pfizer neither left data nor sent the results of the trial to the KNSMOH

#### **2.2.9 MANSUR KABIR.-COMMISSIONER FOR HEALTH, KANO STATE**

Dr. Mansour Kabir, the present Commissioner for Health, Kano State is a physician who had some experience in Public Health from July 1999. His predecessor in office was Dr. Adamu Nuhu – also a practicing physician.

In his response to the Committee's enquiries on his role and knowledge on the episode under reference he stated as follows:

- i) That he could not recollect any mention of an epidemic for his special attention in the hand-over notes he received from his predecessor
- ii) that as a former Deputy Director i/c Federal Vaccine Production Laboratory, Yaba, Lagos, he knew that there was an epidemic in Kano in 1996 and some of his staff took part in its control.
- iii) That there had been no resurgence of measles since a mass campaign jointly conducted by his Ministry with UNICEF, MSF, FMH, on his assumption of duties with above 900,000 children vaccinated
- iv) That Cholera cases have also reduced in the State Government although the KNSG is very concerned.
- v) That a State Ministry for Environment had been created and that the Kano Inner City Project has commenced to improve the environment.
- vi) That Water supply is being improved, although the project was hindered by NEPA's electricity supply.
- vii) That there is an Emergency Preparedness Committee in the State with the Hon. Commissioner of Health as the Chairman.

- viii) That he first heard of the drug trial in December 2000 following which he formed a Committee to look into the issue.
- ix) That the Ministry was being discreet about the episode to protect the public health programs, particularly the immunization programme.
- x) That the State has no Committee for the Approval of Drug Trials.
- xi) That although the drug trial took place at the IDH, Kano, there was neither record of informed consent nor that of people who participated.
- xii) That none of his staff took part in the trial.
- xiii) That record keeping is poor in most of his medical centers and almost zero in epidemics.
- xiv) That he intends to introduce Record Keeping courses in the State's School of Health Technology up to the HND level.
- xv) That he also intends to strengthen the records section of his hospitals.
- xvi) That one "victim of the Pfizer drug trial" had come to him to inform him of his intentions to sue Pfizer as his daughter was one of those recruited for the trial.

He further stated that it was wrong for a foreign drug company to come into the country and carry out drug trials without the consent of the Federal Government, State Government and the subjects. He confirmed that the State MOH would set up an ethical committee whenever there is a need for it.

He confirmed that in conjunction with the MSF, sentinel surveillance for the four major diseases (CSM, Measles, Cholera and Yellow Fever) causing epidemics in Kano was going on and that these efforts have been yielding promising results.

#### **2.2.10 ALHAJI FAROUK USMAN - THE PERMANENT SECRETARY - KANO STATE MINISTRY OF HEALTH.**

Alhaji Farouk Usman became the Permanent Secretary, Kano State Ministry of Health on 30<sup>th</sup> October 2000. He was previously Managing Director of the Kano Broadcasting Corporation. When asked to confirm press reports quoting him to have said that the trial did not cause any deaths or any harm, he emphatically denied having said such a thing.

He did not consider it right for the letter to Pfizer authorizing them to treat patients at the IDH, Kano to have been written by the Director Personnel Management instead of Director of Pharmaceutical Services. He also added

that it is really not good to create room for strangers to come and do whatever they liked in our country.

**2.2.11 DR. DAIYABU MOHAMMED –DIRECTOR PRIMARY HEALTH CARE – KANO STATE.**

Dr. D. Mohammed who is the present Director of Primary Healthcare and Disease Control was with the British Department For International Development from July 1995 to April 1999. He informed the committee that Dr. Takai was the Director – PHC in 1996, and there was no report of the epidemic/drug trial in his handing over notes.

He only became aware of the drug trial through the Washington Post publication. Although he stated that he was unaware of Trovan before now, he felt that if it could be given orally for management of CSM, then it could be a good alternative to other drugs known for the management of meningitis.

**2.2.12 HAJIYA NAFISAT KABIR - FORMER COMMISSIONER FOR HEALTH, KANO STATE.**

Hajiya Nafisat Kabir has a Bachelor of Arts degree in Education; she became a Commissioner in Kano State in November 1994 during the tenure of the late Military Administrator of Kano State – Col. Wase. Her predecessor was Dr. Fayiz Yola while her Director – General at the Ministry of health was Dr. Sanda Mohammed.

During the interview, she attested to the following:

- i) That there was a triple epidemic of measles, cholera and meningitis in Kano State which started beginning of November/December, 1995
- ii) That the focal point for the control activities was the Infectious Diseases Hospital, Kano.
- iii) That she contacted the Federal Ministry of Health for assistance when the epidemic continued to spread
- iv) That at the initial stages both the State and Federal Governments provided medical supplies
- v) That when the epidemics escalated the MSF, Pfizer and Niger Republic and other NGOs came to assist. (see Appendix xxxix).
- vi) That intensive Public enlightenment campaign was launched by her Ministry
- vii) That an epidemic control Committee was set up to coordinate the control programme

- viii) That some individuals in the State made anonymous donations
- ix) That the Federal Government constituted a Task Force with Prof. Idris Mohammed as Chairman.
- x) That the Task Force supervised all those that contributed to the control activities.
- xi) That she could not remember if the request for assistance to the Federal Government was in writing or not.
- xii) That although the KNMOH had no representative on the FG TF, there was a good working relationship with it.
- xiii) That the Chairman of the TF briefed her but briefed the Military Administrator more regularly and that no report was received from the FG after the epidemic was over.
- xiv) that Pfizer wrote to inform her of their intention to donate drugs for the epidemic
- xv) that she met with the then Managing Director of Pfizer – Mr. Sam Oluabunwa once, who came to make the donation
- xvi) that Pfizer did not indicate then that it would undertake a drug trial
- xvii) That she was not informed about the trial, despite her being in the hospital (IDH) every day for several hours throughout the epidemic period.
- xviii) that there was no report of a struggle for bed space between Pfizer and MSF,
- xix) that she was out of town when the Federal Government Task Force Chairman arrived Kano, who consequently reported to her DG and the Governor
- xx) that the Task Force Chairman Prof. Idris Mohammed did not inform her that Pfizer was conducting a drug trial neither did he complain to her.
- xxi) That she became aware of the trial 3 months after the epidemic through a petition from Prof. Idris Mohammed to the Minister of Health against the drug trial by Pfizer.
- xxii) That her Ministry constituted a committee comprising the Director – Medical and Health Services as Chairman, the Director – Primary health Care and the Director – Pharmaceutical Services to investigate the trial.
- xxiii) That she believed that Prof. Idris Mohammed should have discussed with her or with the Military Administrator when he knew something was going wrong.
- xxiv) that the officer in-charge of the IDH did not inform her that Prof. Idris Mohammed had written to stop a drug trial by Pfizer and that he only did that 3-months later
- xxv) that the Federal Government's intervention in the epidemic was good and helpful to the State



- xxvi) that the State Committee was not sidelined by the Federal Government intervention
- xxvi) that Pfizer's donation to the State Government was very helpful during the epidemic. She said that they also left their equipment behind and received formally.
- xxvii) that although no query was issued, she did reprimand some officials of the Ministry for not alerting her of any such trial and for not knowing what was going on in the hospital.

#### **2.2.13 DR. SANDA MOHAMMED – FORMER DIRECTOR – GENERAL, KANO STATE MINISTRY OF HEALTH**

Dr. Sanda Mohammed was the former Director – General, Kano State Ministry of Health. He was appointed to this position mid- 1995; prior to this, he was a Consultant – Surgeon at the Murtala Mohammed Specialist Hospital, Kano.

His testimony went thus:

- i) that In 1996 the State experienced a triple epidemic of cerebrospinal meningitis, cholera and measles.
- ii) That most of the patients came from the municipality but later others came from other parts of the State.
- iii) That all hospitals in the state were designated as treatment centres.
- iv) That the State had no Committee initially for the control of the epidemic.
- v) That the Federal Government came in response to the KNMOH distress call
- vi) That the then Minister of State for Health – Mr. David Sadauki visited Kano and on his return back to Lagos, later sent us a team
- vii) That there was no written request but the Military Administrator went to Abuja to ask for help from the Federal Government for assistance.
- viii) That Prof. Idris Mohammed – Chairman of the Federal Task Force met him in his office and introduced himself and his mission to come
- ix) that his mission was to assist Kano State in the control of the epidemic.
- x) That because of his trust and respect for the Professor Idris Mohammed and Dr. A Nasidi he did not ask for any letter of introduction.
- xi) That the Kano State Government facilitated his work with the provision of official accommodation at Daula Hotel and an official vehicle from the Government House.



- xii) That the base for the Task Force activities was the IDH, Kano
- xiii) That no organisation came to him directly for the purpose of donating drugs.
- xiv) That he was briefed daily by the then Director of PHC&DC – Dr. Ali Guda Takai.
- xv) That there was no problem between the Federal Task Force and the State Ministry of Health.
- xvi) That Dr. Segun Dogunro of Pfizer donated some drugs to the KNMOH Ministry.
- xvii) That Pfizer's letter of offer to donate drugs and request for permission to treat patients were not passed to him.
- xviii) that he signed all letters of acknowledgement of donations to all the donors.
- xix) that the IDH was under the Hospital Management Board.
- xx) that Prof. Idris Mohammed did not mention the drug trial to him
- xxi) that he did not know of the trial and that if he did he would have stopped it or resigned if constrained to allow it to continue.
- xxii) That he recalled being directed by the Commissioner of Health to find out if there was a problem at IDH.
- xxiii) That he convened a meeting of all agencies during which he was informed by participants that there was no problem at the IDH and he thus asked them to continue with work.

#### **2.14 VISIT TO THE INFECTIOUS DISEASES HOSPITAL, KANO.**

The Committee visited the IDH, Kano at about 6.45pm on the 12<sup>th</sup> January 2001. This was due to its very tight schedule imposed by the detailed interviews conducted earlier in the day.

The Committee was appalled by the sorry state of the Hospital and agreed that its graphic depiction by the Washington Post was not an exaggeration.

Some of the observations made by the committee after the visit include the following :

- i) The patient beds were dilapidated and had neither mattresses nor beddings,
- ii) Relations as well as their children attending to AIDS and meningitis patients resided in the same wards where the patients were kept
- iii) The environment was generally dirty
- iv) No treatment cards were available for inspection when requested for.

- v) The Committee spoke to three female staff on duty – a Principal Nursing Officer, a Nursing Officer and a Clinic Assistant all of whom did not work in the hospital as at 1996.
- vi) Within the hospital premises is located an immunization center where healthy children were brought from outside for immunization
- vii) Patients with meningitis, AIDS and measles were on admission at the time of the visit

## CHAPTER 3

### 3.0 PROCEEDINGS OF INTERVIEWS HELD IN ABUJA 19<sup>th</sup> Jan., 2001

These interviews were held in the Federal Ministry of Health in Abuja.

#### 3.1. MSF REPRESENTATIVES, LAGOS OFFICE.

The Chairman introduced members of the Committee to the MSF representatives after intimating them of the Committee's activities. The MSF representatives were:

- |    |                      |   |                              |
|----|----------------------|---|------------------------------|
| 1. | Mr. James Foote      | - | Asst. Country Manager, MSF.  |
| 2. | Dr. Gebrewold Pedros | - | Medical Coordinator for MSF. |

The MSF team submitted their response to the Committee's questions (see **Appendix XI**). The Chairman assured them that they were not under interrogation but rather in a dialogue with partners. During the dialogue with the team, in addition to their written submission, they stated as follows:

- i) that the team could not confirm whether there was conflict between MSF and Pfizer, although did not consider that Pfizer's approach to the clinical trial was ideal
- ii) that they confirmed that Dr. Lodi one of the MSF Doctors who was present during the trial in Kano and was mentioned in the Washington Post report is no longer with the MSF and that he could probably be contacted through the Washington Post.
- iii) That the MSF does conduct clinical trials and would only use drugs that have been tested and recommended for use by the World Health Organization.
- iv) that all records/case files of patients treated by MSF during the epidemic should be with the Ministry of Health, Kano, as it was not their practice to take such documents away. The Chairman requested for a final report on the epidemic as well as follow-up activities by the MSF and therefore, the KN MOH should have them
- v) that one primary reason for the continued presence of the MSF in Nigeria was to facilitate rapid response to epidemics and that MSF intervention in the 1996 epidemic in Kano was between end of February and end of May 1996.
- vi) That the MSF is concerned with the mistake, by the populace, of identifying the MSF as a pharmaceutical company in the face of recent events.

- vii) That the MSF is now involved in surveillance activities that should facilitate rapid response during epidemics and other health emergencies

### **3.2 PROF. G. E. OSUIDE – FORMER D-G NAFDAC.**

Prof. G. E. Osuide (Former DG-NAFDAC), in response to questions stated as follows:

- i) that he was aware of the CSM epidemic in Kano in 1996, and that it affected him personally as his assistant lost his first son during the outbreak.
- ii) That NAFDAC was not aware of the Trovan trial
- iii) That Pfizer had applied for clinical trials in the past and should therefore be familiar with the procedure
- iv) That Pfizer made no formal application to NAFDAC for clinical trial
- v) That such applications, as submitted by Pfizer are usually for special investigations on animals or in vitro analysis.
- vi) that no application to conduct clinical trials was officially made
- vii) that if Pfizer had applied for Clinical trials of Trovan such an application would have been brought to his attention and considered by a committee
- viii) that registration application for use of Trovan for other indications was made after the said trials and that the appropriate NAFDAC desk officer should be able to brief the committee on this
- ix) that NAFDAC has guidelines and procedures for the conduct of clinical trials and that Pfizer did not follow proper procedures
- x) that the letter, allegedly written by a NAFDAC official, Mr. E. U. Usoro, was just for the importation of the drug for investigational use (see Appendix XIIa) .
- xi) that every activity within the organization has distinct patterns and procedures that must be followed
- xii) that, as far as the laws of Nigeria are concerned, there was no clinical trial of this drug for epidemic meningococcal meningitis.
- xiii) that he did not recall receiving any documents from Pfizer on the use of this Trovan for cerebrospinal meningitis
- xiv) that all he could recall was Dr. Ike's letter from the Office of the Minister of Health, Dr. I. Madubuike requesting for NAFDAC's comments on a petition by Prof. Idris Mohammed on the Trovan clinical trial in Kano.
- xv) that there was no letter or license from NAFDAC authorizing Pfizer to conduct the clinical trial.

