Clinical Evaluation Report of

KONTROLLD KOPYA CONTROLLED COPY

according to Annex X of Directive 93/42/EEC Medical Devices as well as MEDDEV 2.7.1

Acriva UD Intraocular Lens Series

(Acriva UD Reviol, Acriva UD BB, Acriva UD BB Reviol and Acriva UD BB Toric)

Replaces Document No. 01.TF.A.17 Clinical Assessment Revision No 03

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1. Introduction

The primary purpose of this document is to provide a clinical evaluation report of Acriva [UD] intraocular lenses with the requirements concerning the characteristics and performance referred to MEDDEV.2.7.1 Rev.3.

The clinical evaluation should rely on data from scientific literature which proposes the intended use of the medical device and the applying techniques to treat the disease. As part of the Essential Requirements, a clinical evaluation in accordance with Annex X must be conducted for all medical devices (Annex I part I, 6a of Directive 93/42/EEC). In low-risk products or products with a long history of successful application, which is Acriva [UD] intraocular lens, clinical investigations referred to the Medical Directive 93/42/EEC, Article 15 and Annex X are required.

As a general rule, confirmation of conformity must be based on clinical data. This includes the requirements concerning the characteristics and performances referred to in Sections 1 and 3 of Annex I, under the device's normal conditions of use, and the evaluation of the side-effects and of the acceptability of the benefit/risk ratio referred to in Section 6 of Annex I.

This analysis is based on relevant and currently-available scientific publications regarding the safety, performance, characteristics, and intended purpose of intraocular lenses. The literature reviewed was based on a demonstration of the device's equivalence to those that we have previously placed on the market.

1.1 Clinical Assessment

Cataract is a condition in the eye that it left untreated, could lead the blindness. The cataract has become one of the most important causes of disability in our aging population, and well over 1.000.000 persons in the United States and perhaps 10% of that number in Canada, most of them elderly, undergo surgery each year for this reason. One of the most sophisticated optical systems found in the nature is the human eye. Table 1.1 shows the prevalence of cataract in population of United States residents. The

table is from "Optical Performance Test & Analysis of Intraocular Lens" book of Junoh Choi, the book has been published in 2008.

Age	Prevalence (%)
43-54	1.6
55-64	7.2
65-74	19.6
75-85	43.1

The clouding of the crystalline lens degrades vision due to scatter and interferes with everyday activities such as driving, watching TV, or reading. A crystalline lens that can change shape therefore varying the power of the eye, and a retina containing photosensitive cells. The earliest treatment for cataract was removal of the cloudy crystalline lens. Removal of the crystalline lens also removes about 20 D of power from the eye and requires the patient to wear high power spectacle lenses. With the advent of intraocular lenses (IOLs), which are artificial lenses designed to replace the natural crystalline lens of the human eye, cataract is often treated with a surgical procedure that replaces the natural lens with an IOL. replacements The intraocular lens (IOL) is a surgically-implanted artificial lens which serves to replace the natural crystalline lens of the human eye. The lens is normally a clear, biconvex structure. The lens is held in place by the zonules, which attach it to the ciliary body. The zonular fibers arise from the basement membrane of the non-pigmented epithelium of the ciliary body and attach just anteriorly and posteriorly to the equator of the lens. The lens is lined on its outer surface by the lens capsule, which is responsible for elasticity, allowing the lens to accommodate. The lens tends to survive fairly well post-mortern because it does not have its own blood supply, but it does not have the same gross appearance

as its clinical appearance in vivo is written in Cataract Surgery book of R. F. Steinert. Hardness of the explanted lens correlates highly with clinical grading of nuclear sclerosis, but not with cortical or subcapsular opacities. One of the effective ways to treat cataract is the removal of the cataractous natural crystalline lens and implantation of an artificial lens called an intraocular lens (IOL). While this replacement lens provides clear passage through the eye with minimal scatter, IOLs have limitations in their performance. Some of the more prominent issues are loss of accommodation, stray light artifacts from lens edges and control of the total ocular spherical aberration. The designs of the IOLs have shown improvements over the years to further imitate natural human vision. A need for an objective testing and analysis tool for the latest IOLs grow with the advancements of the IOLs. Changes in IOL design and corresponding surgical technique have been implemented to reduce the rates of surgical problems and postoperative complications associated with early models. Various IOL designs have been introduced to help enhance pseudophakic vision while minimizing effects of the mentioned limitations. To understand the motivation for different design of IOLs, knowledge of differences between the natural crystalline lens and IOLs are needed. The desire to produce near normal sight following cataract surgery goes back many years. The possible employment of glass lenses within the eye for aphakia was recorded by Casanova, who described an 'itinerant oculist', Tadini, in Warsaw, around 1766 jiggling small shiny objects to be inserted into eyes at the time of surgery. The original posterior chamber artificial lenticulus of Ridley copied nature very closely and the optical and cosmetic effects in successful cases were reported in 1954. Consequently, current cataract patients are receiving IOLs that lack the ability to change the power of the eye. This side effect of this fixed power is that recipients will have severely degraded near vision due to large defocus even though high quality distance vision is provided. The loss of accommodation for pseudophakes requires additional optical appliences, such as reading glasses, to perform near work.

Another difference between the natural crystalline lens and the IOL implant is the spherical aberration content. IOLs with spherical surfaces contribute to the spherical aberration of the eye and degrade the image quality at the retina. The natural crystalline lens typically compensates for most of the positive corneal spherical aberration with inherent negative spherical aberration. The crystalline lens can achieve this aberration control through a combination of aspheric surfaces and a gradient refractive index. Until recently, conventional IOLs have been manufactured with spherical surfaces. For a single lens with spherical surfaces, only positive spherical can be introduced. Consequently, the total ocular spherical aberration can only increase with conventional spherical surface IOLs. Typically though, this induced aberration can be minimized by choosing an asymmetric biconvex form for the lens surfaces.

The Acriva ^{UD} intraocular lens series can be used in treatment of cataract diseases and the surgery technique is standard but the material, design and specifications of the IOL provides high quality vision to patients. The Acriva ^{UD} intraocular lens series have biconvex aspheric surface and Enhanced 360^0 All Square Edge Design. An intraocular implant material should have biocompatibility optical compatibility, mechanical compatibility. According to the Council Directive 93/42/EEC on medical devices, the intraocular lenses are Class IIb medical devices and the safety and performance of an intraocular lens shall be demonstrated by pre-clinical and clinical evaluation, including suitable risk analysis in accordance with ISO 14971. In cases where a test method referenced in this part of ISO 11979 is not suitable for a certain design or a certain application, an alternative test method devised by the manufacturer shall be validated, justified and documented. VSY Biotechnology is the intraocular lens manufacturer and should apply all the essential requirements.

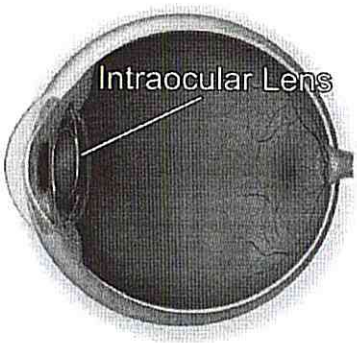
1.2. Device description, function and use

Product: Intraocular Lens

Product Name: Acriva [UD] intraocular Lens Series

Purpose of device: The intraocular lens (IOL) is a surgically-implanted artificial lens which serves to replace the natural crystalline lens of the human eye. Changes in IOL design and corresponding surgical technique have been implemented to reduce the rates of surgical problems and postoperative complications associated with early models. Presently, the only method of curing a cataract is through surgery, which involves the removal of the affected lens. The lens capsule is left behind and the intraocular lens is implanted in the natural lens' place.

Anatomical location of an intraocular lens within the eye:



Acriva [UD] products are around 6.00 mm in optical diameter and soft enough to be folded so that they can be placed into the eye through a very small incision; improvements in microsurgical techniques make it possible to remove a cloudy lens through an incision of only 2.4-2.8 mm, thus avoiding the need for sturing. In the hands of an experienced ophthalmologist, the entire procedure usually takes less than 30 minutes.

Only the user can evaluate the clinical factors involved with each patient to determine if the use of this device is indicated. The user must then decide on the specific technique and procedure that will best accomplish the desired clinical effect. When trying to achieve the maximum potentiality for the ocular optical system, a higher level of optical quality is essential. An IOL of better optical quality could allow a greater spatial frequency spectrum to be transmitted to the retina. The use of IOLs capable of transmitting a broad spectrum of spatial frequencies would allow them to reach higher values of visual acuity—the ocular optical conditions being equal. Moreover , the implantation of an IOL with a superior optical quality could improve the quality of vision in general and in particularly in terms of contrast sensitivity. The implant of intraocular lenses following cataract surgery induces a foreign body reaction to the IOL and a lens epithelial cell reaction. This response of IOL cause mainly from the biomaterial that made of.

The main purpose of our foldable intraocular lenses is to show the highest level of clinically-effective biocompatibility. The ideal IOL material should not incite any inflammatory or immunological reaction. The implantation of intraocular lenses following cataract surgery can induce a foreign body reaction to the IOL as well as a lens epithelial cell reaction. This response is primarily caused by its biomaterial.

Acriva ^{UD} series intraocular lenses are produced from acrylate monomer and the raw-material company is Benz Research &Development which is a very known intraocular lens raw material manufacturer. Benz Research and Development created the first IOL material to incorporate the same UV-A blocking and violet light filtering chromophore that is in the human crystalline lens. The company have entered to IOL materials market in 1998 and have become the preeminent supplier of quality materials and state of the art technology to the IOL industry. The company delivers pure material with 99.9% purity, the quality expected for a polymer implant that may be in the eye for more than 40 years. The company provides raw material of intraocular lenses to IOL companies like Rayner.

The Acriva ^{UD} intraocular lens series have a water content of 25%, are biologically compatible, and are made of a chemically UV-Absorbent acrylic material. They have Ultra Definition (UD) specification and 360^0 enhanced all square edge design. The Acriva^{UD} series intraocular lens has an aspheric structure and aberration control. Due to its special optic design, it maintains high visual quality when correcting the positive spherical aberration of cornea. 360^0 enhanced all square edge design eliminates the risk of

posterior capsule opacification by ensuring posterior capsule contact to the rear surface of the lens for optimal sealing effect.

Acriva ^{UD} intraocular lenses are sterile, foldable intraocular lens (IOL) made of acrylic material with UV-absorbent hydrophobic surface (25% water content).

Acriva ^{UD} intraocular lenses have an aspheric structure with aberration control, provides high visual quality. Clear and yellow chromophore models in monofocal and diffractive multifocal designs. Also Acriva ^{UD} BB with yellow chromophor include monofocal and multifocal toric intraocular lenses. . The product is for single use only and has a shelf-life of three years. It is available in 6.0 mm optic size and 12.50 or 13.00 mm in all size.

2. Classification

According to the classification of medical devices in the council directive 93/42/EEC on medical devices, all implantable devices and long-term surgically invasive devices are in Class IIb. According to the Rule 8 of MEDDEV 2.4 /1.Rev. 9 June 2010, the intraocular lenses are Class IIb medical devices and class IIb medical devices are medium-high risk devices, with examples such are surgical lasers, infusion pumps (non-implantable), ventilators, intensive care monitoring equipment. Routes to compliance are the same as for Class IIa, with the addition of Type Examination of the product by the Notified Body, except for the full quality assurance route (EN 46001), where Type Approval is not necessary.

3. Clinical Data

According to the guidelines document MEDDEV 2.7.1 Rev.3 , Section 4 (5), the clinical evaluation is based on an assessment and analysis of clinical data pertaining to a medical device to verify the clinical safety and performance, associated benefits and risks of the device when used as intended by the manufacturer.

3.1 Market Experience

Acriva UD intraocular lens series are on the market since July of 2009. IOLs have established first in Turkey and have become the market leader. VSY Biotechnology have started to export intraocular lenses to all around the world like Germany, France, Italy, Brasil, Poland, Czech Republic, and so many other countries except United States of America.

Acriva UD intraocular lens series have demonstrated the effectiveness, safety and quality during these years. Acriva UD intraocular lens quality have evaluated and comparison with other products have done by clinical studies. Results have published in journals, also free papers and presentations have accepted to global ophthalmology congresses.

