International Scientific Committee of Ozone Therapy ISCO3

Guidelines and Recommendations for Medical Professionals Planning to Acquire a Medical Ozone Generator

Up-date of the version ISCO3/DEV/00/01 (July 11, 2014). Approved by ISCO3 on 23/09/2019

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1. Background

In June 2012, during the International Ozone Therapy Congress of AEPROMO (Spanish Association of Medical Professionals in Ozone Therapy) in Madrid, the ISCO3 held a meeting, during which was decided to elaborate a document to be offered to any medical professional who is planning to acquire a Medical Ozone Generator (MOG).

This decision is the consequence of multiple questions and requests of help by medical professionals who felt unable to decide which equipment to purchase if based only on technical criteria, but would feel uncomfortable to make a choice based only on the price of the machine.

The original text was written by Heinz Konrad, M.D., who has been working for 44 years with the medical application of ozone, in Sao Paulo, Brazil. To produce these guidelines, we asked a number of manufacturers of medical ozone generators worldwide for help. Not all of them were willing to cooperate and to supply the information we asked for.

The present document meant to be a help and a commercial neutral guideline for all those who plan to buy ozone therapy equipment to be used in medicine, dentistry or veterinary. It is rather meant to be a help and a commercially neutral guideline for all those who plan to buy their MOG.

This up-date version took into consideration new advances in the research area concerning new technologies and new scientific supported application of ozone therapy in clinic. General guidelines and recommendations are also presented for generators used in dental applications.

ISCO3 encourages physicians, scientists, veterinarians and odontologists, in choosing MOG, to consider these international reference guidelines and to request manufactures to provide written manufacturing specifications for purposes of evaluating compliance with the international reference guidelines. It is, however, always the responsibility of each and every user to form his or her own decision concerning what equipment to use and to be diligent, vigilant, and responsible in its use. Generation, control, and administration of ozone gas for any medical use is the responsibility of the treating healthcare practitioner. It is important to use equipment and methods demonstrated through scientific principles and research, good manufacturing practices, and clinical experience to be both safe and effective.[1]

2. Criteria

Technical details to be fit by a MOG was divided into three categories:

a) Which are the **basic** components, resources and technical details **required** in a medical ozone generator?
b) Which are the **highly recommended** components, resources and technical details in a medical ozone generator?
c) Which are the **optional** components, resources and technical details in a medical ozone generator?

Furthermore, we also mention aspects, which should also be taken into account when choosing a MOG that are not purely technical. In order to facilitate the ozone therapist in choosing an appropriate MOG, there is a check list for each aspect in Attachment I.

2.1 Basic Requirements

We start with the resources and technical details we consider **absolutely necessary** in MOG. Some of these will seem obvious to most of our readers, but they must be mentioned:

The machine must produce ozone exclusively from medicinal grade, at least 99,5% pure oxygen, coming from a medical quality certified container, e.g. a high-pressure cylinder. The oxygen for industrial purposes does not qualify for medical uses, because the requirements of hygiene and sterility inside these cylinders are different from the cylinders used for medical purposes. The oxygen tank should adhere to medical quality standards, to avoid the presence of contaminant or others residual gases in the cylinder.

Machines using room air, including oxygen concentrators, do not qualify for ozone therapy. Medical grade oxygen should fit the quality standard of the local Pharmacopoeia. If local Pharmacopoeia is not available, the reference Pharmacopoeia should be:

- European Pharmacopoeia. [2] and European Directorate for the Quality of Medicines, who are responsible for the European Pharmacopeia (Ph. Eur.) monographs.
- United States Pharmacopoeia. [3]
- Japanese Pharmacopoeia. [4]
- Russian Regulation GOST 5583-78 (Industrial and Medical Oxygen). [5]

The quality criteria according the Ph. Eur. is mentioned in Attachment II as a general guideline in case the a local Pharmacopoeia is not available.[6]

There is a tendency to substitute the "old" compressed oxygen cylinders with the oxygen concentrators based on the Pressure Swing Adsorption (PSA) technology. This technology does not reach a sustained concentration of oxygen over 75% and this is leads the production of substances different to ozone.[7*] Modern oxygen concentrators which consistently produce up to 95.5 % O_2 + 4.5 % air, with impurities