- xvi) He further stressed that reference to clinical trials means using human subjects but by his understanding the investigational studies were meant to be in vitro.
- xvii) That any drug that is not on the Essential Drugs List needs to be registered by NAFDAC after multi-centre clinical trials.
- xviii) That a drug could be approved by NAFDAC on emergency basis for use of a single patient (Single Patient Permit) and this can only be by the Minister of Health, through the office of the D-G, NAFDAC
- xix) that the NAFDAC representative at Kano as at the time of the controversial trial was retired Major Aliyu Mohammed.
- xx) That the sample size of the trovan sent from Kano by NAFDAC Representative was too small for analysis, as such they were not tested.
- xxi) Prof. Osuide viewed the conduct of the trial by Pfizer as an act of deception and misuse of privilege.
- xxii) On the apparent contradiction in his comments (**Appendices XIIb and XIIc**), he said it was based on the misleading information provided him by the then Minister of Health Dr. I. Madubuike.

### **3.3 DR. BAWA ABUBAKAR – DEPUTY DIRECTOR (REGISTRATION), NAFDAC.**

Dr. Bawa Abubakar joined NAFDAC in 1996 as a Chief Regulatory Officer in-charge of Registration and presently Deputy Director, (Registration). He is a veterinary doctor with a Masters degree in veterinary medicine from the University of Edinburgh.

He revealed to the Committee that on 3rd July 1996, NAFDAC received a petition on "the illegal clinical trial of the unlicensed drug - Trovafloxacin (Trovan) during the 1996 meningitis epidemic in Kano" written by Prof. Idris Mohammed – Chairman of the Federal Task Force for the Control of the Epidemic, dated 1<sup>st</sup> July 1996, to the then Minister of Health and copied to the Director-General, NAFDAC. He was directed to comment on the letter and confirm the registration status of the drug.

Dr Bawa was interviewed along the same line as the NAFDAC D-G, to confirm some salient issues and he responded as follows:

- i) That although it is his division ((Registration & Regulatory) that handles such requests it had no record of any application or approval for importation or trial of a drug by the name Trovafloxacin (Trovan) from Pfizer before June 1996,

- ii) That he received "a directive" from his Director on this issue much later in 1997 and in his reply he stated among others, "the drug Trovan was not registered and that the R & R Division did not grant Pfizer permit to import the drug or to conduct clinical trials with it."
- iii) That Pfizer submitted an application dated 27th June 1996 and received by NAFDAC on the 1st July 1996 indicating the company's intention to conduct local clinical trials on the drug for a number of indications including cerebrospinal meningitis.
- iv) That no permit was given to Pfizer to conduct clinical trials on the drug, because the application did not comply with NAFDAC's guidelines and procedure for conducting local clinical trials.
- v) That he believed that given the short interval between Prof. Idris Mohammed's petition and the 27th June 1996 application by Pfizer for a clinical trial, Pfizer wrote the application as an after thought with a view to cover up the alleged illegality of the trial reported by Prof. I. Mohammed.
- vi) That on 4th July 1996, Pfizer sent another application to the agency for permits to conduct local clinical trials on three different drug products – Cadura (Doxatosin), Glucotrol XL (Glipizide) and Trovafloxacin.
- vii) That the company paid relevant fees for the clinical trial protocol guidelines that were to be submitted together with relevant documents for evaluation before authorization of the trial and importation of the samples
- viii) That he requested for evidence of the registration of the drug in the country of origin, certificate of manufacture and free sale from the competent health authority in the country of origin authenticated by the Nigerian Embassy in that country, ethical committee clearance and patients' informed consent and completed protocol.
- ix) That up to date, the company has not submitted the completed trial protocol and relevant documents for further action on their application.
- x) That instead, on 9th September 1997, NAFDAC received from Pfizer two separate letters dated 8th September 1997 notifying the agency of the company's intention to import supplies of Trovafloxacin and Alatrofloxacin for investigational and clinical studies purposes for two completely different indications – which are **community acquired pneumonia** and **nosocomial pneumonia** at four centres.
- xi) That the company was requested to submit a trial protocol and other relevant documents.

- xii) That no approval was granted to the company for the trial due to the inconsistencies of the company's documentation and non-compliance with the requirements.
- xiii) That the trial center identified by Pfizer did not meet the requirements because it was neither a tertiary institution nor a place approved by the Health Minister that could grant ethical clearance for a clinical trial.
- xiv) That in emergency situation, the Minister may authorize the use of certain drugs for individual use only
- xv) That he is of the view that strict compliance to the law of the nation should take precedence over any other interest.

In conclusion, he said that from records available in the Drug Registration Division of NAFDAC the drug Trovan has never been registered by the agency and that no approval was granted Pfizer Inc. or their local representative from the division to conduct local trials of the drug at Kano during the 1996 meningitis epidemic.

Attached (**Appendix XIII**) is a submission by Dr Bawa that further clarifies the role of his Department as it relates to the trial.

### **3.4 DR. E. C. CHIDOMERE –SPECIAL ASST. TO A FORMER MINISTER OF HEALTH.**

He was asked in at 6.48 p.m. Dr. Chidomere is a pharmacist with a doctorate degree in Clinical Pharmacokinetics and Drug Metabolism from King's College, University of London. He had enormous experience on issues concerning drug development, production and trials of newly developed drugs. In August 1996, he was appointed Special Assistant to the Federal Minister of Health, Dr. Ihechukwu Madubuike. In his reaction to the Committees questions, Dr Chidomere stated as follow:

- i) that he was appointed to that position after the drug trial had taken place
- ii) that he saw a petition written by Prof. Idris Mohammed and was directed by the HMH to treat it
- iii) that copies of the petition were sent to the Kano State Ministry of Health, the National Agency for Food & Drug Administration & Control and Pfizer for comments.
- iv) That on receipt of their comments he analyzed them and advised the Minister

- v) That the Minister's reply to the petition, which was written and endorsed by him, was based on the comments sent by the addressees (NAFDAC, Kano State Ministry of Health and Pfizer).
- vi) That the Drugs and Related Products (Registration, etc.) Decree Number 19 of 1993 mandates NAFDAC to grant permission for the conduct of clinical trials using an un-licensed drug.
- vii) That NAFDAC legally granted Pfizer the authority to import the drug Trovan into the country.
- viii) That the agency could only depend on the information given by the company on the quality of the drug because it was not in a position to make any pronouncement on it
- ix) That If samples are sent, the analytical protocol and methods of analysis are made available only after the drug is registered.
- x) That investigation on the clinical trial was already in progress before his appointment as the SA to the Hon. Minister.
- xi) That he could not remember the details of Prof. Idris Mohammed's petition but that there was a legal mandate for Pfizer to import the drug.
- xii) That he was aware that Trovan had not been registered in many countries as such the National Drug Regulatory Authorities including NAFDAC were not in a position to make pronouncements on its quality as is the case with every new unregistered drug.
- xiii) He stressed that the QC protocol for the drug as at that time had not been received by NAFDAC.
- xiv) That it is the Agency that approves the use of a drug for investigational purposes and not the Minister.
- xv) That he did not have in his possession the approval given by NAFDAC for the clinical trial and he believes that *clinical trial* and *investigational use* mean the same thing.
- xvi) When told that the former DG, NAFDAC denied issuing any approval for a clinical trial in his statement, he reacted by saying that ... "it means that the Former DG, NAFDAC had at that time misled the Ministry".
- xvii) That according to the Helsinki Declaration informed consent could be provided for minors by relatives and family, and that Pfizer obtained informed consent which he believes was written.
- xviii) He however had never seen such a "written" informed consent and that the report of the Kano State Ministry of Health indicated that Prof. Idris Mohammed should know better.
- xix) That he was informed that the Principal Investigator stated that the approval of a local Ethical review committee was obtained
- xx) That the Ministry did not constitute any committee to look into the matter, but that his office handled everything on the issue



- xxi) That after receiving the comments of the addressees (Kano MOH, Pfizer and NAFDAC) he did not request for Prof I. Mohammed's comments
- xxii) That he did not invite Prof. Idris Mohammed to defend himself after studying the reports from Pfizer and Kano State Ministry of Health because he acted as directed by the Minister.
- xxiii) That he was not sure whether not giving Prof Idris Mohammed the chance to defend himself was fair or not.
- xxiv) When asked why he would rather believe the Pfizer report as against that of the Task Force set up by the Federal Ministry of Health to which he belonged, he commented that everything was based on reports received.
- xxv) That his response to Prof. Idris Mohammed was conveyed on behalf of the Minister and that the Minister probably had other information to which he was not privy.
- xxvi) That Pfizer could not do the wrong thing since no company would want to do wrong knowing the implication as such he trusted their submission.

5. **DR. SULEIMAN ABDULLAHI –PRINCIPAL MEDICAL OFFICER  
IN-CHARGE THE INFECTIOUS DISEASES HOSPITAL (IDH), KANO, 1996.**

He was interviewed about his role in the 1996 Kano Triple Epidemic and the Kovan Trial. He responded as follows:

- i) That he was the Medical Officer in charge of the IDH, Kano, as at 1996 and presently is the State Coordinator for HIV/AIDS control
- ii) That he was aware of the clinical trial and of Prof. Idris Mohammed's protest.
- iii) That he was informed from the Kano State Ministry of Health that Pfizer was coming to render assistance and participate in the treatment of patients
- iv) That none of the NGOs tendered any written permission from the Ministry as evidence to participate in the control activity
- v) That Pfizer informed the IDH that they would use some drugs including new ones
- vi) That he was aware that Prof. Idris Mohammed demanded that clearance letters issued by NAFDAC, FMH and the Ethical Committee be produced within 2 days.
- vii) That Pfizer could not comply with the request.
- viii) That Prof. Idris therefore assigned one Dr. Ajayi-Obe to monitor and ensure compliance with his request.

- ix) That after a few days, the trial was suspended (**see Appendix XIV**) by Prof. I. Mohammed when Pfizer could not tender the necessary approvals
- x) That the Director-General of the Kano State Ministry of Health then, Dr. Sanda Mohammed visited the hospital and directed the resumption of the trial.
- xi) That he was more involved in logistics of patient care than with the clinical trial.
- xii) That Pfizer later brought a document, which Prof. Idris Mohammed found unacceptable.
- xiii) That at that stage Prof I. Mohammed demanded for samples of the drug and pro-drug which he then sent to NAFDAC for analysis
- xiv) That the Task Force with Prof. Idris Mohammed as the head was in charge of patient Management.
- xv) That he was directed to give the Pfizer team a separate ward for the trial.
- xvi) That the MSF was at a stage against the trial.
- xvii) That his hospital had no record of the Pfizer trial as they departed without leaving any documents behind
- xviii) That all records of patients treated by the Hospital should be in the register of the Out-Patient Department
- xix) That he could not remember if Pfizer admitted patients through the Hospital OPD or not
- xx) That the visiting Pfizer Doctors did perform lumbar punctures on patients but that he is unaware of other treatment procedures carried out by them
- xxi) That at a stage the Pfizer team was given 2 days to vacate the IDH by Prof. Idris Mohammed but could not remember the reason for this
- xxii) That about 200 patients passed through the Pfizer team
- xxiii) That the IDH treated about 300 patients/day during the epidemic
- xxiv) That he was not sure if informed consent was obtained by Pfizer before inclusion of any patient
- xxv) That he failed to keep track of Pfizer's activities during the period due to his heavy work schedule including supervision of burials of the dead.
- xxvi) That he did not know about the drug, Trovan, before the trial and Pfizer neither explained the benefits of the trial nor provide any literature on Rocephin and Trovan to him.
- xxvii) He told the Committee that the IDH did not use Rocephin as it was too expensive and the system could not afford it.
- xxviii) That the D-G Kano State MOH was aware of the trial and even gave approval that the trial should continue after Prof. Idris Mohammed had ordered that it be stopped.

- xxix) That the D-G did not consult Prof. Idris Mohammed on the issue before giving directives that the trial should continue.
- xxx) In retrospect, Dr. Suleiman Abdullahi believes the motive behind Pfizer contributions to control of the Epidemic was far from being humanitarian.
- xxxi) That Pfizer should have made their donations to the Kano State Ministry of Health before the trial, which they did not.
- xxxii) That Dr. Agwu Urondu of the Out-Patient Department was in- charge of the ward on arrival of the Task Force and some records could be obtained from the person in-charge of records at that time.
- xxxiii) That he had no report on the epidemic and no one had commended his efforts since the epidemic was controlled
- xxxiv) That he had a cordial relationship with Prof. Idris Mohammed during the outbreak and benefited a lot from his experience

### **3.6 INTERVIEWS HELD ON THURSDAY 25TH JANUARY 2001.**

These interviews were held in the Federal Ministry of Health, Abuja.