A multicenter clinical study is still going on in 7 centers in Turkey. Surgery technique and evaluations have standardized in all centers. 210 eyes of 105 patients have enrolled to the study. According to protocol inclusion criteria were;

- Patients must be undergoing primary intraocular implantation for the correction of aphakia following cataract extraction by phacoemulsification
- Age range should be between 40 - 80 years old
- Patients must be undergoing primary intraocular implantation for the correction of aphakia following cataract extraction by phacoemulsification
- Patients must sign a written Informed Consent form
- Patients should be planning and willing to have a surgery from both of their eyes

Exclusion criteria were;

- Patients with any anterior segment pathology (chronic uveitis, iritis, iridocyclitis, rubeosis iridis, corneal dystrophy, etc.).
- Patients who have uncontrolled glaucoma or who is under current treatment for glaucoma
- Patients with previous retinal detachment or retinal pathology
- Patients with proliferative diabetic retinopathy

- Patients with congenital bilateral cataract
- Patients who have diagnosed microphthalmus or aniridia
- Patients who have had ocular surgery in the operative eye
- Patients who have previously implanted monofocal intraocular lenses in the fellow eye
- Patients who have more than 0.75 D of corneal astigmatism
- Patients who have surgeries with medical complications

a) Capsulorhexis problems which affect centralization
b) If IOL is not in the bag
c) Damage of iris
d) Loss of vitreus
e) Damage of IOL

All patients included will have 1 year follow-up. Post-op 6.month results have been presented in symposiums of Turkish Ophthalmology Society. Visual acuity, contrast sensitivity, patient satisfaction, posterior capsular opacification have evaluated in all patients and 100% of patient satisfaction have been monitored. At this multicenter, prospective clinical study; foldable, hydrophobic surface, diffractive multifocal IOLs were impanted (Acriva UD Reviol MFB 625, VSY Biotechnology) with phacoemulsification surgery. Postoperative data were compared with postoperative 1.day, 1.week, 1.month, 3.month and 3.month data. Refraction values were recorded and uncorrected and best corrected near, intermediate, far visual acuities were measured at all included patients. IOL Powers were determined with immersion method of biometry (Optikon Bioline). Refraction values, uncorrected and corrected near,intermediate and far visual acuities, contrast sensitivity with and without glare at far (Vector Vision CSV-1000 HGT), near contrast acuity were measured at postoperative visits. Subjective describing of patients were examined and patient satisfaction were measured with VF-14 test. 210 eyes of 105 patient were recruited from 7 centers. Preoperative and postoperative values were recorded. Statistically preoperative and postoperative data, and also individually postoperative data were compared between eachother. There was statistically difference between preoperative and postoperative visits at uncorrected visual acuities of every distance. ($p<0.05$) Binocular uncorrected far, near, intermediate uncorrected and corrected visual acuity were respectively determined as 0.42 ± 0.2 ; 0.92 ± 0.2 , J 4 ± 1.2 ; J $1,1 \pm 0,3$ and J $4,4 \pm 1,2$; $1,16 \pm 0,5$. Monocular uncorrected near visual acuity

were determined as J1 at 183 eyes (87,5%) and J2 at 21 eyes (10%) in postoperative 6 months visit. Monocular uncorrected intermediate visual acuity were determined as J1 at 155 eyes(73%) and J2 at 40 eyes (19%) in postoperative 6 months visit. Contrast sensitivity values with and without glare at far distance have found in normal intervals at all spatial frequencies (cpd). Near contrast sensitivity have evaluated with Colenbrander card. Binocular near contrast sensitivity were observed 76,02 ± 14,04 in postoperative and 82 ± 4,21 in postoperative 6.month visit. There was statistically significant difference of contrast sensitivity for far and near between preoperative and postoperative 3.month visits. Posterior capsular opacification (PCO) have observed at 7 eyes (3,33%) in postoperative 6.month visit but only one eye (0,4%) had PCO that necessitated neodymium:YAG laser. VF-14 questionnaire have applied to included patients and on the scale of 100; 98,2 ± 4,6 score have found in postoperative 6.month visit. Acriva ^{UD} Reviol MFB 625 provided high level of visual acuity at all distances and patient satisfaction. While patients had good far and near visual acuity just in postoperative 1.day, intermediate visual acuity and contrast sensitivity improved over time due to neuroadaptation. . 100% of included patients have answered as "Yes" to " Do you offer this surgery and intraocular lens to your relatives? " question.

"Comparison of clinical outcomes with 2 small- incision diffractive multifocal intraocular lenses" have been published at Journal of Cataract and Refractive Surgery in 2012 Volume 38. Acriva ^{UD} Reviol and Acri.Lisa diffractive multifocal intraocular lenses have been studied by İzzet Can, MD, Başak Bostancı Ceran, MD, Gülizar Soyugelen, MD and Tamer Takmaz, MD in Atatürk Training and Research Hospital, Ankara, Turkey. Study design was a comparative case and 60 eyes of 32 patients have recruited to the study. The follow-up was for 6 month. Patients who had previous eye surgery or eye disease that could affect final visual acuity (eg, amblyopia, retinal or macular abnormalities), corneal pathology, glaucoma, or corneal astigmatism higher than 1.00 diopter (D) were not included in the study.Also excluded patients with intensive computer or car use and a meticulous personality because multifocal IOL implantation may be contraindicated in such cases. Uncorrected distance (UDVA), intermediate (UIVA), and near (UNVA) visual acuities; corrected distance visual acuity; distance-corrected intermediate and near visual acuities; and contrast sensitivity measurements with and without glare were determined. Early and late complications and subjective complaints were recorded and evaluated. Both IOLs provided excellent distance and near visual acuity and contrast sensitivity. Acriva ^{UD} Reviol IOL gave better intermediate distance results. All patients in both IOL groups reported spectacle independence for near

and distance. All with an Acriva Reviol MFM 611 IOL also reported spectacle independence for intermediate distance.In addition, all patients in both IOL groups said they would recommend the surgery and the IOL to friends and family. This indicates strong overall patient satisfaction. In conclusion, both microincision IOLs provided good outcomes in presbyopic cataract surgery and had high patient satisfaction. The Acriva Reviol MFM 611 IOL seemed to provide better intermediate visual acuity. You can find the article as Attachment 2.

Dr. Pavel Stodulka from Czech Republic, Gemini Eye Center, Zlin have presented post-op 6.month results of Acriva ^{UD} Reviol MFB 625 multifocal IOL in ESCRS Vienna. 44 consecutive eyes of 25 selected patients recruited at this prospective study. Typical patients seeks glass independency for routine daily activities have included and patients who need fine detail·resolution like jewellers, dentists & dental technicians, night drivers, professional pilots and professional welders have been excluded. Hyperopic patients included in to this study and implantation have been performed at 2.2 mm incisions. Multifocal diffractive IOL Acriva^{UD} Reviol (VSY Biotechnology, Turkey) provided very good uncorrected vision for distance, intermediate and near. YAG rate was 2% in 6 months. None of the patients uses spectacles regularly at 6 months follow up.

Comparison of visual acuity and contrast sensitivity between Acriva ^{UD} Reviol multifocal IOL and Alcon Acrysof monofocal IOL have been presented at ESCRS (European Society of Cataract & Refractive Surgery) in 2010 with post-op 3 month results by Levent Akcay,MD . Post-op 1 year results of Acriva ^{UD} Reviol have been accepted as free paper in 2011. Both of the studies' center was Kartal Training and Research Hospital, Istanbul, Turkey. Acriva UD Reviol had better contrast sensitivity results in comparison with Alcon Acrysof. Exclusion criterias were as follows: patients with an eye disease except cataract (glaucoma, diabetic retinopathy, ocular inflammation, senile macular degeneration and others), patients who have more than 1.5 D astigmatism, patients who have previously had an eye surgery. At pre-op, multifocal group patients' uncorrected far visual acuity was 0.16 and their corrected far visual acuity was 0.31. Three months after cataract surgery uncorrected far visual quality average reported 0.71, corrected far visual acuity average reported 0.85 of multifocal IOL implanted patients. At pre-op the monofocol group, had an uncorrected far visual acuity of 0.29, and corrected far visual acuity reported as 0.53. Three months after surgery uncorrected far visual acuity of 0.71 and corrected far

visual acuity reported as and 0.82. Statistically, there were no significant differences between monocular uncorrected and corrected far vision acuity averages amongst both groups. (p>0.05) We determined that after three months post-op, there was statistically no difference between multifocal and monofocal IOL when it comes to contrast sensitivity in regards to its mean-average at all spatial frequences. (p>0.05) At 12 cpd and 18 cpd frequences , multifocal IOL group's contrast sensitivity average was higher than monofocal IOL group's average but there was still no statistical mean difference. "Visual outcomes after implantation of an aspheric diffractive multifocal intraocular lens" study have accepted to ESCRS as a free paper. This study evaluated the Acriva UD Reviol's visual acuity and contrast sensitivity.

One-year postoperatively the mean log MAR uncorrected distance visual acuity, best corrected distance visual acuity, uncorrected near visual acuity, best distance-corrected near visual acuity and contrast sensitivity was significantly better than preoperative levels. The mean contrast sensitivity increased considerably at all spatial frequencies compared with preoperative levels. There was no patient complaint of severe glare or halos. You can find the papers as Attachment 3 and 4.

Details of the studies also can be found in Clinical Literature Report of Acriva ^{UD} IOLs.

3.1.1. Sold values, period of use

Acriva ^{UD} and Acriva ^{UD} Reviol IOLs series had the CE mark in 14.07.2009 and had a revision with a new model so the other CE mark had taken in 31.03.2010. Acriva ^{UD} intraocular series are on the market since July of 2009 and became the first in Turkey market by gaining a good share Acriva ^{UD} BB , Acriva ^{UD} BB Reviol, Acriva ^{UD} BB Toric and Acriva ^{UD} BB Reviol Toric had the CE mark in 29.04.2011. Acriva ^{UD} BB IOLs series' marketing and sale started after a while of CE mark. They are newly branded.

Since the first establishment on the market, total sales of Acriva ^{UD} IOLs are around 252.000, Acriva ^{UD} Reviol are around 20.000. As it is mentioned, Acriva UD BB IOLs series are new on the market so the marketing and sales are growing day by day. Sold value of all Acriva UD BB, Acriva ^{UD} BB Reviol, Acriva ^{UD} BB Toric and Acriva ^{UD} BB Reviol Toric IOLs is around 7.250.

According to Council Directive 93/42/EEC on medical devices, the intraocular lenses are long term medical devices because of intended for continuous use for more than 30 days. If any complication doesn't occur during or after cataract surgery, the intraocular lenses are intended to use in whole life.

3.1.2 Complaints

According to our VSY Biotechnology complaint management procedure there were no serious complaints in recorder forms about IOL's optical quality, diopter values or patient satisfaction and visual acuity. The complaints were related with general complaints like wrong IOL calculation with biometry and having inaccurate IOL powers. There was a complaint from one hospital about the marks on the IOL surface and after examination the IOL's manufacturing steps and having back-up from surgeon, it found that the problem happened because of viscoelastic marks.

The indications are notified in Instruction for Users. Below indications are listed in the Instruction for Users and also Clinical Literature Report.

Absolute contraindications might be;

- Progressive disturbances on the front segment of the eye such as rubeosis iridis, essential iris atrophy,
- Choroidal hemorrhage,
- Proliferate diabetic retinopathy,
- Severe optic nerve atrophy,
- Severe corneal dystrophy,
- Cataract associated with congenital rubella syndrome,
- Chronic uveitis
- Uncontrolled glaucoma

Relative contraindications like clinic indications that may be harmed or that may have an increased risk by IOL implantation. The individual evaluation of each case must left to the surgeon.

Surgical contraindications might be;

- Flat anterior chamber following clear lens extraction,
- Hyphema,
- Vitreous loss which is a contraindication for posterior chamber lens,
- Zonular damage and presence of,or predisposition to,retinal detachment

Any adverse event and explantation have not been observed related our products in VSY Biotechnology's two years vigilance system. There are no indications of side effects or interactions with medicines.In Ocular Implantation Test Report, there have found that no need to perform this test. Our current or previously supplied devices, any serious adverse event have not been reported in our vigilance system. There was no serious adverse event in the clinical studies.

3.1.3. Customer Satisfaction

Acriva^{UD} intraocular lens provides 100% of patient satisfaction according to published and recorded clinical studies. Multicenter clinical study, "Refractive lensectomy to correct hyperopia with Acriva^{UD} Reviol multifocal IOL implantation" by Pavel Stodulka, MD. "Comparison between 2 small-incision diffractive multifocal IOLs" by Prof. Dr. Izzet Can found that all patients in both IOL groups said that they would recommend the surgery and the IOL to friends and their family. This indicates strong overall patient satisfaction.

3.1.4. Technical Equivalent

The technical equivalence between standard products and Acriva ^{UD} IOLs have been considered. Acriva ^{UD} IOLs' raw materials are purchasing from Benz R&D Company which is selling raw materials to many intraocular lens companies. Benz R&D company have approved themselves and their products' quality with FDA approval. The Acriva ^{UD} IOLs show similarities with other commercially available products in

manufacturing process criteria, raw materials, biocompatibility and characteristic features. Acriva UD IOLs have slightly different designs, specifications when compared to other products in the market. Biocompatibility reports, clinical study results show that Acriva UD Reviol is equivalent and even better in intermediate distance, contrast sensitivity compared to other intraocular lenses.

