IN THE GAUTENG DIVISION OF THE HIGH COURT, PRETORIA

(REPUBLIC OF SOUTH AFRICA)

5/5/15

CASE NO: 992/2015

DELETE WHICHEVER IS NOT APPLICABLE

(1) REPORTABLE: YES/NO

(2) OF INTEREST TO OTHER JUDGES: YES/NO

(3) REVISED

DATE: 5 May 2015 **SIGNATURE:** Jansen

In the matter between:

ALLERGAN PHARMACEUTICALS (PTY) LTD	Applicant
And	
MEDICINES CONTROL COUNCIL	First Respondent
DIRECTOR-GENERAL OF THE NATIONAL DEPARTMENT OF HEALTH	Second Respondent
MINISTER OF HEALTH	Third Respondent

JUDGMENT

JANSEN J

[1] This matter came before me on a semi-urgent basis. It was set down earlier for 17 February 2015, but was not heard due to its voluminous nature and the intricacy thereof. The matter was postponed to 20 March 2015.

[2] At the hearing of the matter, counsel for the respondents sought to file, on the day of the hearing, a fourth set of affidavits (undeposed) by their expert, Professor Walubo (a clinical pharmacologist who has a MBChB, a Masters (M.Phil) in Basic Pharmacology, a Doctor of Medicine (M.D.) in Clinical Pharmacology, two-year post-doctoral training in Clinical Pharmacology and a Masters in Business Administration (MBA)). In the application for the late filing of the affidavit (also not deposed to) it was stated that the applicant's replying affidavit contained new allegations and that the respondents were forced to approach him (on an unknown date) to provide a detailed response to the applicant's replying affidavit. It was further stated that due to prior commitments (of which no details are provided) he was unable to provide a detailed response to the applicants' replying affidavit timeously.

[3] In any event, in the court's opinion, the replying affidavit does not contain new evidence. The mere fact that brief confirmatory affidavits have been appended to the replying affidavit cannot change the facts (and opinions based thereon) in the replying affidavit into "new evidence".

[4] That this "affidavit" for condonation of the filing of a fourth affidavit is woefully inadequate, is obvious. As a result, it was disallowed. The e-mail accompanying the said "application" and the fourth affidavit were e-mailed to the court and the applicant on 19 March 2015 at 5:46pm and contained the following sentence: "***Be informed that the signed and commissioned affidavits shall be served on you tomorrow morning***."

Nature of the application

[5] The applicant seeks declaratory relief to the effect that the applicant's products are medical devices in terms of the Medicines and Related Substances Act 101 of 1965 ("**the Medicines Act**").

[6] The applicant's products are called the Optive range of products and have been sold in the Republic since 2007. The applicant contends that its range of products constitutes medical devices and not medicines. This is

the first issue to be decided in this application. On a previous occasion, the applicant's products were seized by Port Health (by the Director-General of the National Department of Health ("**DG**") and more recently another three shipments during September and November 2014. The reason for the detention of the shipments was that they were allegedly medicines and had been called-up for registration as such.

[7] In the matter of ***Gelderma Laboratories South Africa (Pty) Ltd v Medicines Control Council and Others*** **(54281/2013) [2014] ZAGPPHC 360 (12 June 2014)** heard by Ismail J in this division, it was held that pending the promulgation of medical device regulations, medical devices do not fall to be regulated by the Medicines Control Council ("**the MCC**")

Is the Optive range of products medicines or medical devices?

[8] The first issue to be determined is whether the Optive products constitute medicines or medical devices.

[9] Medicines are defined in section 1 of the Medicines Act as meaning: —

"any substance or mixture of substances used or purporting to be suitable for use or manufactured or sold for use in-

(a) the diagnosis, treatment, mitigation, modification or prevention of disease, abnormal physical or mental state or the symptoms thereof in man; or

(b) restoring, correcting or modifying any somatic or psychic or organic function in man,

and includes any veterinary medicine"

[10] The definition of a medical device in the Medicines Act, in terms of section 1(c) of Act 94 of 1991, is as follows: —

"... any instrument, appliance, material, machine, apparatus, implant or diagnostic reagent –

(a) used or purporting to be suitable for use or manufactured or sold for use in –

(i) the diagnosis, treatment, mitigation, modification, monitoring or prevention of disease, abnormal physical or mental states or the symptoms thereof; or

(ii) restoring, correcting or modifying any somatic or psychic or organic function; or

(iii) the diagnosis or prevention of pregnancy and which does not achieve its purpose through chemical, pharmacological, immunological or metabolic means in or on the human body but which may be assisted in its function by such means; or

(b) declared by the Minister by notice in the Gazette to be a medical device and includes any part or an accessory of a medical device;"

[11] It should be noted that the Optive range of products are Ophthalmic Lubricants/Dry Eye comfort solutions.