#### **3.6.1. DR. STELLA GOINGS – UNICEF DEPUTY REPRESENTATIVE/HEAD OF ABUJA BUREAU.**

The UNICEF Representative introduced herself as Dr. Stella Goings – Head of Abuja Bureau & Deputy Country Representative of UNICEF in Nigeria. During the 1996 epidemic she was the Chief of Health Section and took charge of the UNICEF response in Nigeria. In her presentation she informed the committee as follows:

- i) That she was pleased and privileged to have assisted Nigeria during the epidemic, and recounted the activities of UNICEF during the multiple disease outbreak.
- ii) That UNICEF utilized the expertise of field workers led by Drs. Arthur and Nuhu ( Dr. Nuhu is presently based in Bauchi)
- iii) That UNICEF provided hospital supplies such as oily chloramphenicol injection and CSM vaccines as well as medical equipment through the Federal Ministry of Health.
- iv) That the supplies were from UNICEF Procurement and Assembly Centre (UNIPAC), Copenhagen, Denmark
- v) That UNICEF also carried out information, education and communication through jingles and drama designed to increase awareness among the people on CSM during outbreaks, trained primary health care workers, provided antibiotics like co-trimoxazole

and basic hospital supplies, insecticides, bed nets as well as chloroquine for malaria-ravaged communities in the course of their activities.

- vi) That UNICEF was aware of the Federal Ministry of Health representatives in charge of combating the epidemic in the persons of Dr. A. Nasidi and Prof. Idris Mohammed and that they worked closely with them.
- vii) That the first report of the epidemic was in early November 1995 but calls for assistance were received in March 1996.
- viii) That she was aware that the epidemic was quite devastating and that the impact was felt in eight countries in the Sahel region.
- ix) That UNICEF was aware of the work done by the International Red Cross and MSF at that time but not of Pfizer's role.
- x) That they have checked their records carefully and that no mention was made of Pfizer's presence except in the last few weeks from the publications in the newspaper.
- xi) That UNICEF assistance provided included chlorination of the wells and training of local personnel.
- xii) That she operated from Lagos but was posted to Kano during the epidemic.
- xiii) That it is difficult to give an opinion on the trial since they had no knowledge of it except for what was in the press.
- xiv) She, however presented UNICEF's policies as under listed:
  - No vaccine should be tried except it has been proven safe and efficacious.
  - No individual should participate in a trial except he has been informed and has given voluntary consent to participate in it.
  - The highest standards of safety monitoring are strictly adhered to and a separate independent clinical safety monitoring is conducted.
  - The personnel must be trained, pre-clinical tests, phases 1 and 2 trials must be completed before the clinical trials.
  - Foreign companies should conduct no clinical trials in Nigeria except the drug has been previously tried, tested and approved by the country of origin.

The Chairman requested for the following documents from UNICEF: -

- 1) Convention on the rights of the Child
- 2) Basic Cooperation Agreement and
- 3) Additional information on organizations that participated in the epidemic control.

Dr. Goings promised to cooperate fully as she was of the opinion that the right of the child should never be violated.

**3.6.2. Mr. E. U. Usoro – Former Director of Inspectorate, NAFDAC.**

Mr. Usoro was ushered in at 1.34pm and was interviewed by the committee in his role on the issuance of a letter of clearance. Mr. E. U. Usoro served the FMH for 25 years. Positions he held included Head, Laboratory in FDAC (1988), Assistant Director (Inspectorate), Deputy Director and Director (Inspectorate) until his retirement in July, 1996. He signed the NAFDAC letter to Pfizer and he testified as follows:

- i) That he was unaware of the controversy involving the trial until the Director Food and Drug Services in the ministry informed him.
- ii) That the letter to Pfizer was actually written by him to Pfizer in 1996 on the Directive of the Director-General, FMH.
- iii) That his schedule borders on compliance with NAFDAC laws for importation, sale and manufacture of drugs.
- iv) That he however took the letter to his office and transcribed it on to NAFDAC's letter headed letter and signed.
- v) That he requested for supporting documents from Pfizer before releasing the letter.
- vi) That he asked the DG-NAFDAC's aides to confirm that the DG-NAFDAC had been in touch with Pfizer and that they did.
- vii) That Pfizer needed the letter to meet US FDA's regulations for exporting the drugs.
- viii) That he remembered one of the Pfizer representatives he met at the office of the D-G was Mr. Baale.
- ix) That the directive from the D-G FMOH to endorse the letter was verbal.
- x) That he did not revert to the DG-FMH after he had issued the letter.
- xi) That he believed it was in order for him to sign the letter as the DG-FMH was satisfied with the documents submitted by Pfizer.
- xii) That the draft letter was re-typed and signed on the same day.
- xiii) That he did not consult the Registration and Regulatory Directorate of NAFDAC before releasing the letter.
- xiv) That he understood the authorization was for importation and investigational purposes only.
- xv) That he was also not informed of an impending clinical trial in Kano.
- xvi) That from his experience at NAFDAC he believes that proposals should have been made and interested groups contacted by the

sponsors to make contributions before any clinical trial was embarked upon.

- xvii) That he became aware of the trial through the protest letter sent to the Minister by Prof I. Mohammed
- xviii) That the former D-G NAFDAC, after going through the letter written by him (Mr. Usoro) commented that it would not pass as an endorsement for the trial.
- xix) That no mention was made of humanitarian intentions of Pfizer in all documents submitted

### **3.6.3. DR. A. E. IKE – FORMER SPECIAL ASSISTANT TO FORMER MINISTER OF HEALTH.**

In 1996 Dr. Ike was a Special Assistant (SA HMH) to the then Minister and presently he is a Deputy Director in the Ministry. He testified as follows:

- i) That he was the author of the letter dated 28<sup>th</sup> March 1996 letter to Pfizer Inc inviting Dr. Robert Buhl who was to bring in drugs (see **Appendix XV**)
- ii) That he was instructed by the Minister to write the letter
- iii) That it was the then MD of Pfizer, Mazi Sam Ohuabunwa who actually made the first contact with the Minister about the intentions of Pfizer
- iv) That he did not seek for the opinion of the relevant department of the Ministry before dispatching the letter because the Honourable Minister could have directed whoever he wanted to take action
- v) That he was aware of the protest letter from Prof I. Mohammed and the Minister specifically spelt out the nature of response
- vi) That he dispatched Prof I Mohammed's letters to only KN MOH
- vii) That he also wrote to Prof. Idris to notify him that the matter was being looked into.
- viii) That he advised the Minister to involve the DG-FMH and Director - FDS in the matter.
- ix) That he did not contact NAFDAC when he observed that the drugs which were to be imported (Alatrofloxacin and Trovafloxacin) were unfamiliar to him
- x) That most decisions on the epidemic control were made at the Ministry's Top Management Committee (TMC) and Senior Management Committee (SMC) meetings
- xi) That he did not remember anytime drug trial was discussed at the TMC.
- xii) That the Task Force for the control of the epidemic was set-up by the TMC

- xiii) That the Minister did not seek his advice on the trial.
- xiv) That he was aware that the epidemic's severity resulted in the ban imposed by Saudi Arabia on Nigerian pilgrims.
- xv) That Pfizer made several visits to the Ministry but that he was not involved in some of the meetings.
- xvi) That he specifically mentioned Trovan in his letter because he was requested to include the name by Pfizer.
- xvii) That he had no prior knowledge of the intention of Pfizer to use the drug for clinical trial.

### **3.6.3. DR. SHEHU SULE - DIRECTOR Health Planning and Research (HPR), FMOH**

Dr. Sule is the Director, Health Planning. He told the Committee that as at 1996 he was already the Director, PRS in the Ministry and that he was aware of the outbreak. He informed the committee of his involvement as follows:

- i) that he got information on the outbreak of CSM unofficially
- ii) that information on the epidemic was hoarded due to the fears of its effects on hajj operations.
- iii) that it was one of the worst outbreaks in Nigeria occurring simultaneously in Kano, Katsina, Yobe, Borno and Katsina States.
- iv) that the government tried to establish the facts and sent out people to carry out surveillance.
- v) that reports received were alarming, as many people had already died one month before the event was first reported.
- vi) that lack of funds heavily affected the government's ability to intervene and
- vii) that Dr. Nasidi coordinated the process of combating the epidemic.
- viii) That at the TMC he intimated the Ministry that the University of Maiduguri Teaching Hospital (UMTH) being the center of excellence for infectious diseases should send experts and the CMD, Prof. Idris Mohammed be appointed to head the Task Force
- ix) That during the epidemic the MSF worked at the IDH, UMTH sent experts to assist with drugs, logistics and training whilst Pfizer team brought in a new drug the use of which Prof. Idris Mohammed objected.
- x) That he later learnt that Prof. Idris Mohammed had written the Honorable Minister and copied the SGF on the Pfizer drug trial
- xi) that all four centres of excellence in the country should be kept at peak performance for adequate control should emergency situations arise.

- xii) That members of the Task Force also included staff of the Epidemiological Unit of the Ministry.
- xiii) That the formation of the Task Force was discussed at the TMC and that records could be retrieved from his department
- xiv) That the Minister briefed the TMC on a trip to Saudi Arabia on CSM epidemic and Hajj.
- xv) That he was aware that Prof. Idris Mohammed had problems in getting refund for some of the commitments made in running the Task Force.
- xvi) That since becoming Director HPR, he is aware of only one request for Ethical clearance from the Lagos University Teaching Hospital and ensured that normal procedures were strictly complied with in the conduct of clinical trials, and that no other request for an ethical clearance for clinical trial had been received in his department.
- xvii) That an ethical committee is not an ad-hoc committee but ideally should be a standing/continuous entity and an integral part of the Ministry, forming a link with other local ethical committees.
- xviii) That he was aware that Prof. Idris Mohammed had alerted the Ministry in writing about the trial but was not sure if anyone in the Ministry was notified of the event.
- xix) That he was not aware of any investigation conducted by the Ministry following Prof. Idris Mohammed's protest.
- xx) That the Ministry should have set up a committee to investigate Prof. Idris Mohammed's protest.
- xxi) That Prof. Idris Mohammed should be refunded his money if proven beyond reasonable doubt that he actually incurred such expenses.
- xxii) That he was not aware if any report on the epidemic was submitted by Prof. Idris Mohammed.
- xxiii) That no document on Trovan was sent to him and neither did the Kano State Ministry of Health contact him on the trial in his capacity as the Chairman of the Ministry's Ethical Committee.
- xxiv) That he did not receive any request for the constitution of an ethical committee from Kano or any other institution.

### **3.6.5. PFIZER'S 2<sup>ND</sup> APPEARANCE.**

The Pfizer representatives submitted some of the documents that were earlier requested by the committee and answered a few questions. Mr. Tade, Head of the team, apologized for their inability to present all the documents required but promised to send them at a later date. Among the additional information provided by the Pfizer Representatives were:



- i) That the Principal Investigator did not get more than \$1,000:00 paid in naira (approximately N80,000.00).
- ii) That they were unable to present the ethical committee's clearance letter for the trial.
- iii) That their inability to obtain the other documents is attributed to the restructuring that had taken place within Pfizer.
- iv) That everyone on the investigation team and supportive staff were paid some remuneration after the trial.
- v) That they were not officially notified of Prof. Idris Mohammed's petition.
- vi) That Mazi Ohuabunwa, the then MD Pfizer, was back in the country and arrangements were being made to contact him.

The Committee, thereafter, requested for the following additional documents:-

- a) Submissions on previous trials on Trovan before 1996
- b) Evidence of previous use of the drug on adults/children for the management of CSM.

### **3.7. INTERVIEWS HELD ON FRIDAY 26<sup>TH</sup> JANUARY, 2001**

#### **3.7.1. Prof. Idris Mohammed – Chairman of the Federal Task Force for Control of The Epidemic.**

Prof. Idris Mohammed was ushered in at 11.54 am. He introduced himself as Prof. Idris Mohammed presently working at the University of Maiduguri Teaching Hospital where he was employed in 1984 and that he had been on sabbatical leave to U.K. He graduated from University of Ibadan with an MBBS, degree is a fellow of the Royal College of Physicians, Fellow of West African College of Physicians, and has a Diploma in Tropical Medicine and an MD in Immunology. He was the CMD UMTH, a position he occupied during the 1996 epidemic. He was also the Chairman of Task Force to combat the epidemic in March 1996. In his presentation to the committee he stated as follows:

- i) That he was appointed by the FMOH as the Chairman of the Task Force

- ii) That his letter of appointment did not contain his remuneration (see **Appendix XVI**)
- iii) That other members of the Task Force included the representatives of Kano State Ministry of Health, 3 other members from University of Maiduguri Teaching Hospital (Dr. T. O. Harry, Dr. S. A. Alkali and Dr. A. Garboti), a volunteer from Lagos, Dr. Ajayi-Obe while Dr. Nasidi maintained coordination between the Task Force and the Federal Ministry of Health.
- iv) That other agencies such as the MSF, International Red Cross, and the Kano State Ministry of Health were also represented
- v) That Murtala Mohammed Specialist Hospital, Kano did not send anybody to assist the Task Force despite requests made to that hospital.
- vi) That the 1996 epidemic is the largest in history according to experts, affecting over 109,000 people with over 11,000 deaths.
- vii) That It started in Kano, Katsina and Bauchi spreading to other States including Plateau, Osun and Rivers States, etc
- viii) That several problems such as logistics and cultural were encountered in combating the epidemic.
- ix) That the Task Force was able to combat the epidemic within a period of two months.
- x) that the Task Force was lodged at Daula Hotel initially by the FMOH but subsequently the Kano State Government pledged to take over
- xi) That he footed the bill of expenses incurred in the course of the epidemic control.
- xii) That according to announcement in the media, the epidemic must have started in February and that the Task Force became involved in March
- xiii) That the intervention exercise was concluded by the middle of May, 1996.
- xiv) That he supervised both the control and treatment efforts during the epidemic.
- xv) That the control was effected by vaccination, health education and trainings of the various staff involved.
- xvi) That the Task Force operated from the Infectious Diseases Hospital, Kano while treatment centres were established in every state affected.
- xvii) That he made provision for adequate manpower and liaised with the states concerned.
- xviii) That he also coordinated international control efforts
- xix) That the WHO, UNICEF and UNDP assisted in training personnel while the International Red Cross conducted vaccination only.