3.2 Literature Data

Two main factors have been considered for the selection of literature data. The equivalence of investigated product Acriva UD intraocular lens and give importance to intraocular lens' effectiveness and safety were primary choices.

The equivalence refers to the clinical application (technically) and material properties of Acriva UD IOLs. It must be ensured that the data are used to show the relevant requirements of Directive 93/42/EEC on the conformity of the product. The following description is based treatment and structurally as well as its content to the requirements of the MEDDEV 2.7.1, Section 4.3. (5).

The current state of the art has been collected on a current literature review. For the research of different tools have been used like Google, PubMed, Medline. Scholar Google provides to map the entire state of the art outside of clinical publications. The other search tools are specialized publications with scientific background and cover a wide spectrum of available sources (journals, reports from professional associations, etc.)

3.2.1 Aim

The purpose of the literature review was to evaluate the clinical applicability of the safe Acriva UD intraocular lens series and thus demonstrate the benefits to the patient on the basis of available clinical information on comparable products.

The search of all available publications should ensure that no restricted view of the findings is generated. See Clinical Literature Acriva UD IOL series Report.

3.2.2 Biocompatibility

Acriva UD intraocular lens series conducted biological safety testing accordance with Medical Device Regulation. The biological safety testing is a biological evaluation of medical devices according ISO 11979-5:2006. This test guarantees the biological safety of medical devices and the device is accordance with its' intended purpose.

3.2.2.1 Biological Evaluation

Summary:

The Acriva UD intraocular lens is considered to be safe and secure. Following tests have done to evaluate the safety of the device and its' accordance with the intended purpose accordance with ISO standards.

Expanded test protocols may combine initial evaluation tests. These tests could be sensitization, irritation, systemic toxicity, acute systemic toxicity. All tests and reports have done according to 11979-5:2006.

In sensitization report; closed patch test for delayed-type hypersensitivity test, in irritation test; intradermal reactivity test, in genotoxicity test; Ames test, in cytotoxicity test; extract experiment method in acute systemic toxicity test have been done. In ocular implantation test, the aim was to evaluate the biocompatibility of an IOL material by surgical implantation of the material in the eye of appropriate animal model

Product:

Acriva UD intraocular lenses are artificial lenses replace with the natural crystalline lens of the human eye after cataract surgery and meets the requirements of patient's vision.

Classification:

The intraocular lens Acriva UD is a sterile, foldable, acrylic, state of the art product and according to the classification of medical devices in the Council Directive 93/42/EEC on medical devices, all implantable devices in Class IIb.

Available data of biological safety

According to Council Directive 93/42/EEC, Acriva ^{UD} IOLs are medical devices and have long term use because of they are intended for continuous for more than 30 days. All tests have been evaluated according to ISO 11979-5:2006.

Toxicological symptoms, sensitization potential, biocompatibility of an IOL material by surgical implantation to the eye of an appropriate animal model, irritation potential, presence and degree of cytotoxic effect have been evaluated and the potential of products to induce genetic changes by using test cells or organisms have been investigated according to ISO 11979-5:2006.

In sensitization report, closed patch test for delayed-type hypersensitivity test have done to evaluate potential of medical devices' sensitization. Material types have been determined according to raw material specifications for each model. Biocompatibility tests are performed based on each material type. After 24 h and 48 h observations, no lesion was observed for test material sample and controls.

In irritation test, intradermal reactivity test have been performed to evaluate irritation potential of devices. During the observations at 1 hour, 24hour, 48 hour, 72 hour no lesion was observed for both test material samples and negative controls.

In genotoxicity test, Ames test has been performed to evaluate the potential of products to induce genetic changes by using test cells or organisms. 5 specially constructed strains of Salmonella typhimurim have been used. (TA98, TA 100, TA 1535, TA 1537 and TA 1538) Test have been performed

with and without metabolic activation. The saline test article extract has not been considered to be mutagenic to Salmonella typhimurim tester strains TA98, TA 100, TA 1535, TA 1537 and TA 1538.

In cytotoxicity test, extract experiment method have been used to evaluate the presence and degree of cytotoxic effect on medical devices. All results on confluency, granulation, cell membranlysis, round cell, aggregation, vacuolization, peracute toxicity, picnotic cell have been checked and the test sample has been found noncytotoxic according to the test results.

In acute systemic toxicity test, extraction method have been used to evaluate the toxicological symptoms. Mice treated with test material extracts have been compared with their matching blank extracts. There were no differences between control and test animals during 72 hour observation period.

In ocular implantation test, the aim was to evaluate the biocompatibility of an IOL material by surgical implantation of the material in the eye of appropriate animal model. No adverse event have been observed related to our products.

Conclusion:

Biological evaluation of medical device in Class IIb, Acriva UD intraocular lens, is based both on information from extensive studies on the biocompatibility of various raw materials as well as information about the final product of experience with similar products as medical devices on the market. The data is sufficient for an assessment, so that no further testing according to ISO 11979-5 are required. Biological effects in terms of cytotoxicity, sensitization, intracutaneous reactivity, irritation, and also in terms of acute systemic toxicity can not be recognized.

3.4. Relevance and Acceptance of Data

The assessment of relevance for the purpose of this clinical evaluation is based on the search was carried out according to the available information. Thus, if any abstract shows relevant information on the key issue, they have considered to literature data. Literature search and data selection have done by using

scientific databases as Pubmed, Medline, google scholar-books and journals such as British Journal of Ophthalmology, Journal of Cataract and Refractive Surgery. The search on Google especially gave a general information and also commercially published articles. There have been paid attention to exclude commercially published articles, abstracts and free papers.

3.5. Clinical Relevance

Studies on humans and animals have been considered to clinical literature search. The intended use of the product, it's history and the development of surgery, intraocular lens technology have been searched to understand the manufacturing product, Acriva ^{UD} 's position in the market and to compare with other commercial products.

This first step in the process included developing a literature search strategy and conducting the search. The output is a list of citations to be screened and appraised. The intraocular lens technology has a long history of clinical use and have seen many innovations during these years. There was no difficulty to find relevant clinical literature. Search terms were important at the first step of preparing the Clinical Literature Report. There have developed search strategies i.e., accessed the right databases and constructed the Boolean search logic, that's why we could ensure that our search is comprehensive and that the output is on target. We have found that searches of multiple databases can be valuable such as Medline, PubMed and ScienceDirect.

Typical exclusion terms include non-human studies, single-subject case studies, indications that are not intended and publication dates constraints (e.g., limiting the timeframe to a period most relevant for the subject device). Each abstract have been reviewed for relevance. There have been kept track of the rationale for exclusion of studies which don't fit.

Once the relevant, high quality studies are identified, there have done the summarization of the findings. We've found that pulling key information from the studies into a table prior to drafting the prose summary is a valuable step. The table supports both the objectivity and the transparency of the report, by presenting both positive and negative results in a similar manner – there's no opportunity to emphasize one set of results over another. Also, the table serves as a helpful tool prior to drafting the prose summary (particularly when there are a lot of studies to summarize) – helping to make sure that

important information doesn't get lost along the way.

After the clinical data are collected, there have done a review of the risk analysis to ensure that it addresses all of the safety issues observed with intraocular lenses, and the product literature to ensure that it clearly communicates the intended use of the intraocular lenses, contraindications, and appropriate usage directions and warnings.

In addition to clinical trials, prospective and retrospective studies and other forms of assessment of clinical data on humans have been collected. The clinical study results of Acriva ^{UD} intraocular lenses also have been explained and the literature data have been included (Attachment 1: Clinical Literature Report)

3.6. Evaluation of Literature

There is a very large amount of clinical literature about intraocular lens is available. The lens is normally a clear, biconvex structure. It is located posterior to and loosely apposed to the iris. The lens is lined on its outer surface by the lens capsule, which is responsible for elasticity, allowing the lens to become more spherical in shape for accommodate. The first IOLs in modern medicine, developed and implanted by Ridley in 1949, were polymethylmethacrylate (PMMA) biconvex lenses which were implanted in the posterior chamber. Polymethylmethacrylate, acrylic, silicone, hydrogel, memory lenses, toric lenses and many more IOL designs and materials are available for implantation. Popular acrylic IOLs in clinical use namely hydrophobic such as Alcon Acrysof and Allergan AMO Sensar AR40 are examples of acrylic IOLs. Acriva ^{UD} intraocular lenses are hydrophobic acrylic with 25% of water content and thus provides better similarity with our natural lens and easy to fold while placing the IOL to cartridge&injector system. Especially Acriva UD BB models, which are yellow chromophore IOLs, have the same chromophore structure with our natural lens 3-hydroxy kynurenine according to raw material company Benz R&D. Also manufacturing process of Acriva ^{UD} IOLs is special because of eliminating IOLs which have low surface quality and MTF value.

Acriva UD IOLs offer a very wide diopter range for patients between -20 D to + 45 D and with good MTF results it is providing better contrast sensitivity and visual acuity in every distances according to the published papers. Multicenter clinical study and other single center studies worked on Acriva UD IOLs and good centralization, low pco rates and high patient satisfaction have been observed.

3.7. Critical Acclaim

The clinical literature indicates that the system designed by VSY Biotechnology regarding the relating to the intraocular lenses in the aspects of safety, performance, design characteristics, and intended purpose The literature reviewed was based on a demonstration of equivalence of the device to the device(s) that we have placed on the market. VSY Biotechnology's clinical research of Acriva UD and Acriva UD Reviol have been started since 27.01.2010 and there are studies still going on. There have not been any lens explantation and no serious adverse event have been declared at all studies. The clinical literature showed that there is no risk about product's material, biocompatibility or intended use. The risk might occur because of the user.

3.8. Conclusion

The critical assessment of the objective data collected from the currently available scientific literature/bibliography, evaluated together with our knowledge of the device and of the relevant clinical application/procedures, takes us to the assumption of the device suitably to the intended use and to the acceptability of any possible residual risk associated with its intended use, outweighed by the benefits provided to the user/patient.

Relatively in cataract surgery, most commonly in small incision surgeries and IOL implantation, IOL related complications fall into four general categories: traumatic, inflammatory, infectious, and optical. Inaccuracies in IOL calculations or selection, or postoperative IOL malposition, tilt, decentration, dislocation or dysphotopsia. Postoperative lens opacification/calcification may also result in the need of explant the IOL. Capsular and/or zonular trauma during phacoemulsification may compromise support for an in-the-bag or sulcus supported PCIOL, thus leading to postoperative decentration. Multiple studies have demonstrated that IOL dislocation or decentration occurs with an incidence rate between 0.2 and

0.3%. Signs and symptoms most common at the time of patient presentation include glare, halos, edge effect, reduced visual acuity, increased cylinder manifesting as a refractive shift or instability, iris chafing, uveitis-glaucoma-hyphema (UGH) syndrome, cystoid macular oedema, and corneal decompensation. Other presenting symptoms may be attributed to the edge of the optic, a peripheral Sommering's ring, or capsular opacity entering the pupillary aperture. It is important for the examiner to determine the suspected cause of IOL dislocation before diagnose.

In the published article and papers, there have not seen any adverse event which may result with explantation of the IOL. Pco rates, patient satisfaction and complications have also recorded and analyzed and no risk have been observed for implantation of Acriva ^{UD} intraocular lens series. Quality and Assurance department of VSY Biotechnology is taking care of complaints except clinical studies. According to Q&A, there have not seen any serious complaint except regular ones like wrong calculation of IOL power, inaccuracies in IOL calculations and some marks on the IOL surface because of viscoelastic remainds.

As a general rule, confirmation of conformity with the requirements concerning the characteristics and performances referred to in Sections 1 and 3 of Annex I, under the normal conditions of use of the device, and the evaluation of the side-effects and of the acceptability of the benefit/risk ratio referred to in Section 6 of Annex I, must be based on clinical data. The VSY Biotechnology comply with these requirements.

The Acriva ^{UD} series intraocular lenses (IOLs) perform the fuction of the eye's natural lens and they are designed as hydrophobic acrylic,square edge and exclusively foldable intraocular lenses by treating high quality advanced polymer material. They are sterilized by using autoclave. The biocompatibility tests and clinical studies with the Clinical Literature Report shows that there is no associated risk about the Acriva ^{UD} IOL series. The review of clinical evaluation and product literature is conducted to ensure that the indications for use and product claims are in line with, and supported by, the clinical data. If the product literature contains specific indications or claims and there is no evidence that those indications/claims are supported by clinical data, it's time to take a step back and reassess the product literature. Similarly, if the risk analysis contains significant risks and the only mitigation (or perhaps the major mitigation) is communication through product literature – it's important for us to check to ensure

that those messages are clearly stated. The greater the number of safety issues missing from the risk analysis, the lower our confidence in the overall risk assessment.

It may be noted that the Acriva ^{UD} IOLs proposed use is appropriate due to their composition and preparation, their design and performance can be expected for patients, users and potential safe use of third parties.