[12] The MCC justified its attack on the Optive range of products as allegedly in the interests of public safety, notwithstanding the fact that the applicant demonstrated in its papers that similar products of the competitors are to be found on the shelves of pharmacies and are sold on a daily basis to members of the public.

[13] Furthermore, the applicant refers to various countries across the world where the Optive range of products has been classified, documented and registered as medical devices and not medicines, namely: —

> *"The Australian Department of Health and Therapeutic Goods Administration ('TGA') in Australia; the Medicines and Healthcare Products Regulatory Agency ('MHRA') in the United Kingdom, which ensures and administers compliance with medical device legislation in England, Northern Ireland, Scotland and Wales; the Food and Drug Administration ('FDA') in the United States of America where the Optive range of products trade under the name of Refresh Optive and Refresh Optive Advanced."*

[14] The definition of a medical device which approximates the South African definition the closest is the Australian definition which reads as follows: —

> *"A medical device is:*
>
> *a. any instrument, apparatus, appliance, material or other article (whether used alone or in combination, and including the software necessary for its proper*

application) intended, by the person under whose name it is or is to be supplied, to be used for human beings for the purpose of one or more of the following:

i diagnosis, prevention, monitoring, treatment or alleviation of disease;

ii diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap;

iii. investigation, replacement or modification of the anatomy or of a physiological process;

iv. control of conception;

and that does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but that may be assisted in its function by such means; or

b. an accessory to such an instrument, apparatus, appliance, material or other article." [emphasis added]

[15] Furthermore, the Optive range of products has also obtained the "CC" accreditation mark as a medical device in Europe.

[16] The Optive range of products are further registered globally as a medical device with the Global Medical Device Nomenclature ("**GMDN**") Agency; an internationally recognized body responsible for maintaining the GMDN codes, which is a system of internationally agreed descriptors used to identify all medical device products.

[17] The **South African Draft Medical Devices and IVD Guidelines 2014** in paragraph 5.7 thereof, recognise the use of the GMDN codes. The relevant portions read as follows: —

> *"**GMDN are codes used by regional or national regulatory bodies to consistently describe medical devices. GMDN codes are used to assist in the consistent assessment of devices before they are approved for supply; ongoing monitoring of devices one they are available for supply.***
>
> ...
>
> ***When lodging an application to include a device with the Council on the Medical Device Register..., the Applicant must specify the GMDN code that best describes the devices that they want to include in the Register.**"*

[18] All the above countries are considered to be so-called "benchmark" countries by the MCC, with the results that the standards applied in those countries are acceptable to the MCC. In order to reach their conclusions, these countries were required to satisfy extensive safety and efficacy criteria.

[19] However, the death nail in the respondents' coffin is the following statement by Professor Walubo, its expert witness: —

> "***In this respect, the term artificial tears is a misnomer for most products, including Allergan Optive product range, that identify themselves as such, because they do not mimic the full composition and functions of human tears. The appropriate terms should be "Tear aids".***"

[20] Regarding the classification of the Optive products in other benchmark countries as medical devices the laconic response from Professor Walubo is "***(w)ith clearer*** (sic) ***evidence today, it will not be surprising if these products are reclassified as medicines by these agencies***". This has not been done to date and the court is not inclined to override the expertise of experts in so many countries until they, themselves, believe it necessary

to reclassify the Optive range of products. Given the fact that the eyes of a human is of cardinal importance, one can reasonably expect that the benchmark countries are extremely vigilant regarding eye products and would react to the smallest negative feedback regarding side-effects or complications with any product to be used in the eye.

[21] As pointed out by the applicant in its founding affidavit, which facts are not disputed by the respondents, the applicant's Allergan product range contains carboxmethylcellulose ("**CMCS**") Levocarnitine, erythritol, glycerine, electrolytes and water. These facts are admitted by the respondents.

[22] As pointed out by the plaintiff's expert Dr Christophe Baudouin (the Editor-in-Chief of the *French Journal of Ophthalmology,* the Secretary General of the French Society of Ophthalmology and a member of several international societies, including the prestigious American Ophthalmological Society and the Academia Ophthalmologica Internationalis), the mode of action of CMCS is based on it physical properties which provide a lubricating effect and prolonged residence time in the eye. CMCS increases viscosity and has pseudo-elastic (i.e. shear thinning) properties.