- xx) That the Task Force met daily at the Infectious Diseases Hospital, Kano and sometimes at the hotel.
- xxi) That on a certain day in the office of the Head of the Infectious Diseases Hospital and in the middle of a discussion, he met with certain individuals who were introduced as representatives of Pfizer West Africa.
- xxii) That their mission was to try a new drug for meningitis in the hospital.
- xxiii) That he then asked them for the clearance for the trial from relevant authorities
- xxiv) That they promised to present it on a later date
- xxv) That the Pfizer team told him they believed their new drug was better than existing antibiotics for the treatment of meningitis and that the drug had been used on humans in the past
- xxvi) That at the time of this meeting, the trial had already commenced
- xxvii) That he gave Pfizer two days to present the clearance letter or else he would terminate the trial
- xxviii) That some time after the expiration of the period of grace he terminated the trial via a letter to the Medical Officer-in-Charge (see **Appendix XIV**)
- xxix) That the trial was ordered to continue by the D-G of the Kano MOH, Dr. Sanda Mohammed
- xxx) That he met Dr Sanda Mohammed at the Infectious Diseases Hospital, Kano discussing with the Pfizer team and subsequently ordered the continuation of the trial
- xxxi) That he explained to Dr Sanda Mohammed why the trial could not continue
- xxxii) That he agreed with him, but still went ahead to authorize the continuation of the trial
- xxxiii) That at this point he made a verbal representation on the issue to the Minister
- xxxiv) that he appointed a member of the Task Force, Dr. Ajayi-Obe, a pediatrician, to monitor the trial
- xxxv) that he witnessed how one of the investigators (a foreign doctor in the Pfizer team) withdrew about 10cc cerebro-spinal fluid from an ill child who died an hour later.
- xxxvi) That he obtained samples of the drug from the Pfizer investigators and handed them over to the NAFDAC representative in Kano for analysis.
- xxxvii) that he wrote the Minister on 1st July 1996 and gave the details of what transpired during the trial and copied the DG-NAFDAC, the Presidents of the Pharmaceutical Society of Nigeria and the Nigerian Medical Association.

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- xxxviii) That the letter from NAFDAC did not convey approval for trial, but was only for importation.
  - xxxix) That he received a reply to his letter from the Federal Ministry of Health informing him that Ministry was looking into his report. (see Appendix XVII).
  - xl) That at a later date, another letter which made grievous insinuations against his person was received; but to this he reacted in his letter of 21<sup>st</sup> January, 1997 (see Appendix XVIII).
  - xli) That he lodged a complaint to the Honorable Minister about the non-funding of the Task Force Operations.
  - xl ii) That he was directed to source for funds from anywhere he could to control the epidemic, a response he regarded as strange.
  - xl iii) That he submitted his claims at the end of the epidemic, but was not refunded.
  - xl iv) That he made his submissions on this to the then Secretary to Government of the Federation (SGF) who promised to look into it
  - xl v) That he sent another letter to the SGF in which he intimated him of his intentions to take legal action to clear his name and recover his expenses
  - xl vi) That only the then Military Administrator of Kano State recognized his contributions to the epidemic control and in fact promised to give him a plot of land.
  - xl vii) That the Military Administrator released a vehicle for use of the Task Force and some financial contributions to fuel the vehicle
  - xl viii) That he subsequently noticed a sudden change of attitude from the Military Administrator and that he was later informed that the State Government was of the impression that he had kept some materials and money, supposedly donated to the government by WHO, MSF and UNICEF.
  - xix) That this allegation was confirmed when the Kano State Ministry of Health wrote a letter to him asking him to transfer such materials to them (see Appendix XIX)
  - xx) That in his reply to that letter, he confirmed having received certain items from the MSF meant for the National Program on

Immunization that was then about to be launched by the then First Lady

- xxi) That he was of the opinion that the trial possibly had the support of the Federal Ministry of Health and the Kano State Ministry of Health.
- xxii) That Pfizer representatives he met included Oluabunwa and Dr. Dogunro.
- xliv) That he could remember seeing a copy of the protocol before the commencement of the trial
- i) That the MSF and the International Red Cross threatened to withdraw from Nigeria if the trial continued.
- ii) That he also could not remember if he discussed the trial with Commissioner for Health, but that he will check from his diary
- iii) That Mr. Tunfafi, a PhD Student from the UMTH could have collected some samples from the Pfizer team for his work
- liii) That he never received any response to his letters from NAFDAC
- liv) That Pfizer handled only the patients recruited for the trial, and not those in the general ward
- lv) that all donations were made by the various agencies through the Task Force, except that made by Pfizer
- lvi) That he believed that the true Principal Investigator was Dr. Scott Hopkins and not Dr Dutse
- lvii) That he was not communicated on the letter from the Hon Minister to the Commissioner for Health, Kano concerning his report
- lviii) That he believed that Pfizer's involvement was not humanitarian, but primarily to test its new drug
- lix) That his opinion was confirmed by the immediate departure of the Pfizer on completion of the trial with no plans for the continued management of patients they left behind in the wards they conducted the trial
- ix) That his only mistake was to have allowed the trial to take off at all without documentary evidence of authorization.

- ixi) That in the future, the laws of the country should be strictly adhered to, to avoid such serious violation of our rights
- ixii) That he actually borrowed to run the epidemic control activity and is still expecting the refund of his expenses by the Federal ministry of Health

He submitted the following documents:-

- (a) Letter to the then Military Administrator (see Appendix XX)
- (b) Interim Report on the Epidemic and (see Appendix XXI)
- (c) Foreign Newspaper clippings on the trial (see Appendix XXII)
- (d) A more detailed account clarifying his role during the trial (see Appendix XXIII)

### 3.7.2. 3RD PFIZER APPEARANCE.

The Pfizer made the following additional representations:

- i) That Dr. Dutse was first contacted in March 1996 to be informed that he would be the Principal Investigator.
- ii) That Dr. Dutse was given the protocol in March, 1996.
- iii) That patients were recruited from 1<sup>st</sup> or 2<sup>nd</sup> April 1996 following their arrival in Kano 30<sup>th</sup>/31<sup>st</sup> March, 1996.
- iv) That Dr. Dogunro met Dr. Dutse, alone, on 1<sup>st</sup> April to take care of logistic while the team arrived after the recruitment of patients had begun.
- v) That they had a meeting with Prof. Idris Mohammed in the presence of the Principal Investigator, during which they gave him their proposal and showed him the site of investigation.
- vi) That Prof. Idris was given the protocol and investigator's brochure, and that he questioned their use of Rocephin as standard instead of oily chloramphenicol and wondered why the investigation was not done in other states.
- vii) That Mr. Tunfafi, Stella Egwuogu and some members of the Task Force were asked to work with them by Prof. Idris Mohammed.
- viii) That they met with the DG, Kano State Ministry of Health and that he was informed about Pfizer's intention to conduct the trial.
- ix) That they met with him again after Prof. Idris Mohammed requested that the trial should be stopped.
- x) That the DG while giving the go-ahead for the trial to continue, told them that the hospital belonged to the Kano State Ministry of Health and not to the Task Force.

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- xi) That the DG further said that Prof. Idris Mohammed take a unilateral decision on what happened and
  - xii) That the DG also told them that as far as he as a medical doctor he did not see anything that Pfizer
  - xiii) That in another development Prof. Idris Mohammed he had been accused of collecting N1m bribe
  - xiv) That Prof Idris requested for remuneration instead of honorarium that is usually in cash.
  - xv) That Dr Dogunro was at the Infectious Disease Centre the first 3 days of the trial and subsequently at the
  - xvi) In all, he (Dr Dogunro) made 14 appearances during which he met Prof. Idris Mohammed at the
  - xvii) That Stella Egwuogu was a member of the team with Prof. Idris Mohammed.
  - xviii) That they believed the trial was conducted in good practice.
  - xix) That prior to this, Pfizer had never done clinical trial was not registered in Nigeria or elsewhere.
  - xx) That they possess sound knowledge of the process of registering a new drug.
  - xxi) That all necessary procedures in carrying out the trial adhered to.
  - xxii) That the only loophole was the non-involvement of the Committee, which as at then, was not in place.
  - xxiii) That Prof. Idris Mohammed did not only conduct but also endorsed it.
  - xxiv) That they discussed the site with Prof. Osiagwu but without specifics.
  - xxv) That he admitted Pfizer did give Mr. Usoro a letter written and endorsed by him for the US FDA.
  - xxvi) That the certificates of analysis of the drug should be at the port of entry and should be with NAFDAC.
  - xxvii) That they never met Mr. Usoro.
  - xxviii) That they stopped recruiting patients on the trial without the approval of the Kano State Ministry of Health recruiting patients if they so desired.
  - xxix) That they assumed NAFDAC's letter for importation was also an authority to conduct the trial.
  - xxx) That they could not remember any contact with the Ministry of Health.
  - xxxi) That they held discussions with the DG of the Ministry of Health several times in his office on the same

Concluding, the leader of the Pfizer team (Mr. Tade) expressed fears that Pfizer's discomfort with the appointment of Dr. A Nasidi as Chairman of the committee, because of his known opposition to the trial. He also expressed the fear that the Washington Post might get a copy of the report even before its submission and requested that Pfizer also receive a copy of the report. In response, the committee assured Pfizer that the members of the committee including its Chairman, Dr. Nasidi, are all people of integrity and that all issues discussed will be held in the strictest confidence. It was also emphasized that the report will be that of the committee and not its Chairman, and that the report will be submitted only to the Honourable Minister at whose discretion it will be circulated.

The Committee was quite impressed with the openness of the Pfizer team and further assured them that Dr Nasidi had not shown any bias to any of the parties interviewed.

**3.7.3. Mazi S. I. Oluabunwa – CEO Neimeth International Pharmaceutical Company and Former Chairman/CEO Pfizer Nigeria Plc.**

Mazi S. I. Oluabunwa is the MD/CEO - Neimeth International Pharmaceutical Company. He worked for Pfizer between 1978 and 1997. He was CEO from 1993. He left in 1997. He is also a pharmacist. In his presentation to the committee, Mr. Oluabunwa stated as follows:

- i) that he was bitter with the publications on the clinical trial.
- ii) that he was aware of the epidemic in Kano in 1996.
- iii) that the Kano State government was seeking assistance because of the enormity of the problem during that period.
- iv) that he shared the problem with his colleagues who were interested in the case bearing in mind that Pfizer had been involved in various assistance projects for other countries suffering from natural disasters.
- v) that he later discussed it with Pfizer International who agreed to come down and help with a new drug that had passed through phases 1 & 2 in the USA.
- vi) that Pfizer planned to try the drug in the course of the assistance rendered.
- vii) that he was the one who got in touch with the Federal Ministry of Health and intimated it with the planned assistance and trial of Trovan by his company.
- viii) that they were referred to NAFDAC.



- ix) That NAFDAC agreed that the product should be imported for investigational purposes only.
- x) That after initiating all contacts including meeting with officials of the Kano State Ministry of Health, a cargo load of plane was mobilized for delivering the drugs/equipment directly to Kano.
- xi) That the FMOH assisted his company with the exemption of the drug at Kano.
- xii) That his company got an investigator in Kano, who in turn got others to help in the trial
- xiii) That Dr. Dogunro, Medical Director Pfizer, was in charge.
- xiv) That he was at Kano at the beginning of the trial and was told of the problems with the Task Force Chairman, Prof. Idris Mohammed
- xv) That he met Prof. Idris Mohammed personally and told him it was a humanitarian gesture.
- xvi) That he also met with the Commissioner for Health as well as the Deputy Governor to discuss the matter.
- xvii) That he talked with Prof. Idris Mohammed and tried to assure him that the trial will be conducted in an ethical manner.
- xviii) That he learnt some days later that Prof. Idris Mohammed had raised a lot of questions on the trial and asked that it should be stopped.
- xix) That he was also informed that Prof. Idris Mohammed was not happy with how things were done and that he was not properly compensated.
- xx) That he remembered that the Pfizer team returned in May to work with Dr. Dutse on follow-up studies
- xxi) That they donated drugs to the government during the triple epidemic
- xxii) That he was of the opinion that the trial saved lives and that Pfizer had done something worthy of commendation as there was no commercial benefit attached to it.
- xxiii) That he was sad that a good intention is now disparaged of, judging by the fact that about 10,000 people had previously gone through this trial elsewhere
- xxiv) That although he met the Commissioner for Health, Kano after the trial had started, he has little or no doubt that the then Commissioner was aware of the trial and that everyone contacted in Kano had knowledge of the trial.
- xxv) That the trial was definitely part of the reason for Pfizer's presence in Kano during the epidemic period
- xxvi) That the reason for Pfizer leaving Kano suddenly was because "there was this apparent hostility" developing from other quarters (He