Istanbul, 2nd February 2012

Signature:

Dr. Süleyman Kaynak M.D.

Prepared under the instruction of

Professor of Ophthalmology Vitreoretinal Surgeon

Dr.Ercan Varlibas

General Manager

Report prepared by:

Tuğba Bulut

Clinical Research Associate

4 Attachments

4.1 Clinical Literature Report

4,2 Detailed Information of author ("instruction giver")

Clinical Literature Report for Acriva ^{UD} Intraocular Lens Series

Document information, authorship and approvals		
Prepared by: **Tugba Bulut**	Job title: **Clinical Research Associate**	Date and Signature:
Reviewed and released by: **Dr. Ercan Varlibas**	Job title: **Managing Director**	Date and Signature:

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Replaces Version 01.TF.A.17 Revision 03

Prepared by/Education:
Özge Özcan / Istanbul University Science Faculty Biology Department, Turkey (Support by Prof. Dr. Süleyman Kaynak, see Clinical Evaluation Report)

Device name/model	
Acriva UD	(Intraocular Lens)
Acriva UD Reviol	(Intraocular Lens)
Acriva UD BB	(Intraocular Lens)
Acriva UD BB Reviol	(Intraocular Lens)
Acriva UD BB Toric	(Intraocular Lens)
Acriva UD BB Reviol Toric	(Intraocular Lens)

Scope of the literature search [should be consistent with scope of clinical evaluation]

The term cataract refers to many opacity of various degree of the crystalline lens, which is normally almost completely transparent. There are a variety of methods to classify cataracts clinically, but pathological examination of cataracts may be difficult. The lens tends to survive fairly well post-mortern because it does not have its own blood supply, but it does not have the same gross appearance as its clinical appearance in vivo is written in Cataract Surgery book of R. F. Steinert. A cataract is any opacification (clouding) occurring within the lens of the eye that impedes the passage of light. Because light may not properly pass through the lens, cataracts make it virtually impossible to see clearly. When any person's cataract progresses to the point that daily tasks become difficult, it can create a significant interference with his or her quality of life. Most cataracts are age-related, although occasionally children may born with this condition. Cataracts may also develop after an injury, inflammation or disease. Risk factors for age-related cataracts include diabetes, prolonged exposure to sunlight, tobacco use and alcohol drinking. However vision can be restored by surgically removing the affected lens and replacing it by an artificial one. Changes within the lens nucleus are usually accompanied by changes in other parts of the lens. Aging causes nuclear, cortical and posterior subcapsular cataracts, each to varying degrees. When these changes cause a cataract in the lens, the patient may experience visual impairment, loss of contrast, dulling perception of color, and may also become increasingly myopic

Jacques Daviel started a revolution in ophthalmic surgery on April 8,1747. A couching procedure failed, so through an inferior corneal incision, he inserted a needle behind the lens and delivered it with some loss of vitreous. This was the first report of cataract extraction from its normal position behind the iris but because of opening the anterior capsule, this was an extracapsular extraction. Although the extracapsular (ECCE) and intracapsular (ICCE) methods were developed at nearly same time, it took much longer for the latter to gain popularity. In the last 100 years, old concepts have changed. The simple cataract extraction consisted of opening the anterior capsule and expressing the nucleus. This is the essence of a planned extracapsular cataract surgery (ECCE) as performed today, but there the similarity ends. Subsequent innovations sought to reduce complication rates by repositioning the location of the lens in the eye. The anterior chamber attracted interest for two reasons: first, the greater accessibility of the anterior chamber meant that patients might suffer less surgical trauma; secondly, the lens could be fixated in the angle just behind the scleral spur. The first anterior chamber lenses, introduced by Strampelli in the early 1950's, yielded results which were superior to the earlier posterior chamber models, yet a number of potential hazards were later recognized. In particular, the danger which surgical intervention and lens implantation presented to the delicate corneal endothelium was not anticipated. Corneal dystrophy was reported in many eyes and a secondary surgical intervention to explant lenses became a frequent occurrence.

Phacoemulsification is a technique which was invented and developed by Charles D. Kelman, MD, during the 1960s. He invented a method for performing the extracapsular cataract extraction (ECCE) through a small incision. Some years passed from when technique was invented to when it was actually put into practice. Because of the time needed to complete the experiments, tests and improvements, the irrigation/aspiration (I/A) system of phacoemulsification (Cavitron Kelman), the mother of modern phacoemulsification writes in Phacoemulsification, Principles and Techniques book by L. Buratto, L. Verner, D. Apple and M. Zanini. Phacoemulsification changed all the rules. The majority of cataract surgeries are performed by phacoemulsification using a surgical handpiece with a tip that vibrates at a very high frequency. This tip disintegrates or "emulsifies" the cataractous lens, a process which generates lens fragments or particles within the eye. This technique provides easier implantation and correct positioning of the intraocular lens (IOL) in the posterior chamber and cause a potential market for companies to manufacture foldable intraocular lens.

The lens is normally a clear, biconvex structure. Viewed from the side, it has an elliptical shape, measuring about 3.5-4.0 mm A-P by 9.0-10.0 mm in diameter. It is located posterior

to and loosely appossed to the iris. Lens transparency is a function of regular cell shape, regular cell volume, minimal extracellular space, and minimal scatter elements. The lens is held in place by the zonules, which attach it to the ciliary body. The zonular fibers arise from the basement membrane of the non-pigmented epithelium of the ciliary body and attach just anteriorly and posteriorly to the equator of the lens. Tension on the zonules is reduced by contraction on the ciliary muscle, allowing the lens to become more spherical in shape for accommodation. The lens is lined on its outer surface by the lens capsule, which is responsible for elasticity, allowing the lens to become more spherical in shape for accommodate.

The intraocular lens (IOL) is a surgically-implanted artificial lens which serves to replace the natural crystalline lens of the human eye. Changes in IOL design and corresponding surgical technique have been implemented to reduce the rates of surgical problems and postoperative complications associated with early models. The first IOLs in modern medicine, developed and implanted by Ridley in 1949, were polymethylmethacrylate (PMMA) biconvex lenses which were implanted in the posterior chamber. Despite their successes, a substantial number of problems resulted. Subsequent innovations sought to reduce complication rates by repositioning the location of the lens in the eye.[2] The anterior chamber attracted interest for two reasons: first, the greater accessibility of the anterior chamber meant that patients might suffer less surgical trauma; secondly, the lens could be fixated in the angle just behind the scleral spur. The first anterior chamber lenses, introduced by Strampelli in the early 1950's, yielded results which were superior to the earlier posterior chamber models, yet a number of potential hazards were later recognized. In particular, the danger which surgical intervention and lens implantation presented to the delicate corneal endothelium was not anticipated. Corneal dystrophy was reported in many eyes and a secondary surgical intervention to explant lenses became a frequent occurrence. Other advancements included the development of iris-fixated implants. However these lenses became obsolete due to long-term complications associated with iris erosion and lens instability. Iridocapsular lenses worked well when the haptic was captured by the lens capsule. However, if proper capsule fixation did not occur, the same situation arose as with iris-fixated lenses, e.g., iris erosion and lens instability, which lead to corneal decompensation. These problems led to the development of posterior chamber lenses which were initially placed in the ciliary sulcus, but most recently are routinely placed within the capsular bag for better fixation. The added distance between the cornea and the intraocular lens placed in the posterior chamber is associated with a reduction in endothelial cell "touch" and damage.

The axiom today in the rehabiliton of a patient with a cataract is „small is beautiful". To achieve this goal in present day cataract surgery, there are two basic technical considerations to be addressed by all ophthalmic surgeons : (i) removal of a cataractous lens through the smallest incisions, and (ii) the insertion of an intraocular implant, again, through the smallest of incisions. The first of these has been solved by the gradual evolution and recent innovations in the design of phaco machines. The advent of foldable intraocular lenses (IOLs) is a solution to the second consideration. An intraocular implant material should have biocompatiblity optical compatibility,mechanical compatibility.

Polymethylmethacrylate, acrylic, silicone, hydrogel, memory lenses, toric lenses and many more IOL designs and materials are available for implantation. Obvius advantages of small incision phacoemulsification, such as low-induced astigmatism, rapid visual rehabilitation, and less intraoperative and postoperative complications have led to increase in the use of foldable IOLs. Intraocular materials can be devided into two groups:

- Acrylate, methacrylate polymer
- Silicone elastomers

Hydrogel IOLs are unusual in that they tend to swell in contact in water. The monomer HEMA has been used successfully in copolymerization as a foldable IOL. "Once this IOL is implanted, it slowly unfolds and posterior capsule opacification is observed with this material. „ written in Clinical Ophthalmology and Surgical Approach book by Sandeep Saxena.

The first group contains rigid PMMA IOLs and foldable acrylic and hydrogel IOLs. These IOLs differ in refractive indices, water content, folding and unfolding behaviour and surface properties. Popular acrylic IOLs in clinical use namely hydrophobic such as Alcon Acrysof and Allergan AMO Sensar AR40 are examples of acrylic IOLs. Acrylic lenses have been manufactured in both one-piece and three-piece designs. Acrysof IOL has 5.5 mm or 6.0 mm optic sizes and PMMA haptics. Currently, one-piece acrylic IOLs available for clinical use. Because of its elasticity, soft acrylic IOLs unfold more slowly than silicone. Ist refractive index is highest (1.50) of any available IOL. Since this material is not compressible, therefore, insertion of an acrylic IOL requires slightly larger incision compared to silicone IOLs. The tacky surface of acrylic IOL tends to adhere to surgical instruments and wetting the lens or coating it with viscoelastic may manage this. Acrylic IOLs have lower rate of posterior capsule opacification, which is likely to be a function of lens design, especially the

truncated square edge optic.

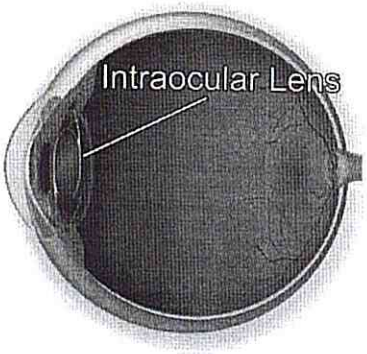
The primary purpose of this document is to provide a clinical evaluation report with the requirements concerning the characteristics and performance referred to MEDDEV.2.7.1 Rev.3. As a general rule, confirmation of conformity must be based on clinical data. This includes the requirements concerning the characteristics and performances referred to in Sections 1 and 3 of Annex I, under the device's normal conditions of use, and the evaluation of the side-effects and of the acceptability of the benefit/risk ratio referred to in Section 6 of Annex I.

This analysis is based on relevant and currently-available scientific publications regarding the safety, performance, characteristics, and intended purpose of intraocular lenses. The literature reviewed was based on a demonstration of the device's equivalence to those that we have previously placed on the market.

Device description, function and use;

Presently, the only method of curing a cataract is through surgery, which involves the removal of the affected lens. The lens capsule is left behind and the intraocular lens is implanted in the natural lens' place. Our products are around 6.00 mm in optical diameter and soft enough to be folded so that they can be placed into the eye through a very small incision; improvements in microsurgical techniques make it possible to remove a cloudy lens through an incision of only 3-3.5 mm, thus avoiding the need for stitches. In the hands of an experienced ophthalmologist, the entire procedure usually takes less than 30 minutes.

Anatomical location of an intraocular lens within the eye:



The main objective of our foldable intraocular lenses is to show the highest level of clinically-effective biocompatibility. The ideal IOL material should not incite any

inflammatory or immunological reaction. The implantation of intraocular lenses following cataract surgery can induce a foreign body reaction to the IOL as well as a lens epithelial cell reaction. This response is primarily caused by its biomaterial. Acriva ^{UD} series intraocular lenses, have a water content of 25%, are biologically compatible, and are made of a chemically UV-Absorbent acrylic material. They have Ultra Definition (UD) specification and 360^0 all square edge design. Acriva ^{UD} BB intraocular lens series have yellow chromophore structure which contains 3-hydroxykynurenine like our natural lens. BB series protect retina and decrease the risk of Age related macula degeneration disease by filtering the toxic effect of blue light between 400-480 nm. The Acriva ^{UD} series intraocular lens has an aspheric structure and aberration control. Due to its special optic design, it maintains high visual quality when correcting the positive spherical aberration of cornea. Haptic designs of monofocal, multifocal of clear and yellow chromophore IOLs are on three line. Acriva ^{UD} and Acriva ^{UD} Reviol intraocular lenses have C-loop, balance and plate haptic designs. Acriva ^{UD} BB and Acriva ^{UD} Reviol BB IOLs have C-loop and plate haptic designs. Acriva ^{UD} T, Acriva ^{UD} Reviol T, Acriva ^{UD} BB T, Acriva ^{UD} Reviol BB T models are toric IOLs and have plate haptic design. Plate haptic designs of all models provide micro incision cataract surgery with achieving implantation from 1.8 mm incision size. The introduction of bifocal and multifocal IOLs in the early 1980s offered cataract patients the potential to obtain a good range of uncorrected vision from near to far. The multifocal IOL takes advantage of the brain's natural ability to adapt to near, far, intermediate vision as it uses the different elements of the lens depending on what it is looking at. Multifocal IOLs do not offer true accommodating vision but rather are an alternative optical mechanism for providing distance and near vision. Acriva ^{UD} Reviol and Acriva ^{UD} BB Reviol IOLs offer far, near and intermediate vision to patients. The product is for single use only and has a shelf-life of three years. It is available in 6.0 mm optic size and 11.00 mm, 12.50 mm or 13.00 mm overall size.
Methods *(i) Date of search*
02.01.2012
(ii) Name of person(s) undertaking the literature search
Özge Özcan
(iii) Period covered by search

Literature data is collecting since three years.
Literature search for this report have been prepared in approx. one month.