[23] According to Dr Baudouin the mode of action of glycerine in eye drops is also based on its physical properties with no pharmacological receptor-mediated properties. In the US, glycerine is described as an ophthalmic demulcent – an agent which is applied topically to the eye to protect and lubricate mucous membrane surfaces and relieve dryness and irritation.

[24] Studies have shown that hydrogenated castor oil may be used to enhance the stability of moisture-sensitive drug products.

[25] Regarding the ingredient sodium hyaluronate, Dr Baudouin testifies that it is the predominant form of hyaluronic acid at physiological pH. He testifies that it is useful for enhancing the availability and retention time of drugs administered to the eye and that it is immunoneutral which makes it useful for the attachment of biomaterials for use in tissue engineering and drug delivery systems.

[26] Erythritol, is a suitable carrier for actives in sachets and capsules, and as a diluent in direct compression tableting. Dr Baudouin testifies that erythritol is included in the formulation of the Optive range of products as a tonicity agent/compatible solute.

[27] Osmoprotection (cell hydration) or normalisation of cellular function in the presence of osmotic stress, is achieved in almost all organisms studied by synthesis or accumulation of small organic osmolytes that may be termed compatible solutes.

[28] Recent research has demonstrated that replacement of salts, such as sodium chloride typically found in ophthalmic preparations, with compatible solutes such as carnitine and erythritol allows ocular surface cells to maintain normal function and water balance, despite the presence of the ongoing hyperosmolar tear film characteristic of dry eye.

[29] Dr Baudouin concludes by stating that the Optive range of eye drops therefore have a dual mode of action – the physical lubrication of the eye and hydration of the corneas and osmoprotection (hydration) by the polyols and carnitine assisting the influx of water into the cells on the surface of the cornea. From what he sets out, it is very clear that the Optive range of products does not fall within the definition of a medical device set out above.

[30] Dr Baudouin also testifies that, in addition, all the ingredients in the products that make up the Optive range are included for their mechanical and physical activities and not for any pharmacological properties: —

[30.1] **Carboxymethylcellulose sodium** for its viscosity-increasing, hygroscopic and pseudo-elastic (i.e. shear thinning properties.

[30.2] **Glycerine** as solvent and also for its physical, humectant and emollient properties.

[30.3] Hydrogenated **castor oil** for its lubricating properties.

[30.4] **Sodium hyaluronate** for its physical and hygroscopic properties, with hyaluronic acid being a natural and biodegradable polysaccharide in the human body. An average 70 kg individual has approximately 15 g of hyaluronic acid in his/her body.

[30.5] **Erythritol and carnitine** for their osmoprotective and/or cytoprotective properties.

[31] Dr Baudouin's evidence demonstrates that the Optive range of products was first made available as medical devices in Europe and the United Kingdom, and was subsequently introduced in New Zealand, Switzerland and Australia as medical devices.

[32] It is emphasised that Dr Baudouin, himself, has had over seven years' experience with the applicant's Optive range of products and speaks from personal experience.

[33] The findings and conclusions by Dr Baudouin have been presented at scientific meetings and have become the accepted state-of-the-art knowledge regarding the fact that the Optive range of products provides lubrication of the eye and hydrates the surface of the eye.

[34] Dr Baudouin has participated in scientific congresses and teaching of doctors/ophthalmologists over many years and in many countries and can, with certainty, state that the Optive range of products are regarded as medical devices by the medical community.

[35] The Optive range of products achieves its purpose by the means set out in the definition for a medical device, and is recognised globally as an ophthalmic and medical device, as opposed to an artificial tear, which is the only product, in terms of the Medicines Act, which would be subject to registration as a medicine.

[36] It is also telling that the so-called expert evidence of the MCC, provided by Dr Walubo, who works for the MCC and whose independence can be

questioned, is clearly defective in that it stems from a clear misunderstanding of the definition of a medical device as contained in the Medicines Act. Most of his evidence is so-called "newer facts" relating to tests on rabbits and the like. Most of it is hypothetical and speculative. Reference is made to the following sentence in his affidavit for example: —

> "***(s)o, having high gram-amounts of one ingredient (CMCS) does not mean that the actions of the final product(Allergan Optive product range) are ascribed to this abundant ingredient (CMCS)***."

[37] Effectively what Dr Walubo seems to do is to seek for fragments of evidence which might indicate that the ingredients of the Optive range of products may have some other effect than that claimed by the applicant.