* *Remarks made by the Ukrainian colleague and also member of ISCO3, Dr. Veronika Vongai about the use of oxygen concentrators as source of medical oxygen for the purpose of medical ozone generation:*
*"*In theory, the PSA technology allows to reach a gas mixture of up to 96% oxygen at the best, so a balance of 4% or more of Nitrogen will remain. However, the oxygen concentrators used in practice, in many cases fall short not only of the theoretical limit for PSA technology, but also of parameters declared in the technical descriptions of these devices.
"For example: a test of four concentrators of different origins, showed that none of them was able to produce an oxygen concentration higher than 89%, at a gas flow rate of 1 L/min. At a gas flow rate of 3 L/min, the oxygen concentration at the machine's exit fell to 70-75%. Therefore, the use of such concentrators is not recommendable, as the presence of Nitrogen oxide and Nitrogen dioxide may occur.
"Also, in many cases, the gas mix at the exit of these concentrators may contain gases characteristic of closed rooms, e.g. Carbon dioxide, ammonia, Hydrogen sulfide, Carbon oxide, steam, as well as airborne aerosols, lythosols, dust, microorganisms, etc.
"Also, the percentage of oxygen at the exit of a concentrator will be reduced as time goes by. An oxygen concentrator providing 96% pure oxygen when brand new may come down to only 70% to 80% oxygen purity after 5000-10000 h of work.
"The speed of decline of concentration efficiency depends on humidity of air, maintenance of carbonic acid gas and a number of other out-of-control parameters of the environment air. For all the above reasons, the uncontrolled use of oxygen sources using PSA technology should not be permitted."

ranging from (4.7 ± 0.5 - 6.0 ± 0.6) % in which the main part is the inert gas Argon (4.5 ± 0.5) % and nitrogen (0.2 ± 0.03) % (unpublished results form: Federal State Budgetary Institution of Science of the Institute of Chemistry of High-Purity Substances of the Russian Academy of Sciences), can be used under the following conditions:

- In countries or adverse environments (emergency, catastrophes or war) with severe health limitations (when there is a favourable risk/benefits balance).
- Topical-dermal application.

The use of oxygen concentrators in another kind of applications, especially in countries with better health systems, is discouraged. In particular, the use of concentrators contraindicated for systemic use until more comparative studies are available that demonstrate its low toxicity and the same therapeutic effect.

All external and internal tubing, connectors, hard or flexible, as well as all external or internal connections and fittings and electrodes coming into contact with ozone must be made of ozone-resistant materials, such as quartz glass, 316 stainless steel, silicone, Teflon, Hastelloy C, Kynar, Halar, polyether ether ketone (PEEK), fluorosilicone, fluoroelastomer FPM (VITON), fluoroelastomer FKM, perfluoroelastomer KPFE (KALREZ), or polychlorotrifluoroethylene PCTFE (Kel-F).[8] No other materials should be used. Silicone may be used externally only. Rubber, Latex or Polyurethane tubing / connections / fittings at any point are totally inappropriate. Unfortunately, these are detailing a potential customer cannot verify before buying the equipment, having to rely entirely upon the information given by the manufacturer.

The MOG must be able to generate the therapeutic, i.e. homogeneous oxygen-ozone mixture with a range of ozone concentration between 1 (one) µg/mL and 80 (eighty) µg/mL. No other substances besides O_2 and O_3 may be present in the produced gas mixture. Concentration between (1-3) µg/mL are mainly used in the procedure of ozonized saline solution. The range (5-80) µg/mL are used in most clinical procedures, and 80 µg/mL are most frequently used in the preparation of ozonized water.[9]

The user must be able to easily identify and adjust the desired ozone concentration, in micrograms by milliliters in the gaseous mixture, with an error margin not above 10 %.[10-12] This may be accomplished either 1) by clear and easily readable lists / tables on the face of the generator, which show the produced ozone concentration according to power input and oxygen flow rate (less precise technologies), or 2) by digital indicators showing the ozone concentration actually measured by sensors directly before the exit nozzle, in technologies who use fixed flow of oxygen and vary the power input (more precise technologies). Step of 1 µg/mL are desirable.