Methods

(iv) Literature sources used to identify data:
- scientific databases – bibliographic (e.g. MEDLINE, EMBASE),specialized databases (e.g. MEDION)
- systematic review databases (e.g. Cochrane Collaboration)
- clinical trial registers (e.g. CENTRAL),
- adverse event report databases (e.g. MAUDE)
- reference texts
Include justification for choice of sources and describe any supplemental strategies (e.g. checking bibliography of articles retrieved, hand searching of literature) used to enhance the sensitivity of the search.

Scientific databases and published articles from journals were used to search and identify necessary data for this report.

PubMed, National Center for Biotechnology Information and Google books have been chose as scientific databases.

Journal of Cataract and Refractive Surgery, British Journal of Ophthalmology, Ophthalmology Source, Eurotimes, Archieves of Ophthalmology have been chose as journals to identify necessary published articles.

(v) Database search details:
- search terms (key words, indexing headings) and their relationships (Boolean logic)
- medium used (e.g. online, CD-ROM (including publication date and edition))
Attach copy of downloaded, unedited search strategy.

Search terms which have used in keywords, titles and methods part of articles were cataract, ICCE and ECCE, intraocular lens, hydrophobicity, multifocal intraocular lens, yellow chromophore structure, cataract surgery, phacoemulsification, cataract surgery complications, intraocular lens complaints, cataract extraction, ICCE and ECCE, Ophthalmology, retina/image quality, intraocular lenses, modulation transfer function.

(vi) Selection criteria used to choose articles

Articles are searched from reputable journals and attached importance to choose articles of known and well surgeons.

Articles which give importance to intraocular lenses' effectiveness and safety were primary choices. Commercial papers are excluded. The most important information to look for when reviewing an article can be summarized by the acronym "PP-ICONS," which stands for the following:

- Problem
- Patient or population
- Intervention

- Comparison
- Outcome
- Number of subjects
- Statistics

There have been paid attention to decide topic or problem important and relevant to cataract surgery and intraocular lenses and also clinical relevance of studies. If the problem studied were not sufficiently similar to your clinical problem, the results would not be relevant. If the patients in the study are not similar to your devices' patient area, for example if they are younger, older, a different gender or more clinically complicated, the results might not be relevant. We have tried to be sure that the comparison fits our questions.

The following variables as indicated in ISO 11979-5:2006 Ophthalmic implants – Intraocular lenses for ophthalmic surgery were searched in the newest validated for scientific articles.

- Safety and performance
- Optical and mechanical properties
- Biocompatibility
- Non-toxic
- Efficiency after cataract surgery
- Comparison results with other products

Objective criteria should be used when assessing the quality of clinical research reports and writing accurate, substantive report. Typical exclusion terms include non-human studies, single-subject case studies, indications that are not intended and publication dates constraints (e.g., limiting the timeframe to a period most relevant for the subject device). Each abstract have been reviewed for relevance. There have been kept track of the rationale for exclusion of studies which don't fit. Obtaining an answer needs to be understood from the concept of clinical relevance. Results of literature search don't just need to show that a treatment or intervention has an effect on a disease. Rather, they need to indicate that, that effect is relevant to the current clinical understanding, treatment and care for the disease or indication. They need to show that the effect is having a positive, meaningful impact upon a patient's prognosis and care or the reverse. This is a crucial point to consider in the development of protocols and in the careful analysis of results, as it is how regulators will review the results. In analysis, numbers are only half the work. One must employ lateral thinking to determine the relevant outcome of a study, followed by a discussion with the relevant medical device community to challenge and validate the study results.

4. Outputs
(i) Attach copy of literature citations retrieved from each database search
(ii) Data selection process
Attach flow chart and associated tables showing how all citations were assessed for suitability for inclusion in the clinical evaluation.

- Potentially relevant literature identified through the search (copy of all citations)
  Literature excluded, with reasons

Title	Published	Sourced	Date	Notes
Intra-Ocular Acrylic Lenses After Cataract Surgery	The Lancet A journal of British and foreign medicine, surgery, obstetrics,physiology,pathology,pharmacology,public health, and news	PubMed	1952	-
Intra-ocular acrylic lenses*10 years' development	British Journal of Ophthalmology	PubMed	1960	-
Multifocal Intraocular Lenses: Overview of Their Capabilities, Limitations And Clinical Benefits	Journal of Refractive Surgery	PubMed	2008	-
Through focus image quality of eyes implanted with monofocal and multifocal intraocular lenses	Optical Engineering	PubMed	1995	-
Distance and near contrast sensitivity function after multifocal intraocular lens implantation	Journal of Cataract Refract Surg	PubMed	2003	-

Title	Published	Sourced	Date	Notes
Adhesion Of Lens Capsule To Intraocular Lenses Of Polymethylmethacrylate , Silicone, And Acrylic Foldable Materials: An Experimental Study	British Journal of Ophthalmology	PubMed	2009	-
Biocompatibility of Intraocular Lens Materials	Curr Opin Ophthalmol	PubMed	2008	-
Multifocal Intraocular Lenses	Ophthalmology Clinics of North America	PubMed	2006	-
Clinical Assesment of Long-Term Safety and Efficacy of a Widely Implanted Polyacrylic Intraocular Lens Material	Am J Ophthalmol	PubMed	2000	-
Influence of glistenings on the optical quality of acrylic foldable intraocular lens	British Journal of Ophthalmology	PubMed	2001	-
Influence of tilt and decentration of scleral-sutured intraocular lens on ocular higher-order wavefront aberration	British Journal of Ophthalmology	PubMed	2006	-

Title	Published	Sourced	Date	Notes
Manual small incision cataract surgery in the United Kingdom	Int Ophthalmol	PubMed	2011	-
Improving Patient Outcomes	Eurotimes	Google	2010	-
Comparative rotational stability of single-piece open-loop acrylic and plate-haptic silicone toric intraocular lens	Journal of Cataract & Refractive Surgery	Google	2008	-
Current technique and results with a plate-haptic lens that effectively neutralizes corneal astigmatism at the time of cataract surgery.	Cataract & Refractive Surgery Today	PubMed	2012	-
Visual function and patient experience after bilateral implantation of toric intraocular lenses	Journal of Cataract & Refractive Surgery	PubMed	2010	-
Early Rotational Stability of the Longer Staar Toric intraocular lens	Journal of Cataract & Refractive Surgery	PubMed	2003	-
Cataract Surgery Should Improve Vision and Health	Supplement to Cataract&Refractive Surgery Healthy Blue Light and the Eye	Google	2008	-
Treatment of Circadian Rhythm Sleep Disorders with Light	Ann Acad Med Singapore	PubMed	2008	-

Title	Published	Sourced	Date	Notes
How much blue light Should an IOL transmit?	British Journal of Ophthalmology	PubMed	2003	-
Visual outcomes after implantation of an aspheric diffractive multifocal intraocular lens	www.escrs.org	Google	011	-
Refractive lensectomy to correct hyperopia with Acriva UD Reviol multifocal IOL implantation	www.escrs.org	Google	2011	-
Early phase results of multifocal Acriva Reviol MFB 625	www.escrs.org	Google	2011	-

- Literature retrieved for more detailed assessment
  Literature excluded from clinical evaluation, with reasons

Literature retrieved for more detailed assessment

Title	Published	Source	Date	Notes
The history of modern cataract surgery	Kugler Publications	Google book	1998	-
Phacoemulsification : Principles and Techniques	Slack Incorporated	Google book	2003	-
Cataract Surgery	Saunders Elsevier	Google book	1995	-
Phacoemulsification Third Edition,Volume 2	Jaypee Brothers Medical Publishers	Google book	2004	-
Clinical Ophthalmology Medical & Surgical Approach , 2nd Edition	Jaypee Highlights	Google book	2011	-

- Literature with relevant useable data included in the clinical evaluation, by outcome:
  - Device performance*
  - Device safety*
  - Device comparability (if applicable)

Title	Published	Source	Date	Notes
Comparative rotational stability of single-piece open-loop acrylic and plate-haptic silicone toric intraocular lens	Journal of Cataract & Refractive Surgery	Google	2008	-
Blue blocking IOLs	Cataract&Refractive Surgery Today	Google	January 2006	-
Rotational stability of the Acrysof SA60TT toric intraocular lenses: A cohort study	BMC Ophthalmology	Biomed Central	2008	-
Transmittance characteristics of ultraviolet and blue-light-filtering intraocular lenses	Journal of Cataract&Refractive Surgery	PubMed	2008	-
Blue light filtering Intraocular lenses in Phacoemulsification Cataract Surgery	Coll. Antrapol	PubMed	2007	-
Comparison of clinical outcomes with 2 small-incision diffractive multifocal intraocular lenses	Journal of Cataract&Refractive Surgery	PubMed	2012	-
Comparison of visual acuity and contrast sensitivity between aspheric monofocal and multifocal intraocular lenses	www.escrs.org	Google	2011	-

Table 1

Assessment of literature

The intraocular lenses have been tested and conform to the appropriate standard ISO 11979-5:2006.

This literature report shows many results, intraocular lenses' effects on eye and comparisons of other commercial products. You can see some articles' and books' summaries about the effects, efficiency, safety and comparison of different intraocular lenses.

- *Intra-Ocular Acrylic Lenses After Cataract Extraction; Harold Ridley M.D. Camb. , F.R.C.S ; 1952: 761.*

Operations of cataract have been practised for 3000 years. In this article, cataract history, extracapsular and intracapsular extraction details can be found. Extracapsular and intracapsular cataract extraction methods in these years are remarkable to read. Operation of cataract extraction and complications that might occur after acrylic lenses implantation have been evaluated. The author have written that in 1952, it is now possible to substitute for the opaque crystalline lens an artificial intra-ocular lenticulus capable of producing an excellent visual result. Such a lens can remain in an eye for at least two years without causing irritation. Aphakia have been explained detailed. It has written that "The manufacturers of perspex (Imperial Chemical Industries) advised their product 'Transpex I' as the variety of polymethyl methacrylate best suited to the purpose, because its composition and optical properties are constant, and, being unpolymerised, it avoids the risk of gradual liberation of free polymeriser which might cause chemical irritation." Also, the history of analyzing the refractive index and diameters during the manufacturing intraocular lenses had explained. There have mentioned that the earliest lenses were made 8.35 mm in diameter but in the human eye it was found, as it could be in no other way, that such a lens was too strong. This article includes the one of the first results of implanting an artificial intraocular lens in the eye. Before this technique's discover, just the extraction of crystalline lens was the method in cataract surgeries.The author had anticipated in the future that the pre – cataract refraction is accurately known and it is intended to insert acrylic lenses in both eyes, it might be desirable to produce lenses to individual specification to attain postoperative emmetropia. It is obvious that the anticipation of author have become real and still post-operative emmetropia is the key goal of every intraocular manufacturers.

- *Intra-ocular acrylic lenses*10 years' development; Harold Ridley M.D.; Brit. J. Ophthalmology 1960; 44: 712*

Harold Ridley have published this paper after ten years of the Intra-Ocular Acrylic Lenses After Cataract Extraction article. It is written that many designs for intra-ocular acrylic lenses which have been and still are being produced show not only that interest in the subject is growing but that the ideal pattern of lens has not yet been devised. When the idea of artificial lenticuli was first conceived in 1948, it was decided, in spite of some evident disadvantages, to place the lens in the natural position rather than in the anterior chamber. Though the mechanical shortcomings of the posterior chamber situation were evident, an attempt was made to copy nature as closely as possible both anatomically and optically. At that time it was feared that a lens resting in the angle of the anterior chamber would inevitably give rise to corneal opacity. Looking back over the past 10 years, it is apparent

that the posterior chamber artificial lenticulus has, for the time at least, fallen out of favour. If a posterior chamber lens is inserted and properly centered after an efficient extracapsular extraction in an eye with a normal iris and an intact zonular capsular bulkhead, not only is the visual acuity satisfactory but almost natural sight is restored. In short if the eye is free from inflammation and the lenticulus is in perfect position, its rim being visible through the peripheral iridectomy, a good and apparently permanent result can be expected. The investigator have been evaluated the posterior chamber lenses', postoperative treatment and early complications. Because of not having new technology phacoemulsification devices, surgeries and healing process of patients were not that fast like today. It has written that patients were leaving hospital in 12 days unlike today. H. Ridley have written that; "When the patient leaves hospital about the 12th day after operation, there will be a deposit of fibrinous exudate on the anterior surface of the lens which precludes good visual acuity. Normally this deposit undergoes gradual absorption during the succeeding 6 to 8 weeks but, if the pupil is allowed to constrict beyond the optimal 3*5-mm." and also at the conclusion of the paper have declared that In spite of thé complications discussed above, the majority of cases, even some of the earliest series, continue to be satisfactory."