[38] Another telling example of his misunderstanding of the term "medical device" is the following statement to be found in Dr Walubo's affidavit: —

> "***The term 'artificial tears' should therefore only be used for products that replace the function of natural tears. Such products may be regulated as either medical devices or medicinal products,***

depending upon their mode of action. These products do not need to stimulate physiological functions of the natural tears. The intended effect may be achieved by physical means only, i.e. by washing the eye surface (effect of dust, smoke), or supplement the aqueous layer of natural tear film with additional water under conditions of significantly increased evaporation (dry heat, air conditioning). By decreasing the exposure to irritants they may be helpful in treatment of 'minor irritations' of the eye." [Dr Walubo's own emphasis]

(All of the above "evidence" is a mélange of paragraphs uplifted directly from the **Manual on Borderline and Classification in the Community Regulatory Framework for Medical Devices** - but not in sequence and also from different paragraphs from the manual. This is clearly not the manner in which one quotes from an article.)

[39] None of what Dr Walubo states, causes the Optive range of products to fall within the definition of a "medical device".

[40] He further ends his affidavit with conclusions not based on facts set out in his affidavit. Once again, he prefaces his "conclusions" by the words "***recent evidence shows that...***" and then sets out the following: —

> "*43.1* ***CMS has pharmacological activity whereby it directly interacts (binds) with the corneal epithelial cells or cellular structures, and stimulate gene expression which leads to improved wound healing of the cornea. In effect, CMCS stimulates some of the physiological functions of the natural tears.***
>
> *43.2* ***Osmoprotectants L-carnitine, erythritol, glycerol and the electrolytes induce their effects via pharmacological and immunological processes of osmosis, inhibition of mediators of inflammation, prevent programmed cell death (apoptosis), stimulate mitochondrial metabolism etc.***
>
> *43.3* ***The other components of Allergan Optive product range (L-carnitine, erythritol, glycerol electrolytes and water) too have pharmacological/chemical activity that contribute to the product's therapeutic effects, e.g., restoration of pH,***

osmolality, anti-inflammatory, etc, by pharmacological/chemical mechanisms similar to those used to restore plasma of pH and osmolality by the same agents after oral or intravenous administration."

[41] Given that Dr Walubo has not given any credible or detailed evidence for his sweeping conclusions (based on the research of others) they can be ignored without further ado. Given the deficiencies in his affidavit it is not surprising that he sought to introduce an entire new affidavit at the commencement of the hearing running into 51 pages. Unfortunately for the respondents, his affidavit was filed wholly out of time and in filing it, the respondents implicitly concede that the initial affidavit of Dr Walubo did not assist them in the slightest as it was not "detailed".

[42] As set out above, the respondents, in seeking condonation for the last-minute filing of the affidavit, states that a "detailed" affidavit is now sought to be introduced by Dr Walubo. The court has no difficulty in rejecting the evidence of Dr Walubo as wholly unconvincing, speculative and mostly relying on so-called "new evidence' which apparently might – in the future – change opinions. Until such time, the "new evidence" has no probative value.

[43] All that this current "evidence" consists of is, as stated, an amalgam of fragments of so-called "evidence', hastily and illogically amassed. The court can only seek guidance from his "expert" evidence and has, in any event, found none. The ***Plascon-Evans Paints Ltd v Van Riebeeck Paints (Pty) Ltd*** **1984 (3) SA 623 (A)** rule therefore finds no application in this matter. As was highlighted by Heher JA in the matter of ***Wightman t/a JW Construction v Headfour (Pty) Ltd and Another*** **2008 (3) SA 371 (SCA)** at [13] –

> ***"A real, genuine and bona fide dispute of fact can exist only where the court is satisfied that the party who purports to raise the dispute has in his affidavit seriously and unambiguously addressed the fact said to be disputed."***

[44] No such real, genuine and *bona fide* dispute of fact has been raised by the respondents.

[45] By way of further example, Dr Walubo seeks to contend that all the benchmark countries, who are specialists in their field, are wrong in classifying the Optive range as medical devices. Contrary to his allegation, the only country which ever classified the Optive range of

products as medicines is Singapore. In any event, even this contention is inaccurate. Optive MD was first approved in Singapore as a pharmaceutical product on 27 May 2010, and reclassified, soon thereafter, on 11 October 2011, as a medical device. Far from "new evidence" allegedly changing the thought patterns of the benchmark countries, the opposite is true.

Is the Call-up Notice referred to by the respondents applicable to the Optive range of products?