- believes it was due to Prof. Idris Mohammed's interference and others)
- xxvii) That the trial was open and real and there was no "hidden agenda" as being insinuated
  - xxviii) When asked why there was no mention of the trial in their letter of 1st April 1996, he replied that he believes it was subsumed as part of the activity helping to relieve the problem, adding further that over 10,000 people had previously passed through the trial.
  - xxix) When asked why the Pfizer's donation was made about 1½ weeks into their presence in Kano and after they had actually commenced the trial, he responded by stating that this could have been due to the way things were sequenced, adding that the primary need was to save patients lives and donate after.
  - xxx) That he was told by his team that the success rates of the treatment procedures by others were lower than Pfizer's and could have resulted in jealousy by others
  - xxxi) When asked why anyone should be jealous since no other pharmaceutical company was present He replied that he did not know.
  - xxxii) That the Honorable Minister's involvement bordered strictly on Pfizer's letter to the Federal Ministry of Health requesting their assistance in having their goods cleared at the port of entry.
  - xxxiii) That the goods arrived the country on 28<sup>th</sup>/29<sup>th</sup> March 1996 same date the letter of invitation to Mr. Buhl was written
  - xxxiv) That all processes involved were strictly adhered to by Pfizer
  - xxxv) That in the history of trials done by Pfizer much of the remaining activities depended on the principal Investigator.
  - xxxvi) That he was of the view that there should have been a waiver for the trial to be conducted as the intent was to save lives
  - xxxvii) That this was the first such a trial (phase III) conducted in Nigeria
  - xxxviii) that all communications with the Federal Ministry of Health were made through the office of the Honourable Minister but that he could have discussed the issue with the Permanent Secretary, Federal Ministry of Health
  - xxxix) That Pfizer International group left Kano a few days after the trial when they had time to discuss with Dr. Dutse, Principal Investigator
  - xl) That much of his responses are based on the information received from representatives of his company who were frequenting Kano to monitor the progress of the trial
  - xli) That he had a meeting with the DG-NAFDAC in his office to discuss the issue but not with the then Director (FDS)

At the end of his testimony, Mazi Ohabunwa submitted some documents to the committee (see Appendix VI)

**3.7.4. 3RD APPEARANCE OF DR. ISA DUTSE –THE PRINCIPAL INVESTIGATOR:**

He stated further as follows:

- i) Treatment forms for each patient were with Pfizer and that he was not sure whether there were addresses on them stressing that probably only initials were used.
- ii) That he was told by Pfizer that they had informed Kano State Ministry of Health and had obtained approval from them for the trial
- iii) That they had excellent cooperation from Kano State Ministry of Health officials, which further reinforced his belief that they obtained the approval.
- iv) That the Commissioner and the DG came around the ward while the trial was in progress
- v) That he believed the DG Kano State Ministry of Health had knowledge of the trial as he had visited the IDH a couple of times and spoken with him on the issue
- vi) That he could not remember who authorized that the trial should continue and only got to know from Prof. Idris Mohammed's letter that he had stopped the trial.
- vii) That he did not participate in the development of the protocol but was handed a ready protocol by Dr Hopkins
- viii) That the trial started on 3<sup>rd</sup> April, 1996
- ix) That Prof. Idris Mohammed had been given the protocol and was also at a meeting in which he gave the go ahead to continue with the trial.
- x) That Pfizer officials had actually visited Kano early March 1996 with the Investigator's brochure which was released to him for his perusal
- xi) That the team returned to Kano 1-2 days before the trial commenced
- xii) That Dr. Ajayi-Obe came in after the trial had begun
- xiii) That she, in a way, participated in the investigational activities but was not very involved
- xiv) That he first met Dr. Hopkins at Tahir Guest Palace, Kano, after which they discussed the most suitable site for the investigation
- xv) That the last patient was recruited on the 14<sup>th</sup> April 1996 and discharged 5 days later
- xvi) That the last patients were managed by them
- xvii) that Dr. Hopkins left 3 days after the trial had begun while Debra and Dunne stayed on until shortly after the 14<sup>th</sup> April 1996

- xviii) That the MSF managed most of the patients at the IDH
- xix) That he was not actually involved in the control of the epidemic at the Infectious Diseases Hospital, Kano although he saw a lot of patients at the Murtala Mohammed Hospital.
- xx) That he participated strictly as a doctor but that he did not keep records of the investigation.
- xxi) That the publication on Trovan (see Appendix XXIV) was sent to him for the first time when the committee showed him during the interview
- xxii) That he was shocked that Pfizer could publish such a data without showing him or intimating him with the details
- xxiii) That he was actually paid ₦100, 000.00 at the end of the trial.

In general, he again expressed his regrets in issuing the ethical committee clearance, after the trial, stressing that it was a mistake and that he had learnt his lessons from this mistake.

### **3.7.5 Highlights Of Findings Of the Kano State Ministry of Health Investigation Committee.**

The Chairman, thereafter, requested Dr. Mohammed Sani Ado – Kano State Representative to brief the Committee on the finding of the Kano State Ministry of Health Investigation Committee. In responding, Dr. Ado said that the Kano State Ministry of Health officials interviewed could not acknowledge any knowledge of the trial. They also found out that the Federal Ministry of Health formed a Task Force headed by Prof. Idris Mohammed on learning of the epidemic and that the Kano State Ministry of Health was not happy that they were not notified when the Task Force was constituted. They also learnt that most of the intervention activities were under his control and that people came from elsewhere to assist in the intervention. In all, there were vehement denials of knowledge of any clinical trial by the Commissioner for Health and Permanent Secretary. The Permanent Secretary claimed he learnt of the trial through Prof. Idris Mohammed's letter and that the Commissioner threatened to go to court.

He said it was difficult to get the best out of Dr. Suleiman Abdullahi who incidentally was on the committee and did not sign the report as he felt it was not fair that he should be on the committee bearing in mind his precarious position in the controversy.

He also acknowledged that the government of Kano State was aware of the trial and that it gave the permission for it to continue but could not remember

who gave the instruction. He also revealed that oral instruction to continue the trial came from Dr. Sanda Mohammed.

Dr. Ado was then told that Dr. Suleiman Abdullahi had confessed that the Kano State Ministry of Health knew of the trial and that he gave a copy of Prof. Idris Mohammed 's letter to the Committee. He responded that there seemed to be some gap in communication. A member was of the view that the Federal Ministry of Health should be questioned for setting-up a Task Force without naming members, giving terms of reference as well as funding its activities.

The Chairman explained that, after setting-up the Task Force, it was concluded that the TA or SA of the Minister should communicate with its head. He added that the urgency of the situation was no excuse for the Ministry's inability to fine-tune its terms of reference. He added that the Task Force's terms of reference were mentioned generally in the letter and that the magnitude of the epidemic covering 19 States was probably responsible for the shoddy preparation. Another member stressed that the Federal Ministry of Health cannot absolve itself from blame and that it lacked the political will to tackle the pressing situation.

At this point, the Chairman explained the way the Task Force was constituted; the letter forming the Task Force was copied to all State Ministries of Health and relevant agencies, he further explained that the budget had been prepared prior to the setting up of the Task Force and as such no budgetary provisions were made for its activities. He presented the letter. He added that information on the epidemic was received through Agencie Francaise Press (AFP) following which he traveled to Kano for on the spot assessment of the situation.

His experience at Kano showed that the DG – Kano State Ministry of Health did not seem to be aware of the enormity of the problem. He later informed the Honourable Minister about the outbreak, as the Minister was not aware also. He narrated that, he worked closely with MSF representatives and tried to establish the case index and found 3 different epidemics occurring at once – meningitis, cholera and measles. He was then asked why the report of the epidemic was not tendered to the Committee. He responded that he relied on data received from various States, which did not come in at the same time. He was told that the report could contain mention of the trial but he said that Prof. Idris Mohammed did not submit the report to him as he, Prof. Idris Mohammed, worked with the Minister directly. He, however, worked on a joint report with him.

Generally, the current Committee perceived a lack of empowerment of Prof. Idris Mohammed's Task Force by the Federal Ministry of Health. Dr. Ado also told the Committee that Dr. Kura had left the service of the government and may not be available for interview. The committee insisted that he must present himself.

### 3.8. INTERVIEWS HELD ON 31/01/2001.

The meeting commenced at 2.03 pm. Mr. R. K. Omotayo - DFDS presided over the meeting in the absence of the chairman, Dr. A. Nasidi who was away to Benin on a national assignment in respect of the kerosene explosions in Edo State.

#### 3.8.1 2<sup>nd</sup> Appearance of Dr. Sanda Mohammed - Former DG Kano State Ministry of Health.

In his response questions he stated as follows:

- i) That there never was any meeting on the trial with Pfizer in his office.
- ii) That his meeting with Pfizer was by chance at the IDH, Kano
- iii) That a meeting was holding during his visit to the IDH, Kano and upon enquiring if there was any problem, the group replied there was none.
- iv) That he was not sure if he met Prof. Idris Mohammed at that meeting
- v) That he did not know that the trial was going on at the IDH
- vi) When told that the Pfizer spokesmen testified that they had had a meeting with him, he responded that there was no formal meeting
- vii) That it was when he was assured that there was no problem that he gave the go ahead to all involved go on with his job.
- viii) When Pfizer's letter to the Kano State Ministry of Health on their donations in which the trial of a new drug was mentioned was read to him, he responded that the letter came in a mail and was minuted to his office to be signed, adding that he did not go through the letter thoroughly as the schedule of his office was quite demanding.
- ix) When asked as to why he was not involved in the process of approval for Pfizer's participation in the treatment of patients in

hospitals in the state, he responded that as at then his powers were limited as such, he could not approve or disapprove anything.

- x) When asked which role the Kano State Ministry of Health play in the control of the epidemic he responded that the Kano State Ministry of Health did all within its powers in providing personnel, equipment and accommodation.
- xi) That he personally hosted one of the teams that came to assist in his LGA in his family house.
- xii) that at the end of the activities, the Kano State Ministry of Health had a party for the team from Niger Republic and presented them gifts in appreciation of their efforts.
- xiii) that in fact, an alarm was raised only when the Kano State Ministry of Health could not cope with the outbreak.
- xiv) that he left the Kano State Ministry of Health as Permanent Secretary, a few months ago as such he is not in a position to access documents-
- xv) that he was aware of the Federal Ministry of Health's letter to the Kano State Ministry of Health forwarding Prof I. Mohammed's report for their comments.
- xvi) that he was aware that a three man committee instituted to investigate the drug trial comprised of Dr Mukhtar A. Kura, Director Medical & Health Services, Dr. Aliyu Muktar, Director Pharmaceutical Services, Dr. Abdulmumini Usman -Consultant Epidemiologist.
- xvii) that he agreed with the conclusions of the Committee.
- xviii) that it was an act of contempt on the Kano State Government that the Epidemic Control Task Force did not bother to provide a daily briefing on its activities to the Kano State Ministry of Health.
- xix) that the suspension of the trial 8 days after it had begun was rather belated and that it should have been stopped right from the start.
- xx) that Dr. Suleiman Abdullahi the Principal Medical Officer in-charge of the Infectious Diseases Hospital, Kano, did not inform the Kano State Ministry of Health of the trial.



- xxi) that the Kano State Hospital Management Board had a supervisory role over all hospitals.
- xxii) that since Prof. Idris Mohammed had access to the late Military Administrator of the state, he should have told him of what was going on at the Infectious Diseases Hospital, Kano.
- xxiii) that it was possible Prof. Idris Mohammed visited other states during the 8-day interval prior to his stopping the trial, as the epidemic was wide spread through many states.
- xxiv) That he was worried that the Committee's report may be biased because one of its members was a party to the events that took place during the 1996 epidemic in Kano and that such a person could prejudice the final report.

The Ag. Chairman however assured him that members of the Committee are men and women of high integrity and cannot be influenced by anyone to give a biased report. In response, he stressed that he would appreciate that the Committee takes note of his observation for the purpose of objectivity.

### **3.8.2 4<sup>th</sup> Appearance of Dr. Isa Dutse – Pfizer's Principal Investigator.**

Upon his request to be granted audience before the Committee, he was ushered in and testified as follows:

- i) that he intended to clarify further that Pfizer Central Research paid him as the Principal Investigator the sum of \$20,000:00 (Twenty Thousand US Dollars) which was given to him at the Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) conference.
- ii) That the money was given to him by Dr. Scot Hopkins (the actual amount paid into his domiciliary with the U.B.A was \$19,000:00)
- iii) That he was made to understand that this payment was according to the policy of Pfizer Inc.
- iv) That he had previously worked as an Assistant Investigator on a CSM study for Pfizer in 1986 with Dr. Fakunle as Principal Investigator.
- v) That his only recruits on the 1996 Trovan trial were 2 house officers namely Dr. Hussein Haruna and Dr. Shehu Yussuf.
- vi) That following the trial, the US FDA sent him a paper indicating some discrepancies in some of the test results.



- vii) That he saw the letter stopping the trial only after it had been completed but was told about it by Dr. Suleiman Abdullahi
- viii) That he could not recall any meeting with the Professor Idris Mohammed afterwards
- ix) that on hindsight, he was of the view that the informed consent should have been documented and that thumbprints plus signatures of the witnesses (nurses) should have been obtained.
- x) He also said he did not sign any contract agreement with Pfizer.

### **3.9 Interview held on the 1st February 2001:**

#### **3.9.1 Major Aliyu Mohammed (Rtd) – Deputy Director, NAFDAC Inspectorate, Kano.**

Major Mohammed is a pharmacist and presently a Deputy Director, Inspectorate, NAFDAC – North West Zone, Kano. He presented the following to the committee:

- i) that he was in Kano in 1996 during the epidemic as NAFDAC representative.
- ii) that he was not aware of the drugs brought in by Pfizer but that he did not clear the drugs.
- iii) that he got to know about the drugs through Prof. Idris Mohammed's letter.
- iv) That Prof. Idris Mohammed also came to confirm the status of a particular letter purportedly giving Pfizer authority to conduct a clinical trial.
- v) That he had told Prof. Idris Mohammed then that the letter was not an authority to conduct a clinical trial but to import the drugs.
- vi) That before then, he was not aware that a trial was being conducted
- vii) that NAFDAC did not participate in the clearance of the drugs possibly because when the drugs arrived NAFDAC office at the Airport was closed or that alternatively, the drugs could have been received at the baggage hall to which NAFDAC personnel have no access.
- viii) that there was no record of NAFDAC clearance of Trovan in their Kano office.
- ix) That when a consignment arrives in their absence, it is normally moved to the warehouse and on resumption of duty an officer normally goes round to check such consignment.