Ridley have written early and late complications regarding the cataract surgery and acrylic intraocular lens implantation. The cause of late complications can generally be traced to bad surgery or inadequate aftercare. In the early stages an attempt may be made to re center the lens and raise the iris over its edge, but firm adhesions soon develop and usually render full replacement impossible. A lens lying free in the anterior chamber and resting against the cornea must be removed by a simple operation to prevent irreversible dystrophy. It was soon found that insertion of a posterior chamber acrylic lens after deliberate intracapsular extraction was followed in the majority of cases by dislocation and this procedure was abandoned. These technical modifications have greatly improved the prospects of good and lasting results, for since they were introduced there have been few posterior dislocations.

- *Multifocal Intraocular Lenses: Overview of Their Capabilities, Limitations and Clinical Benefits, Micheal C.Knorz, MD; Journal of Refractive Surgery 2008; 24: 216*

Approximately 90 million people in the United States are currently presbyopic. IOLs, which traditionally have been targeted to correct for distance vision, have recently been modified to improve the condition of presbyopia. These technologies are also being developed and used in cataract surgery to replace the functioning of the natural crystalline lens, improving the quality of life of cataract patients by reducing their need for spectacles. M.C.Knorz have evaluated multifocal intraocular lenses in this editorial. At that time, multifocal intraocular lenses were on the market since 20 years. Contrast sensitivity testing has confirmed the decline in visual performance with age, and wavefront science has helped explain that this decline occurs because of increasing spherical aberration of the human lens. Because the optical wavefront of the cornea remains stable throughout life, the lens has started to come into its own as the primary locus for refractive surgery. It is written that; monovision remains the most frequently used compromise to address the reading disability caused by presbyopia. Monovision typically provides approximately 1.50 diopters of depth of field. The author have explained about multifocal IOLs' specifications, preferable techniques, advantages and disadvantages.

Multifocal IOLs allow multiple focal distances independent of ciliary body function and capsular mechanics. Once securely placed in the capsular bag, the function of these lenses will not change or deteriorate. Additionally, multifocal lenses can be designed to take advantage of many innovations in IOL technology that have already improved outcomes, including better centration, prevention of posterior capsular opacification, and correction of higher order aberrations. The fundamental challenge of multifocality remains the preservation of optical quality, as measured by modulation transfer function on the bench or

contrast sensitivity function in the eye, with simultaneous presentation of objects at two or more focal lengths. Another significant challenge for multifocal technology continues to be the reduction or elimination of unwanted photic phenomena, such as halos. One question that the designers of multifocal optics must consider is whether two foci, distance and near, adequately address visual needs. Acriva ^{UD} IOL series provide far and near focus with intermediate vision by neuroadaptation. .Aberrations cause incoming light that would otherwise be focused to a point to be blurred, which, in turn, causes a reduction in visual quality. This reduction in quality is more severe under low luminance conditions because spherical aberration increases when the pupil size increases. Pupil independent multifocal intraocular lenses which are diffractive ones provide better visual acuity in every light condition. The advantages of diffractive optics when compared with refractive optics for the correction of presbyopia have been well established in pseudophakic bifocal IOL trials in Europe and the United States. These two items, the limitations of keratorefractive surgery and the advances in diffractive optics, have rekindled major interest in anterior chamber IOLs as potentially the best method of correcting moderate to severe ametropia as well as presbyopia.

The editorial ends with the conclusion of that multifocal IOLs offer a useful compromise and are here to stay until a means to restore the accommodation of the human lens is discovered.

- *Through focus image quality of eyes implanted with monofocal and multifocal intraocular lenses; Artal P, Marcos S, Navarro R, et al.; Opt Eng 1995; 34:778*

Several kinds of studies on the optical performance of different types of IOLs have been performed: optical bench testing, ray tracing, and clinical studies on the visual performance (mainly acuity and contrast sensitivity) in patients implanted with IOLs. All those studies are useful to test the optical design in new IOL types or to evaluate the clinical success of IOL implantation. Clinical (psychophysical) tests can be affected by non-optical problems in the patients' visual systems. All these facts are good reasons for the need for direct optical measurement of retinal image quality in eyes implanted with IOLs. This should be the most appropriate kind of method to obtain a final complete evaluation of the optical performance of implanted lenses. In this paper, there have extended the double-pass method to investigate the actual differences of image quality as a function of focus in eyes implanted with two different types of IOLs: monofocal and bifocal. New designs of multifocal IOLs permit to extend the depth of focus by different means. The objective determination of through focus image quality after the IOL is implanted in the eye would permit a complete evaluation of the lenses. In this study, a double-pass method is applied to determine the retinal image quality of eyes implanted with intraocular lenses (IOLs). The double-pass technique is based on imaging an object onto the retina. Then a fraction of the light is reflected back and the external retinal image (aerial image) is used to estimate the aberrations of the eye, point and line spread functions, and the ocular MTF. The effect of focus on image quality was measured in two groups of patients that had been implanted with either monofocal or multifocal IOLs. Measurements have been obtained in two groups of four patients each, implanted with either monofocal or multifocal IOLs. They ranged from 50 to 71 years old. Some of the patients implanted with monofocal IOLs had residual astigmatism (up to 1 D). All the patients were chosen after a long postoperatory period and based in clinical success. They passed a complete ophthalmological exam with good records of clean capsules, iris shape, pupilary reflex, visual acuity, and contrast sensitivity. For comparison purposes, the two lenses used in this study were also tested in an optical bench in air to record the single pass point spread functions of IOLs alone at different focuses (from —6 D to 3 D). From these measurements, MTFs and image quality parameters were computed. The results show that the overall retinal image quality is reduced in eyes with multifocal lenses with respect to that implanted with monofocal IOLs. The retinal image quality results

in the case of multifocal IOLs are more homogeneous. On average, eyes implanted with monofocal IOLs have a modulation in the retinal image a factor of 2 larger than that in multifocals. Although the depth of focus is larger in multifocal IOLs (4 to 5 D) than in the monofocal IOLs (2 to 3 D), some patients implanted with monofocal IOLs have higher image quality than those implanted with multifocal IOLs in a range of about 4 D around the best focus. Depth of focus depends on pupil size. The results presented in this paper correspond to a 4-mm pupil diameter. This is a typical pupil size for indoor situations common in normal conditions for reading. All the results of depth of focus will be different for smaller or larger pupil diameters. Image quality results as a function of focus are qualitatively different when obtained in vitro and in vivo measurement. The implantation process and the effect of the eye's dioptrics reduce the final image quality in the eye in comparison with the intraocular lens. In the case of bifocals IOLs, in vitro measurements show clearly defined peaks for near and far focus, whereas in the implanted eye, there is a range with a similar image quality. In conclusion, this paper demonstrates the usefulness of the double-pass method in assessing the image quality in eyes after implantation of IOLs in cataract surgery.

- *Distance and near contrast sensitivity function after multifocal intraocular lens implantation;Robert Monte´s-Mico´, OD, MPhil, Jorge L. Alio´, MD, PhD;J Cataract Refract Surg 2003;29:708*

Multifocal intraocular lenses (IOLs) are designed to reduce dependence on eyeglasses after cataract surgery, and the IOL is gaining acceptance as a potential refractive surgical option in selected patients. Monofocal IOLs were designed to provide vision at 1 distance, typically far. Patients with traditional monofocal IOLs usually require glasses for near distance tasks such as reading. Patients with multifocal IOLs use 2 focal points for sharp imaging on the retina depending on the object's distance. Multifocal IOLs enable projection onto the retinal plane of images set at various distances. Patients can use this feature after becoming accustomed to the IOL, which involves a cortical process of elaboration and selection.23 Because patients need time to become accustomed to the IOL, the visual response may vary depending on the time after IOL implantation. Therefore, the differences in some studies may reflect the different evaluation times after IOL implantation. The objective of this study is to see whether there is a correlation between contrast sensitivity at distance and near over a period of time after multifocal IOL implantation. To confirm whether correlations identified with the multifocal IOL are accurate, we also examined contrast sensitivity in age-matched control eyes with monofocal IOLs. Contrast sensitivity was measured with the Stereo Optical Functional Acuity Contrast Test at distance and near in 21 patients with a refractive multifocal IOL (Array SA-40N, AMO). A control group with a monofocal IOL (SI-40NB, AMO) was also studied to allow comparison of results. Contrast sensitivity was measured 1, 3, 6, 12, and 18 months after IOL implantation. The Array (AMO) is a 5-zone refractive multifocal IOL that has been approved for clinical use in the United States and Europe. Patients with multifocal IOLs use 2 focal points for sharp imaging on the retina depending on the object's distance. Multifocal IOLs enable projection onto the retinal plane of images set at various distances. Patients can use this feature after becoming accustomed to the IOL, which involves a cortical process of elaboration and Selection. In conclusion, the Array multifocal IOL provided excellent contrast sensitivity at distance that was comparable to that obtained with monofocal IOLs between 3 months and 6 months after implantation. At near vision, results improved over time but were always lower than at distance and in monofocal near corrected patients, although acceptable to avoid near visual function degradation. In all cases, contrast sensitivity improved over time, suggesting a learning process resulting from a brain adaptation phenomenon that overcomes the contrast sensitivity decrease at the initial stages after surgery. This article proves that brain adaptation is very important especially in contrast sensitivity.

- *Multifocal Intraocular Lenses; Stephen S. Lane, MDT, Mike Morris, PhD, Lee Nordan, MD,Mark Packer, MD, FACS, Nicholas Tarantino, OD, R. Bruce Wallace III, MD, FACS; Ophthalmol Clin N Am 19 2006: 89*

Laboratory studies of accommodation have confirmed the essentials of Helmholtz's theory and clarified the pathophysiology of presbyopia. What remains is for optical scientists and materials engineers to design an intraocular lens (IOL) that provides unaberrated optical imagery at all focal distances. This lens must compensate for any aberrations inherent in the cornea and either change shape and location or employ multifocal optics. Accommodative IOLs have made their debut around the world (CrystaLens, Eyeonics and 1CU [Aliso Viejo, California], HumanOptics [Erlangen, Germany]). Clinical results indicate that restoration of accommodation may be achieved, at least to some extent, with axial movement of the lens optic. Another unique design involves the light adjustable lens, a macromer matrix that polymerizes under ultraviolet radiation (LAL, Calhoun Vision, Pasadena, California). An injectable form of this material might enable surgeons to refill the capsular bag with a flexible substance and subsequently adjust the optical configuration to eliminate aberrations.
Although these designs show promise for restoration of accommodation and elimination of aberrations, multifocal technology also offers an array of potential solutions. Multifocal IOLs allow multiple focal distances independent of ciliary body function and capsular mechanics. Once securely placed in the capsular bag, the function of these lenses will not change or deteriorate. Newer dual optic designs (Synchrony, Visiogen [Irvine, California], and Sarfarazi, Bausch & Lomb [San Dimas, California]) may allow greater amplitude of accommodation. Flexible polymers designed for injection into a nearly intact capsular bag continue to show promise in animal studies. In this article, a global multicenter open label study's results are shown. Some study results have explained. One of them is completed in the United States and Europe comparing bilateral implantation of the AcrySof ReSTOR apodized diffractive IOL with that of the AcrySof MA60BM monofocal IOL. The trial implanted 566 subjects with the AcrySof ReSTOR IOL and 194 subjects with the AcrySof MA60BM. The study examined patients 120 to 180 days postoperatively from the second eye implant. Patient inclusion criteria included age over 21 years, bilateral cataract removal using phacoemulsification, with an IOL implanted in the capsular bag, and completion of bilateral implantations within 90 days of each other. The inclusion criteria required a potential postoperative visual acuity of 20/40 (0.34 logMAR) or better, astigmatism less than 1.0 D, and clear intraocular media. Data were collected for distance and near visual acuity, pupil size, contrast sensitivity, night driving, visual disturbances, quality of life, spectacle use, and safety, and sub studies collected data on defocus and intermediate vision. In addition to efficacy data, safety data were collected. Data were collected for distance and near visual acuity, pupil size, contrast sensitivity, night driving, visual disturbances, quality of life, spectacle use, and safety, and sub studies collected data on defocus and intermediate vision. The results show that except near visual acuity patient satisfaction differs too much between monofocal and multifocal IOLs. Freedom from spectacle wear was categorized by subjects selecting "never" in queries regarding the use of glasses postoperatively. Eighty percent of patients who were implanted with bilateral ReSTOR lenses reported never wearing glasses, and 17% reported occasional use of spectacles. Only 8% of the monofocal group reported spectacle freedom. Multifocal lenses can be designed to take advantage of many innovations in IOL technology that have already improved outcomes, including better centration, prevention of posterior capsular opacification, and correction of higher order aberrations.