[46] The second issue to be determined in this application is whether the Optive range of products was called up for registration in terms of *Government Gazette* No R2179 of 28 October 1977 as medicines in terms of section 14(2) of the Medicines Act which Call-up notice reads as follows: —

> "***The Medicines Control Council has, by virtue of the powers vested in it by section 14 (2) of the Medicines and Related Substances Control Act, 1965 (Act 101 o 1965), by resolution approved by the Minister of Health, determined that artificial tear solutions and contact lens solutions are subject to registration in terms of the provisions of the said Act as medicines falling under***

pharmacological classification 34 of Category A in regulation 4 (a) of the regulations made in terms of the said Act, with effect from the date of publication this notice."

[47] It is emphasised that this Call-up notice only finds application should the court hold that the Optive range is medicines. For reasons set out above, the court holds that the Optive products are medical devices.

[48] Furthermore, it should be noted that when this Call-up Notice was published, there was no definition of a "medical device" in the Medicines Act. Hence only medicines were subject to Call-up Notices.

[49] The respondents correctly concede that if the Optive range of products are medical devices then they are not subject to regulation. However, as stated, they contend that the Optive range of products are medicines.

[50] This court has held that the Optive range of products is not medicines as defined in the Medicines Act and hence the Call-up Notice does not find application. In the matter of ***Treatment Action Campaign and another v Rath and others*** **[2008] 4 All SA 380 (C)** at paragraph 31, it was also pertinently held that it is not for the Medicines Control Council to decide

whether a substance is a medicine, but that it is a question to be decided by a court: —

> ***"The question whether or not any particular substance is a medicine must be determined with reference to provisions of the Act and when its identity is questioned. The attributes of the substance and the claims made in respect of the substance will determine if it is a medicine within the meaning of the Medicines Act.***
>
> ***The question for determination is whether VitaCell is subject to registration as a medicine. The answer to this question will turn on the interpretation of the 2002 call up notice. I agree with Mr Budlender's submission that it is not for the MCC to decide whether the substance is a medicine. <u>It is for the courts to decide that question</u>."*** [emphasis added]

[51] As has been stated earlier in this judgment, the Optive range of products are universally recognised as medical devices, namely ophthalmic lubricants, as opposed to artificial tears.

[52] When one analyses the Call-up Notice, in the manner prescribed by Wallis JA in the matter of ***Natal Joint Municipal Pension Fund v Endumeni Municipality*** **2012 (4) SA 593 (SCA)** at paragraphs [17] to [27], it refers only to "artificial tear solutions" and not ophthalmic lubricants.

Conclusion:

[53] Given what has been set out above, the Optive range of products are medical devices and not subject to registration, absent any regulations to do so.

Order

[54] In the premises the following order is made: —

1. The products identified in annexure "**FA1**" to the founding affidavit ("the Optive range of products") as emanating from the applicant are medical devices as defined in section 1 of the Medicines and Related Substances Control Act 101 of 1965.

2. In the absence of the promulgation of appropriate regulations in terms of section 35(1)(xxvii) and/or (xxviii) of the Medicines and Related Substances Control Act 101 of 1965, the first respondent and/or the second respondent, are not empowered to deal with the authorising, regulating, controlling, restricting or prohibiting the registration, manufacture, modification, importation, exportation, storage, transportation, sale or use of Optive range of products in respect of its safety, quality and efficacy in the Republic.

3. The Optive range of products are not subject to: —

3.1 Registration in terms of section 14(2) of the Medicines Act; and the

3.2 *Government Gazette* 5790 dated 28 October 1977 (promulgated in terms of section 14(2) of the Medicines and Related Substances Control Act 101 of 1965) determining that artificial tear solutions and contact lens solutions are subject to registration in terms of the Medicines Act as medicines falling under pharmacological classification 34 of Category A in regulation 4(A) of the

regulations made in terms of the Medicines Act ("the Call-up Notice")

4. The first and second respondents are forthwith directed to release all and/or any of the Optive range of products detained by them, including specifically the products listed in the table annexed marked "**FA5**" to the founding affidavit.

5. The Respondents are ordered, jointly and severally, the one paying, the other to be absolved, to pay the costs of this application, including the costs of two counsel where engaged.

JANSEN J

JUDGE OF THE HIGH COURT

For the Applicant **Advocate AC Botha**

Instructed by **Goldman Judin Inc** (Ref: Mr Judin/R Hsiao/A0005 -011 – 595 2300)

For the Respondents **Advocate W.R. Mokhari SC and Advocate H.A. Mpshe**

Instructed by **The State Attorney**, Pretoria (Ref: 0084/2015/Z64/jb - 012-309 1623)