- x) That it was the responsibility of the airport officers (non-NAFDAC staff) to keep the drugs which could then be "cleared" before their arrival.
- xi) That he had never seen a copy of Prof. Idris Mohammed's protest letter,
- xii) That notification of information of a drug depends on importer, some inform and arrange for clearance, others do not
- xiii) That either the customs or security agents could have cleared the consignment or airline staff may have taken it to the office of an agent and then taken it out before it is seen by NAFDAC staff.
- xiv) That NAFDAC personnel are not on duty on Saturdays and since the goods arrived on Sunday this also could explain why NAFDAC was not involved in the clearance
- xv) That following his explanation to Prof Idris Mohammed that the NAFDAC document was for importation, (he Prof Idris) returned with 2 vials of injection samples for analysis
- xvi) That he also informed Prof. Idris Mohammed that 2 vials of samples were insufficient for analysis
- xvii) That during the epidemic he was aware Prof. Idris Mohammed made trips outside Kano
- xviii) That he was aware that the Pfizer investigators left Kano unceremoniously, immediately after the investigation
- xix) That he had not seen Prof. Idris Mohammed's protest letter
- xx) That he was unaware of Kano State Ministry of Health's investigation on the issue.
- xxi) That no investigation committee invited him on this issue until now

### **3.9.2 Interview of Dr. A. Nasidi Director, Special Project, Federal Ministry of Health by the Committee on the 23rd February 2001.**

The committee interviewed Dr. Abdulsalami Nasidi who was actively involved in the epidemic control efforts. The interview was presided over by Dr. P. H. Amodu.

He is a medical doctor and a public health officer in the employment of the Federal Ministry of Health. He also specializes in Virology. He is currently the Director in charge of Special Projects in the Ministry. In 1996 he was a Deputy Director/Chief Consultant Epidemiologist and he therefore had responsibility for epidemic control. He provided the committee with the following information:

- i) That the extent of the outbreak of meningitis was not initially known.
- ii) That his division mobilized teams to go out and assess the situation in nine affected states in early January 1996.
- iii) That he found that there was in Kano a triple epidemic of cholera, measles and meningitis of greater magnitude than they expected in Kano.
- iv) That members of the other teams returned with equally alarming reports.
- v) That on presentation of his report, the Top Management Committee of the ministry decided to set up a Task Force to tackle the epidemic with Prof. Idris Mohammed as Chairman.
- vi) that his role was to coordinate and facilitate the work of the Task Force and control of the epidemics.
- vii) That this included sourcing for funds to purchase medical supplies for the control of the epidemic and liaising with international agencies such as WHO, UNICEF etc. (see Appendix xxxix)
- viii) That the Task Force Chairman was expected to pass all his requests through his (Nasidi's) office to the Minister of Health.
- ix) That before the formation of the Task Force the sum of ₦6m was provided for his division's team in two installments.
- x) That the amount was released by two installments of N3 million each.
- xi) That although a budget of ₦23m was later made and approved for the Task Force by the Ministry, no funds were released to it till the end of the epidemic (See Appendix XXV).
- xii) That neither himself nor Prof. Idris Mohammed was refunded their expenses for the control of the epidemic.
- xiii) That at the end of the epidemic he was owing ₦5,517,075.50.
- xiv) That instead, the SSS was made to arrest and interrogate him.
- xv) That the TMC of the ministry, during the 1996 epidemic, approved standard operating procedures and guidelines for the control of epidemics. (see Appendix XXVI).
- xvi) That the federal government must intervene whenever a disease has the potential to spread from one state to another or to neighboring sovereign states.
- xvii) That during the epidemic the WHO funded training of Health workers on case management and adherence to WHO standard operating procedures for the treatment of meningitis; this resulted in a drop in the case fatality rate by more than 50% (see Appendix XXVII for WHO's contribution).
- xviii) That although he had to shuttle through all the states in which the epidemic raged he came back to Kano from time to time.

- xix) That on one of his visits to Kano, Prof. Idris Mohammed informed him that rather than assist with the control of the epidemic Pfizer was actually conducting a clinical trial with their new antibiotic product Trovan.
- xx) That Prof. Idris Mohammed was worried that Pfizer was trying their new drug on critically ill children.
- xxi) That himself and Prof Mohammed both saw a young American female doctor struggling to collect cerebrospinal fluid from a child.
- xxii) That when confronted she referred him to her boss.
- xxiii) That later in the evening, Dr. Hopkins and other members of the Pfizer team came to his hotel and met him in the presence of Prof. Idris Mohammed.
- xxiv) That he told them what they were doing was wrong since there was already a drug that was effective and that they did not obtain the necessary permission.
- xxv) That he asked them what would happen if their drug failed.
- xxvi) That for two hours he tried to dissuade Dr. Isa Dutse (who then was convinced and elated at the potentials of oral Trovafloxacin) and pointed out the danger of using an unproven oral therapy in the treatment of critically ill children.
- xxvii) That much later Dr. Dutse expressed to him his regrets for participating in the trial.
- xxviii) That both Prof. Idris Mohammed and he, Dr A. Nasidi telephoned the then Minister to notify him about the Pfizer drug trial.
- xxix) That the minister informed him that he was aware of the trial and he would furnish him with more details later, which he never did.
- xxx) That he advised the minister to listen carefully to what Prof. Idris Mohammed had to say.
- xxxi) That when it was apparent that the Minister was not going to help him and Prof. Idris Mohammed to stop the trial, they both informed the then National Security Adviser— Alhaji Ismaila Gwarzo with a view to attracting the attention of the former Head of Government.
- xxxii) That in response to Prof. Idris Mohammed's letter of 1st July 1996 which was minuted to him (see Appendix XXVIII), he recommended that a thorough investigation of the drug trial should be conducted.
- xxxiii) That he had no further knowledge of the matter after that recommendation.
- xxxiv) That there was no independent investigation of Prof. Idris Mohammed's report of the drug trial at that time.
- xxxv) that the drug trial was rather unfortunate and that the government of Nigeria must put in place measures that would protect our populace from such external invasion and abuse.

- xxxvi) That our governments must duly recognize and utilize indigenous technical expertise and advice
- xxxvii) That those who are appointed as ministers and to other high public offices must always be mindful that their primary responsibility is to the populace they were appointed to serve.
- xxxviii) That since the commencement of the work of this committee he had received threats to his life.
- xxxix) That in spite of his several protestations to the minister and request to be relieved of his appointment as chairman of the committee because of his prior knowledge of the problem, the then minister still stuck to his earlier directive saying that he needed someone who knew about the event to get him the facts.

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**CHAPTER 4****THE COMMITTEE'S VIEWS ON THE MAJOR ACTORS****4.1 PFIZER:**

- a. The company applied to and obtained approval from NAFDAC to import the drug Trovan into Nigeria for investigational purposes.
- b. The company conducted the clinical trial on the premise that NAFDAC's approval authorizing importation of Trovan for investigational purposes was sufficient authority to do so.
- c. The drug trial was conducted without the oversight of an ethical review committee.
- d. The company did not follow necessary procedures for the conduct of a clinical trial. There was no formal application in the prescribed manner to NAFDAC for the conduct of a clinical trial in Kano in 1996.
- e. No report of the clinical trial was submitted to any Nigerian authority until the commencement of this investigation.
- e. The company was allowed to use the Infectious Diseases Hospital, Kano on the basis of their offer of a compassionate program of intervention in the control of the epidemic.
- g. Although Pfizer claimed to have informed the Kano State Ministry of Health about the clinical trial, the company's letters to the Kano State Ministry of Health did not at any point in time state that there was going to be a clinical trial, even though the drug Trovan was mentioned.

**Conduct of The Drug Trial.**

Although, Pfizer claimed to have adhered to good clinical practices, when examined on the basis of protocol, informed consent, ethical clearance, treatment regimen and inclusion & exclusion criteria it was observed that:

- a. There was no record that they had informed consent.
- b. There was no ethical approval for the conduct of the trial.
- c. There was no adequate patient record in the trial. (see **Appendix XXIX** for their claims)
- d. There was no adequate follow-up activity.

- e There was no record on drug reconciliation i.e. how much was brought in and utilised.
- f. The way Pfizer came in and left showed that their presence in Kano was just for the trial as they left when the epidemic was still raging.

#### 4.2 Dr. Isa Dutse –Principal Investigator for the trial.

- a. He was the principal investigator for the trial only by name. He was neither in charge of the technical aspect of the trial nor was he administratively in control. Dr. Scott Hopkins of Pfizer Central Research was the de-facto principal investigator while he (Dutse) was used as a good physician to facilitate their work.
- b. Dr. Dutse neither contributed to the development of the protocol nor was he given sufficient time to study the protocol before the commencement of the trial.
- c. As principal investigator he had no record either of the patients recruited or the outcome of the investigations. The Pfizer team took away to the USA all documents pertaining to the trial - this further confirms our earlier observation that Dr. Dutse was the principal investigator only by name.
- d. Very much to his regret, Dr. Dutse admitted to have single-handedly issued an ethical clearance certificate to Pfizer at a time an ethical committee was not in existence at the Aminu Kano Teaching Hospital; this he did in response to a request from Pfizer a few months after the trial
- e. The possibility of a breakthrough that would have resulted from the successful use of oral Trovafloxacin as compared to other routes especially during an epidemic probably influenced his sense of judgement. This is apart from other benefits associated with conducting the trial.

#### **4.3. NAFDAC:**

##### **Key Players: –**

<b>Mr. E. U. Usoro</b>	<b>– former Director, Inspectorate,</b>
<b>Prof. G. E. Osuide</b>	<b>– former D-G</b>
<b>Major Aliyu Mohammed Rtd.</b>	<b>- DD Kano office</b>

#### **4.3.1. Mr. E. U. Usoro – Former Director of NAFDAC Inspectorate.**

- a. As the acting Director-General he admitted writing the letter addressed to US FDA (and copied to Pfizer) authorising the importation of Trovan into Nigeria for investigational use.
- b. He stressed that his letter was not authorization to conduct clinical trial, but a clearance to import the drug for investigational use only

#### **4.3.2. Prof. G. E. Osuide – Former Director-General of NAFDAC.**

- a. Prof. G. Osuide the then Director-General NAFDAC admitted he was out of the country at the time the letter was written and that Mr. E. U. Usoro acted for him.
- b. He confirmed the letter written by Mr. Usoro did not constitute approval for the trial of the drug in Nigeria but authorized the importation of the drug for investigational purposes.
- c. He also clarified to the Committee the difference between approval for clinical trial and approval for importation for investigational purposes.
- d. The letter written by Prof. Osuide on this issue dated 14th August 1996 reference number I. D. 72/I/126 confirmed his stance above.
- e. Subsequent minutes written by Prof. Osuide dated 1st November 1996 to the then Honourable Minister of Health, purportedly written after consultations with the Minister however, contradicted his earlier stance.
- f. In his presentation to the Committee Prof. Osuide maintained his assertion that the letter written by NAFDAC did not in any way convey approval for a clinical trial.
- g. He expected Pfizer who had conducted clinical trials in Nigeria in the past to know exactly what to do to obtain approval for clinical trial



**4.3.3. Major Aliyu Mohammed Rtd – Deputy Director i/c NAFDAC North-West Zone, Kano.**

- a. He was in Kano at the time of the epidemic and the drug trial in 1996 and was in charge of the North-West Zone of NAFDAC at the time.
- b. He confirmed receipt of samples of the drug from Prof. Idris Mohammed, which he despatched to the office of the DG NAFDAC.
- c. He admitted telling Prof. Idris Mohammed that a letter to US FDA signed by Mr Usoro was not an authority to conduct the trial

**4.4 Federal Ministry of Health.**

**The key actors:**

- |                          |  |
|--------------------------|--|
| -Dr. Ihechukwu Madubuike | - former Minister of Health            |
| -Dr A. E. Ike            | - former SA to the Minister of Health, |
| -Dr. E. C. Chidomere     | - former SA to the Minister of Health, |
| -Dr. J. D. A. Makanjuola | - former D-G, FMOH                     |
| -Dr. A. Nasidi           | - former Chief Epidemiologist          |

**4.4.1. Dr. Ihechukwu Madubuike**

- a. He was the Honourable Minister of Health in 1996.
- b. He facilitated the issuance of a duty exemption by the Federal Minister of Finance for the importation by Pfizer of Trovafloxacin and other drugs/medical supplies for "control of the epidemic."
- c. He neither sought nor considered the need for expert advice on the expediency of introducing a new drug for the treatment of meningitis in an epidemic situation.
- d. He apparently relied more on his Special Assistants and by-passed the most relevant departments like the Primary Health Care & Disease Control and the Food & Drug Services departments of the Ministry.
- e. He neither set up a committee to look into Prof. I. Mohammed's report of "an illegal trial of unlicensed drug in Kano" nor invite him for discussion on the matter.
- f. He under-funded the task force for the control of the epidemic.

- g. Did not react to S.O.S from his Staff and the Chairman of the Task Force when alerted on the incident
- h. Without calling Prof Idris Mohammed to discuss his report on the drug trial and asking for his comments on the views expressed by the KN MOH on the report, the Minister caused Dr Chidomere to write Prof Idris an undeserving and distasteful letter
- i. He did not respond to the invitation of the committee for interview.