- *Biocompatibility of Intraocular Lens Materials; Liliana Werner Current Opinion in Ophthalmology 2008;19:41–42*

The article provides a review of recent findings regarding uveal and capsular biocompatibility of materials used in the manufacture of intraocular lenses (IOLs) that are currently available or under development. Intraocular lenses are being progressively implanted in much earlier stages of life (refractive lens exchange, pediatric implantation) and are expected to remain in the intraocular environment for many decades. Each currently available foldable acrylic lens design is manufactured from a different copolymer acrylic, with different refractive index, glass transition temperature (above this temperature the polymer exhibits flexible properties and below it remains rigid), water content, mechanical properties, etc. Materials used in intraocular lens manufacture should, therefore, insure long-term uveal and capsular biocompatibility, as well as ultimate transparency after implantation. The biocompatibility of intraocular lens materials should be assessed in terms of uveal biocompatibility, related to the inflammatory foreign-body reaction of the eye against the implant, as well as in terms of capsular biocompatibility, determined by the relationship of the intraocular lens with remaining lens epithelial cells within the capsular bag.

Overview of biomaterials used in the manufacture of IOL optics have explained in the paper. Biomaterials (polymers) used for the manufacture of IOL optics can be divided into two major groups: acrylic and silicone. Acrylic lenses can be further divided as follows: rigid, e.g. manufactured from poly (methyl methacrylate) (PMMA); foldable, manufactured from hydrophobic acrylic materials. Inflammatory response of the eye after IOL implantation, lens epithelial cell proliferation: after intraocular lens implantation: capsular biocompatibility, anterior-posterior capsule and interlenticular opacification, long term biocompatibility: biomaterial calcification problems have been evaluated separately. More recently, yellow hydrophobic acrylic IOLs containing a blue light-filtering chromophore (besides the standard chromophore for protection against UV radiation) have become available in the market. The addition of a covalently bonded yellow dye results in an IOL UV/visible light transmittance curve that mimics the protection provided by the natural, precataractous adult human crystalline lens. There is indirect evidence showing that this addition may result in a reduction of the risk for macular degeneration or its progression. Clinical studies demonstrated that the biocompatibility of this yellow lens is overall similar to that of the same lens manufactured without the blue light-filtering chromophore.

Secondary cataract or PCO is the most common postoperative complication of cataract surgery. This complication has been the object of a recently published review. In terms of IOL material capsular biocompatibility, the 'sandwich' theory states that a hydrophobic acrylic IOL with a bioadhesive surface would allow only a monolayer of LECs to attach to the capsule and the lens, preventing further cell proliferation and capsular bag opacification. We performed two immunohistochemical studies on the adhesion of proteins to different IOLs that had been implanted in human eyes obtained postmortem, which confirmed the presence of greater amounts of fibronectin (protein mediating adhesion) on the surfaces of a hydrophobic acrylic lens (AcrySof, Alcon). Even though differences among materials exist, however, in terms of PCO prevention it appears that the geometry of the lens, with a square posterior optic edge, is the most important factor. Animal as well as clinical studies also demonstrated that this feature should be present for 360 ^{0}around the optic, as the optic–haptic junction of single piece lenses may represent sites where the edge barrier effect is absent. Long-term biostability of new IOL biomaterials may be assessed by tests such as those used in accelerated hydrolytic and UVaging studies, among others. Considering the reports on IOL optic calcification of some hydrophilic appears to be an excellent model for screening new materials for calcification potential. The biocompatibility of IOL materials should be assessed in terms of uveal biocompatibility, related to the inflammatory foreign-body reaction of the eye against the implant, as well as in terms of capsular biocompatibility,

determined by the relationship of the IOL with remaining LECs within the capsular bag. Research on factors to optimize IOL biocompatibility, minimizing postoperative inflammatory reaction and preventing opacification within the capsular bag, as well as any form of IOL opacification, is increasing in significance with the increase in popularity of procedures such as refractive lens exchange.

- *Influence of glistenings on the optical quality of acrylic foldable intraocular lens; Tetsuro Oshika, Yasuhiko Shiokawa, Shiro Amano and Kikuo Mitomo; Br. J. Ophthalmol. 2001;85;1037*

The use of foldable intraocular lens (IOL) has been increasing as these lenses most enhance the benefits of phacoemulsification cataract surgery. Among the foldable IOLs, acrylic foldable IOLs are especially growing in popularity because of stable clinical results and a low incidence of posterior capsule opacification. There are, however, several complications of acrylic foldable IOLs, one of which is the formation of glistenings in the optic. This study's aim is to assess the influence of glistenings on the optical quality of acrylic foldable intraocular lens. The glistenings are thought to be fluid accumulation in the microvoids of the optic, which are likely to be caused by temperature changes and not material changes. It has been known that glistenings can be induced in vitro by warming a lens and then cooling it to room temperature. In this study, there have been produced an in vitro model of glistenings in the acrylic foldable IOL and have been evaluated its optical quality.

Acrylic foldable IOLs (MA60BM, AcrySof, Alcon Surgical, FortWorth, TX, USA) of +15.0 dioptres in the wagon wheel packaging were used in this study. The optical bench tests were carried out in accordance with the ISO standard when the test methods are described in the standard (ISO 11979 2:1999(E) Optical properties and test methods). Resolving power of the IOL was determined using the optical bench apparatus. In the current experiment, there have immersed the IOLs in water at 37°C for 48 hours and then at 25°C for 24 hours. After the immersion, the IOLs were kept in the air and various degrees of glistenings were created by changing the duration of exposure to the air. The longer the duration of exposure to the air, the more the glistenings faded. The intensity of backward scattering was assessed by measuring spectral transmittance with a spectrophotometer. Modulation transfer function(MTF) have been measured in a model eye at a 3 mm aperture. In the current study, there have experimentally induced glistening particles in the optic of acrylic foldable IOLs, ranging in degree from 1+ to 4+ . Although the 1+ glistenings could be photographed, their instability made the optical bench test on this lens impossible. Nevertheless, judging from the experimental results of the 2+ glistening lens, data of the 1+ glistening IOL should have been similar to those of the control lens. Other optical parameters tested in the current study were scattering, MTF, and resolving power at various contrasts with and without the veiling glare light source. As shown in the results, the glistenings up to 3+ had little influence on these parameters. The degrees of scattering calculated by equation 1 were 3.9% for the control lens, 5.9% for the lens with 2+ glistenings, 11.1% for 3+ glistenings, and 21.7% for 4+ glistenings. In the measurements of spectral transmittance, the IOLs with clinically compatible level of glistenings (2+ and 3+) showed results similar to those of the control lens. On the other hand, very severe glistenings (4+) deteriorated spectral transmittance especially at longer wavelength. The diameter of glistening particles has been reported to be approximately 10–20 μm. Other optical parameters tested in the current study were scattering, MTF, and resolving power at various contrasts with and without the veiling glare light source. As shown in the results, the glistenings up to 3+ had little influence on these parameters. In practice, glistenings are frequently seen in acrylic foldable IOL after several months postoperatively but very few cases have led to significant clinical consequences. Moreover, the formation of glistenings is not limited to acrylic foldable IOL, but can be seen

with poly(methylmethacrylate) and silicone IOLs. As in acrylic foldable IOL, glistenings in these latter biomaterials have not been shown to cause any adverse clinical sequelae.

- *Treatment of Circadian Rhythm Sleep Disorders with Light: Joshua J Gooley; Ann Acad Med Singapore 2008;37:669-76*

The human circadian system is normally synchronised with the solar day, insuring that alertness and performance peak during daytime hours and consolidated sleep occurs during the night. In circadian rhythm sleep disorders, the pattern of sleep-wake is misaligned with the patient's circadian system or the external environment, resulting in insomnia, fatigue, and deterioration in performance. Appropriately-timed exposure to bright light can reset the timing of sleep and wake to the desired times, and improve sleep quality and daytime alertness. In the absence of environmental time cues, cycles of sleep-wake, physiology, and gene expression continue to exhibit a near-24-hour circadian rhythm. This article, the investigators have examined the physiological basis for bright light therapy, and we discuss the application of light in the treatment of circadian rhythm sleep disorders including advanced and delayed sleep-phase disorder, free-running disorder (nonentrained type), shiftwork disorder and jet lag disorder. The review article explains that light treatment of circadian rhythm sleep disorders is mediated exclusively by the activation of ocular photoreceptors. Specialised retinal ganglion cells which contain the blue light-sensitive photopigment melanopsin project directly to the circadian clock in the SCN. Consistent with a primary role for melanopsin in mediating the effects of light therapy, clinical studies have established that exposure to bright monochromatic blue light (460 nm) is more effective than green light (555 nm, the peak of sensitivity of the three-cone photopic visual system) at phase-resetting the circadian system and suppressing nighttime release of the pineal gland hormone melatonin. Acriva ^{UD} BB IOL series filter the blue light just until 480 nm not like other IOLs which filter until and beyond 500nm. This article proves that these IOLs are badly effective in circadian rhythm with causing sleep disorders.

Bright light therapy for circadian rhythm sleep disorders is an effective treatment option for sleep-wake disturbances. Appropriately-timed exposure to bright light can shift the sleep-wake cycle to earlier or later times, in order to correct for misalignment between the circadian system and the desired sleep-wake schedule. Laboratory studies have established that the human circadian system is exquisitely sensitive to light, and that the efficacy of light in resetting circadian rhythms is determined by the dose, spectral content, and time-of-day that the light is administered. In field studies and in the clinical setting, these principles have been applied successfully to treat circadian rhythm sleep disorders.

- *Cataract Surgery Should Improve Vision and Health: Martin A. Mainster, Patricia L.Turner;Cataract and Refractive Surgery Today Supllement Healthy Blue Light and the Eye March 2008;7.*

It has been known for over 50 years that blue light is important for vision in dim environments. A rapidly growing body of scientific evidence now documents that blue light is vital for optimal systemic and mental health. Blue-blocking IOLs were designed almost a decade before the discovery of retinal ganglion photoreceptors and their important role in good health and quality of life. UV-blocking IOLs have provided pseudophakes with their best possible photoreception for over 3 decades. Blue blocking IOLs sacrifice rod and retinal ganglion photoreception for ineffective photoprotection against an unproven hazard. The phototoxicity-AMD hypothesis posits that photic retinopathy (retinal phototoxicity) from repeated environmental light exposure causes AMD. Many mechanisms other than light have been postulated for AMD, including choroidal sclerosis, RPE dysfunction, genetic defects, retinoid deficiency, and inflammation. Blue light provides 7% of cone-mediated photopic vision and 35% of rod-mediated scotopic sensitivity.

Thus, blue light is much more important for vision in dim than bright environments. Cone photoreceptors image headlight-illuminated objects during night driving, but rods provide the remaining visual field. Driving, mobility, and peripheral vision problems are all associated with rod- but not cone-mediated dark adaptation parameters. When you get up at night and lighting is too dim to see color, you are using rod-mediated vision. The spectral efficiency of melatonin suppression peaks at 460 nm in the blue part of the spectrum. This blue-light dependence arises because retinal ganglion photoreceptors express the blue-light sensitive photopigment melanopsin. Blue light provides 55% of melatonin suppression, which is a standard surrogate for retinal photic input to nonvisual brain centers, including the suprachiasmatic nuclei. Circadian rhythmicity is often disturbed in aging and in people with insomnia, depression, and memory loss. Circadian dysfunction occurs in coronary artery disease, hypertension, diabetes, Alzheimer's disease, and many forms of cancer. Health risks are correlated with the degree and dúration of circadian disruption. Numerous clinical studies have shown the risks of disturbed circadian photoentrainment and the benefits of optimal rhythmicity. According to Mainster's graphic, it has been explained that blue-blocking IOLs offer 14% to 21% less scotopic sensitivity than UV blockers. This graphic can be also found in Acriva ^{UD} BB IOLs' brochure and shows the light loss from blue blocking IOLs in scotopic and photopic conditions between 350 to 700 nm. The filtering nanometers show that light loss increase while the filtering range getting closure to 500nm. Acriva ^{UD} BB IOLs are providing better vision in dark environments too by not blocking the blue light and just filtering until 480 nm.

