To,

The Municipal Commissioner & Chairman, AMC MET

Ahmedabad Municipal Corporation.

Respected Madam,

A team of three of us, has been appointed to investigate the incidence in detailed and submit findings including suggestions about the incident happened at the C.H. Nagri Eye Hospital after giving intravetrel Avastin to the patients [18 patients] having retinal vascular disorders due to various reasons like Diabetes, senile, age related macular degeneration, Hypertension etc.

We have reviewed all the aspects including theatre asepsis, injection details, patient status, laboratory details and other relevant factors. We are hereby submitting the report.

Sincerely yours',

(DR. SHASHANK PATEL)
Director
M & J Institute of Ophthalmology Western Regional Institute

(DR. BHARAT GHODADRA)
Medical Superintendent
GCS Medical College

(Professor & Head of Dept of Ophthalmology)
AMC MET Medical College

DATE: 18th January, 2016
First / Preliminary Report

To
The Commissioner & Chairman, AMC MET

Respected Madam,

An Independent inquiry committee has been constituted on 13th January, 2016 by the Municipal Commissioner & Chairman, AMC MET comprising of Dr. Shashank Patel, Dr. Bharat Ghodadra and Dr. Beena Desai to investigate the incident in detail and submit findings including suggestions about the incident happened at the C.H. Nagri Eye Hospital after giving intravitreal Avastin to the patients [18 patients] having retinal vascular disorders due to various reasons like Diabetes, senile, age related macular degeneration, Hypertension etc. on 12th January, 2016 between 11:30 am to 1.00 pm. The patients were advised for follow up on next day at 9.00 am. On follow up i.e. on 13th January, 2016, 15 patients complained about swelling, pain, watery discharge etc.

We have visited the C.H.Nagri Eye Hospital first on 14th January, 2016 subsequent to 15 and 16 January on follow up visit.

During our visit, we have inspected OT complex, Wards, Procedure Room of C.H.Nagri Eye Hospital. We have also examined affected patients at bed side. We inquired about ocular complaints and clinical events taken place following intravitreal procedure and subsequent management given by the hospital authority with the patients and their relatives.

We also had a detailed interaction with the hospital authority including Medical Superintendent, RMO, Treating doctors, Resident doctors, Para Medical and technical Staff and support staff about the Procedure and Protocol for injecting Avastin, OT protocol, treatment and post procedure care protocol.
We have also checked Fumigation and sterilization records (ANNEXURE-1), microbiological report of used Avastin vial (Batch No. B7031B10) (ANNEXURE-2), AC/PC TAP and vitreous fluid of every affected patients (ANNEXURE-3).

1. **Use of Avastin Injection**

Avastin is a monoclonal Anti Body used as an anti – VEGF agent to treat different retinal vascular pathologies e.g. WET ARMD, Diabetic macular oedema, retinal vascular occlusion with macular oedema, vasculities etc. Sporadic incidences of drug hyper sensitivity in the form of sterile endophthalmitis, uveitis and Vitritis are reported worldwide with the use of this drug intravitreally but considering its wide spread as anti – VGEF agent for successful treatment of various above mentioned retinal vascular pathologies and cost effectiveness, Inj. Avastin is very commonly used not only in India but worldwide. Such international reports regarding sterile endophthalmitis and other concerned literature are attached herewith for reference. **ANNEXURE – 4.**

2. **Patient Profile**

There were 18 patients reported for intra vitreal treatment procedure on 12	extsuperscript{th} January, 2016. The details of which are annexed herewith as **ANNEXURE – 5.**

The patient mentioned in annexure – 5 diagnosed having WET ARMD, Diabetic macular oedema, retinal vascular occlusion with macular oedema, vacutities hence advised intra vitreal Avastin.

We also came to the know that, out of 16 patients, 6 patients had taken intra vitreal Avastin before as part of their treatment – the details are annexed herewith as **ANNEXURE-6.**

We have inquired preliminary with most of the patients and their relatives, who have complaints of swelling, watery discharge and pain etc on 14	extsuperscript{th} January, 2016 at 11.00 am. We had observed that 7 patients were symptomatically better who had been operated in previous night with emergency vitrectomy. The other 8 patients were being operated in the OT during our first visit.

3. **Standard Protocol for intra vitreal injection procedure**

The standard protocol for intra vitreal injection procedure is attached herewith as **ANNEXURE- 7.** Upon investigation, observation and interaction with Medical / Para Medical Staff we found that, the hospital authority has followed all protocols. The procedure for intravitreal injection of Avastin has been performed by qualified ophthalmic surgeon and there is no lacunae or negligence found on that part.
Out of above mentioned 16 patients intra vitreal injection was injected in OT in 15 patients and one patient was injected in other OT under sedation. Though intravitreal procedure was performed in two different Operation Theatres. However hyper inflammatory uveal response was seen in all 16 cases of both theaters.

On the same day, other two patients were injected Avastin from another batch batch No: B7034802 in OT along with cataract surgery and they were found clinically normal next Post op day.

In the same OT where injection Avastin was given to 15 patients; one separate patient was injected with Triamcinolone Acetoneid. However this patient had no complaint of inflammation or pain on next day, on follow up visit.

So it can be concluded that 16 patients who were injected Avastin from single vial Batch No: B7031810 had hyper inflammatory response irrespective of theatre location and procedural protocols.


Considering the response of the injected drug or adverse effects e.g. hyper inflammatory response in the form of sterile endophthalmitis, UVEITIS and VITRITIS patients treated with Avastin are seen on follow up visit after 24 hours as per standard protocol.