#### **4.4.2 Dr. A. E. Ike**

He was the Special Assistant to the Honourable Minister of Health, Dr. I. Madubuike.

- a. He admitted that he wrote a letter inviting Robert L. Buhl of Pfizer International to Nigeria to deliver emergency medical supplies including the drugs Alatrofloxacin and Trovafloxacin without reference to the relevant department in the ministry, the Food & Drug Services Department.
- b. He admitted that he did not have previous knowledge about the drug Trovafloxacin. He should, therefore, have advised that more information be sought.
- c. He acknowledged the petition of Prof. Idris Mohammed but did not pass the petition to the relevant departments
- d. He also considered that a committee should have been constituted to investigate the matter.

#### **4.4.3. Dr. E. C. Chidomere – Former Special Assistant to Dr. I. Madubuike.**

- a. He was the successor to Dr. Ike and it was during his tenure that Prof. I. Mohammed's report was treated by the Minister's office.
- b. He admitted that he did not communicate to Prof. I. Mohammed the responses received from Kano State Ministry of Health, Pfizer and NAFDAC requesting for his comments.
- c. His letter to Prof. I Mohammed did not address the issues raised and was in bad taste

#### **4.4.4. The TASK FORCE**

- a. The Top Management Committee of the Federal Ministry of Health set up the Task Force.
- b. The membership of the Task Force consisted of Prof. I. Mohammed (Chairman) and
  - i) Representatives of teaching hospitals in affected States
  - ii) Members of the Kano State Ministry of Health
  - iii) Representative of MSF and some other agencies involved in dealing with the epidemic
- c. The task force used the Infectious Diseases Hospital, Kano as its operational base for the control of the epidemic nationwide
- d. The Task Force was under funded by the Ministry.

#### **4.4.5. Dr. A. Nasidi – then Chief Consultant Epidemiologist, Federal Ministry of Health.**

- a. He was the ministry's member/facilitator of the task force for the control of the epidemic.
- b. He was aware of the drug trial and advised that the trial be discontinued
- c. He reported the incidence of the drug trial verbally to the Minister of Health .
- d. He joined Prof. Idris Mohammed to report the drug trial to Alhaji Ismaila Gwarzo, the then National Security Adviser who did nothing.
- e. He advised the Ministry of Health in writing to investigate the drug trial.
- f. He has expenses that are yet to be settled
- g. He mentioned threats to his life at various times in relation to the drug trial.

#### **4.4.6. Dr. J. D. A. Makanjuola – Former DG Federal Ministry of Health.**

- a. He was Director-General of the Federal Ministry of Health at the time.
- b. Mr. Usoro alleged that he passed the draft letter from Pfizer to him for endorsement.

- c. All efforts to reach him were unsuccessful; as such he did not appear before the committee.

#### **4.5 KANO STATE MINISTRY OF HEALTH.**

**Key actors:**

- |                        |  |
|------------------------|--|
| -Hajiya Nafisat Kabir  | – then Commissioner for Health             |
| -Dr Sanda Mohammed     | - DG                                       |
| -Dr Sulaiman Abdullahi | – Principal Medical Officer (PMO) i/c IDH. |

##### **4.5.1. Hajiya Nafisat Kabir – Former Commissioner of Health.**

- a. Hajiya N. Kabir was the Commissioner at the time of the trial.
- b. She denied that Pfizer informed her of the trial.
- c. She regularly visited IDH where she met with Prof. I. Mohammed who always briefed her on efforts to control the epidemic.
- d. She claimed that Prof. Mohammed reported more frequently to the Military administrator.
- e. She recalled that the Military Administrator told her that there was a problem at the IDH but gave no details.
- f. She said that she only got to know of the trial about three months later when she received a letter from the Minister of Health requesting for her ministry's comment on the report submitted by Prof. Idris Mohammed.

##### **4.5.2 Dr. Sanda Mohammed – Former DG.**

- a. He was Director General Kano State Ministry of Health at the time of the trial
- b. He stated that he visited the Infectious Diseases Hospital, Kano regularly at the time of the epidemic.
- c. He denied knowledge of a drug trial but from oral and documentary evidence from key players like Pfizer, Prof. I. Mohammed, Dr. Dutse, Dr. Suleiman and Dr. Dogunro the Committee has cause to believe that he was aware of the drug trial and could have aided its continuation after Prof Idris ordered the stoppage on 11/4/1996.

**4.5.3 Dr. Suleiman Abdullahi – The Principal Medical Officer i/c IDH, Kano.**

- a. He was the head of the hospital at the time of the trial.
- b. He admitted that he was aware of the trial.
- c. He testified that he was overwhelmed by the enormity of the epidemic, which was further compounded by the nurses strike action.
- d. He confirmed that he received a letter from Prof. I Mohammed stopping the trial on 11/04/96
- e. He did not forward Prof. I Mohammed's letter to the higher authorities.
- f. He confirmed that Dr. S. Mohammed then Director General Kano State Ministry of Health was aware of the trial and gave the approval for its continuation after Prof Idris's stoppage order.

**4.6 AMINU KANO TEACHING HOSPITAL, KANO.**

**Key officers: Dr. Sadiq S. Wali, Dr. Musa Borodo, and Dr. Hussein Haroun**

**4.6.1. Dr. S. S. Wali / Dr. M. Borodo.**

- a. Dr S.S. Wali is the Chief Medical Director of Aminu Kano Teaching Hospital (AKTH).
- b. Dr. Wali at the time of the epidemic was the honorary Chief Medical Director of the Aminu Kano Teaching Hospital and personal physician to the late Head of State.
- c. Dr. Musa Borodo is the Chairman Medical Advisory Committee .
- d. They testified that they were unaware of the trial and that there was no standing ethical committee at AKTH at the time the trial.
- e. They confirmed that the ethical clearance letter issued by Dr. Dutse was irregular.

**4.6.2. DR. HARUNA HUSSEIN**

- a. He was a House Officer at the time of the trial and presently a registrar with AKTH.
- b. Dr. Isa Dutse recruited him for the study.

#### 4.7 PROF. IDRIS MOHAMMED

- a. He was Chairman of the Task Force appointed by the Minister of Health to control the epidemic
- b. He met with the Pfizer team and was shown the protocol before the commencement of the trial.
- c. He gave a go-ahead for the trial pending the submission by Pfizer of relevant approvals from NAFDAC and the Minister,
- d. He directed Dr. Ajayi-Obe to monitor the trial and collect on his behalf, the letters of approval earlier demanded by him.
- e. He notified the Commissioner of Health about the trial by Pfizer before its commencement.
- f. When the approvals he demanded were not forthcoming eight days later, he ordered a stoppage of the trial by a letter to the Principal Medical Officer in-charge of the Infectious Diseases Hospital, Kano.
- g. He testified that to his surprise the trial was continued purportedly with the approval of the Kano State Ministry of Health.
- h. In his effort to stop the continuation of the trial, Prof. I Mohammed reported the case to the HMH on the 9th April 1996 before issuance of the letter of stoppage.
- i. On the 14th April 1996 further attempts were made by Prof. I Mohammed accompanied by Dr Nasidi to stop the trial by briefing the National Security Adviser - Alhaji Ismaila Gwarzo about the trial at Kano.
- j. On the 3rd of July 1996, Prof. Idris Mohammed personally submitted his report on the "illegal Trovan trial" to the Minister of Health's office.
- k. Prof. Idris Mohammed considers as libelous the final response of the then Minister of Health to his report on the "illegal trial of an unregistered and unlicensed drug by Pfizer in Kano 1996."
- l. In spite of not being provided with funds to control the epidemic Prof. I. Mohammed should be commended for his efforts in successfully bringing the epidemic under control and for being the first to sound the alarm on the drug trial.
- m. The committee recommends that the Federal Ministry of Health should refund expenses incurred by him in the course of controlling the epidemic.

Attached (**Appendix XXVIII**) is a submission by Prof Idris Mohammed which further gives details of his involvements.

**4.8. MEDECINS SANS FRONTIERE (MSF)**

- a. MSF established a presence in Nigeria during the epidemic.
- b. It is noteworthy that they contributed substantially to the control of the epidemic. Amongst other things, they vaccinated 2.9 million out of 5.1 million people vaccinated, treated 30,000 out of 56,700 cases of meningitis.
- c. Their total financial commitment in the control of the epidemic was \$2.935m.
- d. The major objection of the MSF to the trial was that it was interfering with their work. This was eventually resolved with the allocation of separate wards for MSF and Pfizer.
- e. Against the established tradition, the MSF was found to have published a paper on the epidemic using data gathered from Nigerian workers on the field without any regards or reference to such workers (**see Appendix XXX**)
- f. Also contrary to the Ministry's public health rules, such a publication was made without approval of the Ministry of Health

## CHAPTER 5

### TECHNICAL REPORT/REVIEW OF THE TRIAL

The terms of reference are as follows:

A. Review of Scientific evidence with the following points in mind.

- (i) If Oral Trovan had ever been used in the treatment of meningitis before.
- (ii) If alatrofloxacin had ever been used in the treatment of meningitis before.
- (iii) Is the sample size for the trial adequate or not?
- (iv) What is the WHO recommendation for the management of epidemic meningitis and sporadic meningitis?
- (v) Is there any WHO or FMOH or any other scientific group document recommending Trovan for managing meningitis? If yes, where are they?
- (vi) Are there any documents guiding the trial of new drugs, particularly in developing countries, and in particular, among children? If yes, where are they and what did they say?
- (vii) What is the advantage of the drugs we know specifically used for meningitis? – Chloramphenicol, oily Chloramphenicol, Ceftriaxone, Penicillin and Trovan.
- (viii) What are the recommended routes of administration in epidemic and sporadic meningitis?
- (ix) Look and weigh the adverse side effects of each of these drugs on adults and children.

#### **Ethics**

- (x) Was there a protocol for this study or not? If yes, developed by whom and how was it processed?
- (xi) Was there any other relevant document submitted for the study, to whom and by whom?
- (xii) Did the protocol submitted conform to national and international standards?
- (xiii) Were deviations from the protocol?
- (xiv) In the process of conducting the trial, did the group actually obtain ethical committee approval? Comment on what ethical approval is and why it is necessary.



- (xv) Was there any informed consent? Did they bring any format? Was it done properly? Verbal or written?

### ***Management***

- (xvi) Did they follow protocol?  
 (xvii) Any lapses in the management of patients?  
 (xviii) Dosage.  
 (xix) Efficacy of the trial (comment on belief on less mortality for Trovan group compared to Ceftriaxone).  
 (xx) Background of Foreign Doctors that managed patients compared with the roles played by Nigerian doctors.  
 (xxi) Role of the Principal Investigator.

### ***Presentation of Results.***

- (xxii) What happened when clinical trials were concluded.  
 (xxiii) To whom is the result sent?  
 (xxiv) Who is the custodian of the data obtained?  
 (xxv) How is the data analysed and presented?  
 (xxvi) Role of State of hospital (IDH) – based on reports and personal observations.  
 (xxvii) What happens again in the event of another epidemic?

The terms of reference were treated under two broad categories namely:

- (a) Trovan use and;  
 (b) The trial

The inferences arrived at were as follows:

### **TROVAN USE:**

Prior to the 1996 clinical trial, there is evidence that Alatrofloxacin was used in children with meningitis in a multi centre Phase 1 pilot study between May and November 1995. This report was presented at the First International Paediatrics Infectious Diseases Conference in Monterey, California (21st – 22<sup>nd</sup> September 1995). Also, there is a reported use of oral Trovafloxacin by normal volunteers in an earlier undated study (see Pfizer's submission to the FDA). However, it would appear that oral Trovan was first used in paediatric meningitis patients during the Kano epidemic of 1996 .

Furthermore, there was no evidence from WHO, FMOH or any other scientific body recommending Trovan for use in the management of meningitis. Later, however, in a 1997/98 WHO publication, it was said that:... "New drugs such as meropenem, cefpirom or trovafloxacin may have a role, but at present, these are very expensive and not in common use". (see Appendix XXXI).

For proper assessment of the efficacy of three drugs used, there is need to compare the Case Fatality Rates (CFR) vis-à-vis the sample sizes of the patients treated with the drugs. At the IDH during the period of the epidemic when the trial took place, 1,243 (86.2%) patients received oily chloramphenicol, 100(6.9%), ceftriaxone and 98 (6.8%) had Trovan, bringing the total number of patients treated to 1,441 patients. In each of the groups the following case fatality was recorded: oily chloramphenicol, 10.1%, ceftriaxone and 6.2% and Trovan group, 5.6%, respectively (see Appendices XXXII & XXXIII). A strict comparison of the efficacy of the three drugs cannot be judged from this data, even though Trovan appears to be the most efficacious of the three. A more detailed statistical analysis of the data and a review of the data submitted to FDA (this committee was constrained by time from deeply reviewing this) might provide a better understanding of the effectiveness of the therapies. (see Appendix XXXIV)

The adverse effects attributable to ceftriaxone use include haematological abnormality, liver damage and kidney dysfunction. Chloramphenicol, on the other hand, is known to cause bone marrow depression. For Trovan, the common side effects associated with most antibiotics, such as nausea, diarrhoea, vomiting and skin rashes are also exhibited but toxicity to cartilage and tendon, which is peculiar to the quinolones, is also manifested in Trovan use. There is, also, need for caution in patients with CNS disorders and liver problems.