ARTICLE AND FREE PAPERS OF VSY BIOTECHNOLOGY

- *Comparison of visual acuity and contrast sensitivity between monofocal and multifocal intraocular lenses ; L.Akcay, N.Tutas Gunaydın, I. Sayman, A. Kaplan, O. Dogan;ESCRS XXVIII Congress of the ESCRS;2010*

Multifocal intraocular lenses (MIOL) are enhanced lenses that provide far and near vision without the use of spectacles for patients after cataract extraction. With multifocal IOLs, images of near and far objects' can focus at the retina at the same time to provide near-far vision while the monofocal IOLs achieve sharp vision solely for far vision. Optic design is based on the two optic principle at MIOL. Purposed of the study is to evaluate the best corrected visual acuity and contrast sensitivity after cataract extraction and aspheric multifocal (Acriva Reviol) and monofocal (Acrysof IQ) intraocular lenses (IOL) implantation. The study site is Dr. Lutfi Kirdar Kartal Training and Research Hospital, 1.Eye Clinic, Istanbul, Turkey. In this prospective study, two IOLs were tested. 40 eyes of 20 patients were included. 10 patients implanted bilaterally with each type of IOL. Patients with an eye disease except cataract (glaucoma, diabetic retinopathy, ocular inflammation, senile macular degeneration and others), patients who have more than 1.5 D astigmatism, patients who have previously had an eye surgery have been excluded from the study. All routine examinations have been performed at post-op intervals of 1day, 1week, 1month, 2month and 3months. One month and three months after surgery, best corrected visual acuity (BCVA) for distance and contrast sensitivity for distance was measured by CC-100 Topcon LCD with optical correction. Tested spatial frequencies were 1.5, 3, 6, 12, 18 cycles per degree. Contrast sensitivity and visual acuity have been measured in the same environment at the same light level. The average age of the Monofocal IOL implant patients' recruited for this test was 66.3 years old. The multifocal IOL implanted patients' age average was 65 years old. At pre-op, multifocal group patients' uncorrected far visual acuity was 0.16 and their corrected far visual acuity was 0.31. Three months after cataract surgery uncorrected far visual quality average reported 0.71, corrected far visual acuity average reported 0.85 of multifocal IOL implanted patients. At pre-op the monofocol group, had an uncorrected far visual acuity of 0.29, and corrected far visual acuity reported as 0.53. Three months after surgery uncorrected far visual acuity of 0.71

and corrected far visual acuity reported as and 0.82. Statistically, there were no significant differences between monocular uncorrected and corrected far vision acuity averages amongst both groups. (p>0.05) Because of monofocal group's not providing near vision, just multifocal group' s near visual acuity have been measured. MIOLs' were implanted into 20 eyes' with results showing far corrected near visual acuity to be determined J1 at 15 patient eyes and J2 at 5 patient eyes. There was no significant difference between the monofocal and multifocal IOL groups BCVA for distance. We determined that after three months post-op, there was statistically no difference between multifocal and monofocal IOL when it comes to contrast sensitivity in regards to its mean-average at all spatial frequences. (p>0.05) At 12 cpd and 18 cpd frequences, multifocal IOL group's contrast sensitivity average was higher than monofocal IOL group's average but there was still no statistical mean difference. The multifocal group had higher contrast sensitivity at 12 and 18 cycles per degree.

In this short term study,postoperatively at the end of the 3rd month control patients with multifocal IOLs had better contrast sensitivity at 12 and 18 cycles per degree and better far visual acuity with no statistically significant difference.

- *Visual outcomes after implantation of an aspheric diffractive multifocal intraocular lens; L.Akçay, I.Sayman; Congress of the ESCRS;2011*

The purpose of the study is to evaluate distance, near vision and contrast sensitivity after aspheric diffractive multifocal (Acriva ^{UD} Reviol) intraocular lens (IOL) implantation. Twenty eyes of 11 patients were included in the study. Uncorrected distance visual acuity, best corrected distance visual acuity, uncorrected near visual acuity, best distance-corrected near visual acuity, contrast sensitivity and patient satisfaction were evaluated preoperatively, 1 month and 1 year postoperatively. One-year postoperatively the mean log MAR uncorrected distance visual acuity, best corrected distance visual acuity, uncorrected near visual acuity, best distance-corrected near visual acuity and contrast sensitivity was significantly better than preoperative levels. The mean contrast sensitivity increased considerably at all spatial frequencies compared with preoperative levels. There was no patient complaint of severe glare or halos. The aspheric diffractive multifocal IOL provided good distance and near visual acuities, good contrast sensitivity and high satisfaction.

- *Clinical Outcomes of Two Different Small Incision Diffractive Multifocal Intraocular Lenses: Comparative Study; İzzet Can, M.D., Prof.; Başak Bostancı Ceran, M.D.; Gülizar Soyugelen, M.D.; Tamer Takmaz, M.D., Journal of Refractive and Catarct Surgery 2012;59-67*

Although few multifocal IOLs that can be implanted through incisions of 2.0 mm or smaller are available, they are reported to resolve some of the problems of conventional small-incision IOLs. In addition to multifocality, these IOLs must have the same good uveal and capsular biocompatibility as conventional monofocal IOLs. Most important, they must remain perfectly centered in the capsular bag to restore visual performance and quality of vision and to prevent dysphotopsia symptoms.

In this study, there have been a comparison and there have been evaluated the clinical results of 2 multifocal IOL models implanted through 1.7 mm clear corneal incisions using a biaxial microincision cataract surgery (MICS) technique. In this prospective, comparative study, Acri.Lisa 366 D (Group 1) and Acriva Reviol MFM 611 (Group 2) IOLs were implanted each in 30 eyes with B-MICS technique and patients were followed for at least 6 months

postoperatively. Groups were comparable and standard for all their preoperative and intraoperative data. Patients who had previous eye surgery or eye disease that could affect final visual acuity (eg, amblyopia, retinal or macular abnormalities), corneal pathology, glaucoma, or corneal astigmatism higher than 1.00 diopter (D) were not included in the study. Also excluded were patients with intensive computer or car use and a meticulous personality because multifocal IOL implantation may be contraindicated in such cases. Nuclear hardness have been evaluated by biomicroscopy and the LOCS III scale. Refraction and corrected distance visual acuity CDVA) were determined by Early Treatment Diabetic Retinopathy Study (ETDRS) charts and transformed into logMAR units for statistical analysis. Corneal toricity was assessed by corneal topography. Central corneal thickness was measured with an ultrasound pachymeter. Biometry was performed 5 times by the immersion method. Intraocular lens power was calculated by targeting emmetropia. All patients had a follow-up of 6 months or longer. The examinations at 1 day, 1 week, and 1, 3, and 6 months included monocular and binocular uncorrected and corrected distance (6 m), near (33 cm), and intermediate (60 cm) visual acuity measurements (ETDRS chart); detailed slitlamp biomicroscopy; and corneal pachymetry. At 3 months, contrast sensitivity was measured (CSV 1000E, Vector Vision) and corneal topographic measurements were performed. The mean 6-month postoperative refractive astigmatism was 0.43 ± 0.20 D in Group 1 and 0.34 ± 0.25 D in Group 2 (P =.114). In all eyes, the topographic simulated keratometry was 0.61 ±0.27 D preoperatively and 0.59 ± 0.24 D postoperatively. Both IOL groups had a statistically significant increase in uncorrected distance visual acuity (UDVA) and CDVA postoperatively (P=.000). There was no statistical difference UNVA, J 1.46±0.73 and J 1.23±0.50 (p=.155) in Acri-Lisa and Reviol groups respectively. Reviol group showed significantly better results for UIVA (J 2.23±0.72) than Acri.Lisa group (J 3.06±0.90) (p=.000). Mesopic CS results, complication and dysphotopsic complaint rates were not significantly difference between the groups. In no case were the symptoms severe, and no patient had mentioned the symptoms to the surgeon before completing the questionnaire. One eye (3.3%) in each group developed posterior capsule opacification (PCO) 4 months and 5 months after surgery. Acri-Lisa 366 D and Acriva Reviol MFM 611 seemed to be effective multifocal IOLs in order to take the advantages of microincisional cataract surgery techniques. Both designs provided high level of distance and near visual acuities and CS results in addition Acriva Reviol IOL gave much better and satisfactory results for intermediate distance.

- *Refractive lensectomy to correct hyperopia with Acriva UD Reviol multifocal IOL implantation:Pavel Stodulka; ESCRS; 2011 September*

Purpose of the study is to evaluate the clinical results of Acriva^{UD} Reviol (VSY Biotechnology, Turkey) at hyperopic patients. This is a prospective study and all eyes were operated by the same surgeon with the implantation of Acriva^{UD} Reviol MFB 625. The study site is Gemini Eye Clinic, Czech Republic. 44 consecutive eyes of 25 selected patients recruited at this prospective study. Typical patients seeks glass independency for routine daily activities have included and patients who need fine detail resolution like jewellers, dentists & dental technicians, night drivers, professional pilots and professional welders have been excluded.

Hyperopic patients included in to this study and paid attention to patients don.t have any other intraocular pathologies. Phacoemulsification and implantation have been performed at 2.2 mm incisions. All patients have 6 months follow up regularly. Mean age was 51± 5 years and mean implanted IOL power was 27,3 ± 3,69 D. Mean preoperatively distance best corrected visual acuity was 0,78 ± 0,14. Distance corrected visual acuity for far, mid and near distance have measured. Halo and glare, PCO rate have been evaluated at the

patients. Mean ucorrected visual acuity increased from 0,18 to 0,54. Mean BCVA preop. 0,78 remained unchained and ended up 0,80 at 6 months. Mean best distance corrected visual accuity for near was J 1,2 at 6 months. Mean best distance corrected visual acuity was for intermediate was J 1,75 at 6 months. Distance corrected near visual acuity achieved J1 at %85 of patients in post-op 1.month, %88 in post-op 3.month. Multifocal diffractive IOL Acriva^{UD} Reviol (VSY Biotechnology, Turkey) provided very good uncorrected vision for distance, intermediate and near. YAG rate was 2% in 6 months. None of the patients uses spectacles regularly at 6 months follow up.

- *Early phase results of multifocal Acriva ^{UD} Reviol MFB 625 IOL : Mehmet Baykara; ESCRS; 2011 September*

Purpose of the study is to determine early results of visual performance for near-intermediate-distant vision, keratometric value changes, photopic complaints, patient satisfaction in Multifocal Acriva ^{UD} Reviol MFB 625 diffractive IOL implantation. The site was Uludağ University, Bursa, Turkey. Convenient 12 eyes of 6 patients who went phacoemulsification surgery and intraocular multifocal lens implantation are included in this prospective analysis. Before procedure informed consent was taken for every patient. In 12 eyes of 6 patients uncorrected distant visual acuity average increased 0,4 to 0,8. On the other hand uncorrected near visual acuity average increased 0,2 to 0,8. Preoperative anterior chamber volume average 131,42 was and changed to 167,87 after postoperatively. Patient satisfaction in photopic condition was reported good for distant, intermediate and near vision. In postoperatively early phase patient satisfaction in near intermediate and distant reported good with Acriva ^{UD} Reviol MFB 625 diffractive IOL(%95). Long term follow-up and large series will be helpful and needed in determining material security and reliability.

Conclusion

A number of the references cited are from textbooks, since the design, principles of operation and use of intraocular lenses is so well-established. Clinical study-based literature clearly shows that there is no doubt about the biocompatibility, quality, efficacy and safety of intraocular lenses. The risks associated with the use of intraocular lens are acceptable when it is weighed against the benefits to patient.

Acriva ^{UD} IOLs series are on the market since July of 2009 and they have proved their quality by published articles, free papers and presentations which show results of clinical studies. The clinical literature search also showed that there is no risk associated with Acriva ^{UD} IOLs. The intraocular lenses have been tested and conform to the appropriate standard ISO 11979.

There are no indications on side effects or interactions with medicines. There might three type of contraindications such as; Absolute, Relative and Surgical. Absolute contraindications might be; Progressive disturbances on the front segment of the eye such as rubeosis iridis, essential iris atrophy, choroidal hemorrhage, proliferate diabetic retinopathy, severe optic nerve atrophy, severe corneal dystrophy, cataract associated with

congenital rubella syndrome, chronic uveitis and uncontrolled glaucoma. Relative contraindications like clinic indications that may be harmed or that may have an increased risk by IOL implantation. The individual evaluation of each case must left to the surgeon. Surgical contraindications might be; flat anterior chamber following clear lens extraction, hyphema, vitreous loss which is a contraindication for posterior chamber lens, zonular damage and presence of, or predisposition to, retinal detachment. These effects are not caused by intraocular lens or it's material.

The authors of the data are known scientists, whose study results in norms were taken over. The conclusions are established. The upraised literature corresponds „state of the art" and the medical ones practice. The origins are up-to date publications, up-to-date literature or norms and writs. The development „state of the art " was considered during the preparation.

Appendix 1. Articles and abstracts of literature from table 1.