This standard protocol has been observed by the Medical and Para Medical staff of C.H. Nagri Eye Hospital.

5. Management and Response to the complication by Hospital Authority

On the follow up visit i.e. on 13th January, 15 patients were found complaining about swelling, pain, redness, watering between 9:00 to 10:00 AM.

From clinical records it was found that, on follow up examination that, all 15 patients had fibrinous reaction in anterior chamber and hypopyon. Therefore as per standard protocol, All patients were given sub conjunctival injection of Gentamicine + Dexona + Mydrin by qualified clinicians after informing the patient and their relatives. They were assessed after 30-40 minutes. All patients showed improvement in the form of decrease in symptoms e.g. pain, watering and decrease in inflammation in anterior chamber were noted on slit lamp examination. All patients were advised to get admitted in the wards for observation and further management. On admission, as per standard protocol immediately ocular ultrasound was performed in all cases by expert retinal clinicians. From the record it was found that ultra sound examination showed vitreous activity in the cavity along with
intraocular inflammation. It was then decided by expert retinal clinicians at 2.00 pm to inject intravitreal antibiotic and steroid injections with Anterior chamber tap for microbiology. Detailed counselling was done with all patients and their relatives. After obtaining written informed consent, all patients were injected intravitreal antibiotic and steroid injections.

All cases were re-assessed by retinal consultants along with invited vitreo-retinal experts Dr. Alay Banker and Dr. Shaileen Parikh between 7.30 p.m. to 8.00 p.m. Based on clinical findings and ultrasound findings, 7 patients with severe intraocular inflammation and associated risk of diabetes were decided to take for immediate pars plana vitrectomy with vitreous fluid tap and injection of vancomycin + amikacin + dexamethasone. The operative procedure was done by the team of expert vitreoretina surgeons during 10.00 pm till 12.30 midnight. Other 8 cases were observed overnight for intravitreal injection response and topical medication continued.

On next day (14/1/2016) all 15 patients were reviewed and evaluated again by expert vitreo-retinal surgeons team including invited experts. Out of 15, 7 Cases operated on previous night (13/1/2016) showed remarkable improvement in reduction of intraocular inflammation. Result of immediate vitrectomy in those 7 patients suggested faster recovery in the reduction of intraocular inflammation. Therefore for better outcome, remaining 8 patients were subjected to do vitrectomy surgery with vitreous fluid tap and intravitreal injection of vancomycin + amikacin + dexamethasone on 14/1/2016. Surgery were done between 9 a.m. to 12.30 p.m. by same expert vitreoretinal surgeon team.

(Source: Indoor case paper study and discussion, deliberations with Medial & Para Medical Staff)

It was observed that, the standard care for hyper inflammatory uveal response has been observed and standard care has been provided in time as per protocol.

Review of literature reveals that sporadic incidences of sterile endophthalmitis or severe intraocular inflammation are noted following intravitreal injection of Avastin worldwide. (Source published articles. ANNEXURE-4)

Sheth C. H. Nagri Municipal Eye hospital has catered this treatment to the poor and needy citizens from 2007 onwards. Since July 2007 they have treated different retinal vascular diseases successfully to approximately 7000 patients as per hospital data record.

(ANNEXURE-8)
On examining the records and other evidences, preliminary we can conclude that prima facie,

A) the treatment of the patient diagnose with retinal vascular disorders due to various reasons like Diabetes, ARMD, Hypertension etc. has been done with standard protocol and care.

B) All patients who had developed hyperinflammatory response in form of sterile endophthalmitis; had been diagnosed immediately on the basis of their complaints and treated immediately for the same as per the standard protocol of care.

C) Emergency primary vitrectomy were done in all needed patients in time by expert vitreo retinal surgeon team as per standard protocol of care.

D) On examining the data and the record submitted by Micro Biology Department of Smt. NHL Municipal Medical College, it can be concluded that all patients’ vitreous tap did not show any growth of micro organism; therefore they all seems to have developed sterile endophthalmitis.

E) On prima facie we do not find any short fall or lacunae in any procedures of standard protocol of care by treating medical and paramedic staff members. We also do not find any medical negligence in treatment of those patients as per standard protocol of care.

The hospital authority has submitted samples of the inj. Avastin 100mg from similar Batch No: 87031810 to Food and Drug Control Department, Sola Civil Hospital. Upon receiving the report from the Food and Drug control when received shall be submitted to this committee for further evaluation and conclusion.

6. Suggestions:

After our preliminary review we would like to submit following suggestions for prevention of such incident in future:

- The magnitude of complications of multidose vial injection in such a mass can be reduced by decreasing the number of patients per day. However this may delay the treatment to the needy patients immediately and this may also cause chances of contamination of the drug which should be look into carefully.
- The experts should update their knowledge of treatment by attending different conferences and follow the guideline which is published by All India Ophthalmology Society / speciality societies.

S.M. Patel

[Signature]
• Public education regarding the drug action & reaction should be displayed in the waiting area and other effective places in the hospital.

This preliminary report is submitted for taking immediate care and course of action by the hospital authority including both clinical and administrative. We shall submit the final report after receiving the drug evaluation report.

We sincerely thank Municipal Commissioner & Chairman of AMC MET for keeping faith in us and appoint us as team of expert. We sincerely thank the patients and their relative for their cooperation for our investigation in spite of their stressful conditions. We also thank the hospital staff and other concerned authority for their kind cooperation during our investigation and observation.

(Signed)

(DR. SHASHANK PATEL) (DR. BHARAT GHODADRA) (DR. BEENA DESAI)

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