In addition to these, a post-marketing surveillance since the introduction of Trovan in the USA and Europe sometimes in 1998, 152 cases of serious hepatic events associated with drug therapy have been reported. These include nine spontaneous cases involving hepatic failure where patients required liver transplant. Following this and 14 cases of acute liver failure strongly associated with Trovan, the US FDA restricted its use through the issuance of a public health advisory to physicians. In that notification, the US FDA instructed as follows; " Trovan should not be used for more than two weeks, and therapy should be discontinued if the patient experiences any clinical signs of liver dysfunction". On the basis of these observations, European Agency for Evaluation of Medicinal products -EMA) banned the use of Trovan. In a World Health Organization Alert Notice 86 of 18<sup>th</sup> June, 1999 for the same hepatotoxicity a warning for the use of this drug was made.

Following this warning, NAFDAC Nigeria also issued an alert on the same product in 1999 (see Appendix XXXIV).

Presently Trovan and Trovan I.V are (alatrofloxacin) restricted to patients with life-threatening infections treated in hospitals only. Because of its ability to cause borne marrow development problems in young animals, It is not currently recommended for use in infants or children

Analysis of the adverse events by body system among the subjects treated with Trovan in this study showed that all body systems were affected. However, the most affected were **musculoskeletal** system, symptoms of which included *arthralgia, arthritis and painful= swelling* (21% in Trovan group as against 13% in ceftriaxone), **gastrointestinal**, which includes *Abdominal pain, constipation, diarrhoea, enteritis, haematemesis, nausea and vomiting*, – (17% in Trovan group versus 25% seen among ceftriaxone group), the **central and peripheral nervous system** – which included *convulsion, dizziness, headache, neuropathy, oculo-motor nerve paralysis, paralysis* – (13% trovan group as against 21% in ceftriaxone group), followed by **cardio-vascular system**, which included *peripheral oedema, vasculitis* –( 4% for all the groups.) (for details see Tables 6.2 and 6.4 in Pfizer's final report).

Specifically, analysis of case report forms submitted by Pfizer showed that some specific adverse effects were recorded among some patients (See Appendix XXXVIII).

The comments on other drugs in the treatment of meningitis, as well as, the WHO recommendation for the management of sporadic and epidemic meningococcal meningitis is contained in its publication, referenced WHO/CHO/98.6; WHO/EMC/BAC/98.2; Pg. 13 & 14.(see Appendix XXXI)

The Protocol, prepared by Pfizer Central Research Laboratory, conformed to national and international standards. It was given to Dr. I. Dutse, the Principal Investigator, who accepted it. The sample size of 200 was considered statistically adequate by the investigators. The protocol allowed the doctors the discretion of their clinical judgment, but the cases of patients 0069 and 0002 showed significant deviations. Patient 0069 continuously received doses of oral trovafloxacin for 3 days, showed no improvement and died on the third day without a change of therapy. The report to U.S. FDA showed patient 0003 was placed on admission for 5 days, received i.m. ceftriaxone instead of i.v. alatrofloxacin on day one, and oral Trovan on days 2–5; but the hospital treatment sheet showed a 3-day admission of 3rd to 5th of April. This discrepancy, throws some doubt on the report. Apart from the fact that there was no evidence of drug reconciliation, patient 0003, was given a combination of test and standard drugs.

There were many other deviations from the protocol observed by the committee from documents submitted. On the whole, the observations confirmed most of the deviations reported by the investigators among which treatment of patients older than the study age group, patients with dosing deviations and patients from whom CSF could not be obtained were the most serious. Of all these deviations, management of patients 0069 and 0003 constitutes a serious deviation which compromises patient care.

Additionally, although the protocol mentioned the possibility of elevated liver enzymes in experimental animals it did not consider carrying out any liver function test either before or after the treatment.

The protocol was designed specifically to validate the safety and efficacy of Trovafloxacin in treating epidemic meningococcal meningitis (EMM).

### **Informed Consent:**

Although Pfizer claimed to have obtained verbal informed consent, using 'an informed consent form' the evidence for this was not included in the final report of the study. Such forms if shown, could have indicated whether the witnesses endorsed them (attesting to oral consent of each of the patients).

Methods used to recruit patients and obtain informed consent and assent (for children usually 7+ years) in pharmaceutical research should be transparent. Parents must be given sufficient information to obtain their consent whilst the competent children must be given sufficient information to promote understanding before assent is sought and obtained without coercion. Both parties must be reminded of their rights to withdraw at any time if they so desired and that their subsequent treatment will not be affected by such withdrawal. The committee could not establish the veracity of claim that the investigators followed this.

### **Ethical Issues**

Ethical approval is mandatory for all clinical trials, as it is an opportunity to review, assess and monitor the trial by the Ethical Committee. The normal procedure for obtaining an Ethical Committee approval is for the Principal Investigator to apply to the Ethical Review Committee, of the institution in which the trial is to be conducted, with a copy of the protocol attached. Ethical Clearance, once obtained, should be forwarded to NAFDAC with the approved protocol. **THERE WAS NO ETHICAL APPROVAL FOR THIS TRIAL BEFORE AND DURING THE TRIAL.** This is contrary to the earlier

claims by Pfizer that the study could not have been initiated without ethical committee approval which according to them was obtained prior to study.

There were three U.S. Doctors involved in the trial, namely: Scott Hopkins, Debra Williams and Mike Dunne. Although medically qualified and experienced in handling infectious diseases of this nature (see Appendix XXXV), these doctors who formed part of the medical team were not cleared nor licensed by the Nigerian Medical Council to practice in Nigeria.

Besides the diagnostic aspects of laboratory tests such as microscopy, gram stain, latex and serological tests, the results of clinical laboratory tests of liver and renal functions, and haematological studies normally monitored to help doctors in the cause of treatment were not made available while the trial was in progress. The samples were apparently taken outside Nigeria for analysis and results made available only to U.S. FDA and not to any Nigerian Health Authority and agency.

It is usual to make copies of the report available to the sponsor, Principal Investigator and NAFDAC but this was not the case with this trial. Neither the PI, NAFDAC nor the institution where the trial was carried out got copies of the report. In addition, the follow-up was not well planned and this affected its outcome. Compensations to the participants was minimal or non existent, as such a clear case of exploitation of the ignorant was established.

Given the frequency and severity of the outbreak of epidemics in Kano area, the IDH, as we found out during our visit, was grossly inadequate in space, infrastructure and equipment. A lot of urgent attention has to be given to all these aspects to improve the general state of the hospital.

### **Patient Records**

No patient record given to the committee by Pfizer was complete with patient names and address. Samples of cards which was claimed to have been given to each of the patients was also not made available by the investigators. Therefore, no such documents were available for analysis

### **Repeat Scenario**

As the committee is writing this report, cases of measles and CSM were occurring in many States of the Federation. The IDH is again seeing cases of measles and some CSM. It is again not ready and Nigeria could experience

the 1996 scenario. If the chaotic situation is allowed to recur then any fast agent could exploit the situation again.

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## **CHAPTER 6**

### **CONCLUSIONS AND RECOMMENDATIONS.**

#### **6.1 CONCLUSIONS.**

The committee, after review of all documents available to it and evidence from all interviewed concluded as follows:-

1. The trial of oral Trovafloxacin (Trovan) and its intravenous pro-drug Alatrofloxacin (Trovan IV) by Pfizer did take place at the Infectious Diseases Hospital, Kano from 3rd –18th April 1996.
2. Two hundred (200) Nigerian children who were critically sick with meningococcal meningitis were recruited for the trial.
3. Ninety nine - (99) of the children were treated with Trovafloxacin/Alatrofloxacin whilst 101 received Ceftriaxone, an antibiotic already well established and accepted internationally for the treatment of meningitis.
4. Eleven (11) fatalities occurred out of the 200 children.
5. Of the 11 fatalities, 5 occurred in the Trovan while 6 in the Ceftriaxone group
6. Unknown number suffered adverse events of varying degrees
7. Pfizer's primary motive for intervening in the epidemic seems to be to try its new drug – the Trovafloxacin – (Trovan)
8. Based on his memo of 14th March 1996 (see Appendix XXXVI) and other evidence available to the committee, Dr. Scott Hopkins was the true Principal Investigator
9. Pfizer Inc. committed N12 million for the trial and made donation for the epidemic worth N6.3 million
10. Pfizer's medical team (investigators) treated only 200 patients who were subjects of the trial as against an estimated 110,000 victims of the epidemic.
11. Pfizer did not follow laid down procedures for conduct of clinical trials in spite of their being conversant with the guidelines.
12. Pfizer's doctors from the USA although well qualified (see Appendix XXXV For CVs) failed to obtain license to practice before participating in the trial in Nigeria
13. As earlier pointed out in item 8 above, Dr. I. Dutse though presented as the Principal Investigator appeared not to have played that role
14. The purported approval for the trial issued by NAFDAC was actually an authority to import the drug.

15. NAFDAC as a regulatory agency failed in its responsibility by not stopping the trial or taking any action when alerted by the chairman of the Task Force.
16. By its inappropriate response to Prof. Idris Mohammed's report of the drug trial, the Federal Ministry of Health failed in its duty to protect the health of the ailing children
17. The FMH constituted a Task Force that it failed to empower administratively and financially.
18. Although the key officials of the Ministry of Health Kano pleaded ignorance of the trial, the committee has cause to believe that the then Director-General was aware and could have aided the continuation of the trial after Prof Idris stopped it
19. Although Pfizer alleged that Prof. Idris Mohammed requested that the equipment used for the trial be given to him after completion and that inability of the company to do so did not go down well with him, the committee could not ascertain the veracity of the allegation.
20. Prof. Idris Mohammed's prompt and sustained alert on the drug trial did not receive the necessary attention it deserved from the Federal Ministry of Health and the Kano State Ministry of Health, despite his efforts at drawing attention to the possible dangers to the health of the children involved.
21. The voluntary and international agencies such as WHO, UNICEF, Nigerian Red Cross, German Red Cross, International Red Cross, the Governments of the Republic of Niger and Cuba, and in particular MSF should be commended for their invaluable contributions to the control of the largest epidemic of meningitis ever recorded.
22. Despite all efforts by the committee to obtain from Pfizer, the Principal Investigator and the Kano State Ministry of Health, the line-listing with names of the Patients involved in the trial, none was made available to us
23. In general, the committee is of the opinion that the trial violated the Drugs and Related Products (Registration, Etc.) Decree Number 19 of 1993, the Declaration of Helsinki on Ethical Principles for Medical Research involving human subjects and the Convention on the Right of the Child adopted by the General Assembly of the UN on 20th November 1989 (see Appendix XXXVII)



## 6.2. RECOMMENDATIONS.

The committee after extensive review and due consideration of the facts available to it recommends as follows:

1. For breaching the Drug and Related Products (Registration, etc) Decree of 1993, the Helsinki Declaration on Ethical Principals for Medical Research involving Human Subjects and the 1989 United Nations Convention on the Rights of the Child, Pfizer Inc. should be sanctioned appropriately.
2. An unreserved apology to the government and people of Nigeria and Kano State in particular, should be tendered by Pfizer accompanied by appropriate restitution
3. Any individuals, groups, or corporate organization intending to conduct clinical trial should be conversant with and made to adhere strictly to all the relevant Nigerian laws, regulations, guidelines and procedures
4. Henceforth all doctors and other health professionals entering Nigeria to assist in health programs, emergencies, epidemics etc. must be duly cleared and licensed by the Professional regulatory bodies
5. Ethical Committee clearance must remain a mandatory requirement for any trial on humans
6. Dr. Isa Dutse the naïve and exploited "Principal Investigator" of the trial should be reprimanded and considered for disciplinary action by his institution.
7. The then leadership of NAFDAC should be reprimanded for equivocation on its advice to the Minister of Health on Prof. Idris Mohammed's report on the drug trial
8. To avoid ambiguity in letters conveying approval for either importation or clearance to commence clinical trial standard formats of such letters should be prepared by NAFDAC
9. NAFDAC should be fully equipped and allowed to operate at entry and exit points so as to facilitate its onerous task of safeguarding the lives and health of Nigerians.
10. NAFDAC should train and re-train its staff in monitoring and auditing of clinical trials.
11. NAFDAC should periodically review the guidelines for clinical trials to update the requirements and ensure strict compliance.

12. That NAFDAC upon giving approval for importation of an unregistered product, including investigational drugs must monitor its safety and efficacy
13. Any Task Force constituted for a National assignment must have its membership identified, its role clearly defined and more importantly be properly funded.
14. During emergencies there should be adequate consultations and coordination among the various tiers of government for timely and effective control
15. Ministers should utilize the expertise of the relevant Departments within their Ministries rather than relying solely on their Special Assistants
16. Kano State Government should probe further the role of the former Director-General Kano State Ministry of Health during the drug trial.
17. That the Infectious Diseases Hospital, Kano should be promptly relocated from the densely populated area of Kano where it is presently located.
18. The hospital should be expanded and equipped to serve adequately the teeming population of Kano State.
19. The Infectious Diseases Hospital, Kano must improve its records department
20. State governments should be encouraged to establish Infectious Diseases Hospitals that are well equipped and properly manned in view of the frequent outbreaks experienced in the last decade.
21. Prof. Idris Mohammed and members of his task force should be commended for their role during the epidemic.
22. He should also be commended for his effort at stopping the drug trial.

23. That Prof. Idris Mohammed should without further delay submit formally his official report as Task Force Chairman for the control of the epidemic.
24. That all claims following the epidemic control be verified and promptly settled by the Federal Ministry of Health.
25. Specialized experience in pediatrics by investigators should be pre-requisite for conduct of such clinical studies in children.
26. We recommend that the Minister of Health should constitute an ad hoc national ethical committee whenever the need arises.
27. The FMOH should intensify supervision of NAFDAC and all its parastatals.