The measurement / estimation of current ozone output can be made in real time by several manners:

a) Direct method, by single or double beam photometric system, and
b) Indirect method, by Algorithm Calculation Measurement (ACM)
c) Hybrid method, by using both direct and indirect methods.[10,12]

Whichever the method used, accuracy should be ± 10 % or better.

The photometric direct system measures in real time the concentration of a gas in contact with it and will require more or less frequent adjustments and calibrations. It is precise and trustworthy when compared to a wet chemistry method. Those which use a mercury lamp may be unstable, may need more frequent

calibration, and may lose precision after a time. Mercury-vapor lamp will be limited in medical devices in the European regions by RoHS regulations. The photometric system using LED is preferable. Half live time of the lamp should be communicated by the manufacture.

The ACM method seems to be the simplest / sturdiest method. It determines the concentration by mathematical algorithm without contact with the gas. However, its exactness will depend to great extent on the good quality of the generator's components and the technically optimal design of the equipment. The ACM method provides an ozone concentration accuracy of ± 10% or better within full range of delivered concentrations in an ozone production of at least 20 min of continuous operation at 30 µg/mL and 5 min at maximum available concentration.

The Mathematical Count (MC) [different from ACM] method is the least accurate method to estimate ozone concentration. It is based on regulating flow rates and voltage applied to the generator tube after which the values are tabulated. The flow is regulated using different means, the simplest with the O_2 bottle flowmeter. The voltage is controlled by some kind of switch or potentiometer set in three or four positions. However, its exactness will depend to the quality of the input oxygen sources and the oxygen flow control. In this case, the concentration must always be verified frequently by the manufacturer with calibrated ozone analysers. Therefore, the use of generators using MC as estimation method to assay ozone output should be limited to these cases: 1) In countries or adverse environments (emergency, catastrophes or war) with severe health limitations (when there is a favourable risk/benefits balance). 2) Topical-dermal application.

Because it is not practical, the wet chemistry method is not feasible in a clinical environment. Nevertheless, it is the ideal reference method used to calibrate the other methods including photometers. There is also the ultrasound method, which is able to determine both the oxygen and the ozone concentration in the gas mixture.

The measure of ozone gas concentration should be compensated by the manufacture according to the influence of the temperature and pressure, and should be standardized to the pressure of 1 atm (760 mmHg [1.10325 bar], and temperature of 0 °C [273.15 K]. Those conditions should be referred as "International Standard Conditions," and the units generated as "normalized ozone concentration" preferable expressed as µg/NmL.

The equipment must have a fully reliable internal cooling / ventilation system that ensures correct system cooling, switched in such manner as to interrupt operation in cases of overheating.

The material of which the oxidation chamber is made must be of highest quality, so as to be able to withstand long term and frequent exposure to the high electric energy as well as the oxidation which may be caused by ozone. The most recommended material for these is quartz glass. Electrodes should be made of titanium or 316 inox stainless steel, preferentially avoiding direct metallic contact with O_2/O_3 mixture. Metallic electrodes should have a double dielectric barrier.

The exit syringe nozzle with the standard Luer Lock must be protected against the accidental inflow of any air born or liquid contaminants when not in use. This may be easily accomplished with a simple filter.

A syringe port must be available, allowing easy attachment and detachment of the syringe to be filled, and which will not allow any ozone to escape from the generator into the ambient air. Such syringe port must be easily disinfected. When O_3 is used for injection, the gas should flow through an ozone resistant

sterilizing filter 0.2 µm before being used. Hydrophilic filtering media will provide additional safety against accidental liquid entrance into the MGO.

The O_3 output flow should be between 3 L/h (50 mL/min) and 50 L/h (833 mL/min). The output flow will determine the time the generator needs to fill a syringe or a bag. The output flow is inversely proportional to the concentration. The more modern models of medical ozone generators do not adjust the ozone output by regulating the input flow of oxygen. All generators should indicate output flow.

Concentration and flow rate should be certified by an external laboratory and certification should be attached to the documents of the MOG. Manufacturers may calibrate the MOG using the concept of normalized milliliter to guarantee the right amount of ozone with variable temperature and atmospheric pressure. Is desirable that the MOG measures the temperature and atmospheric pressure of the environment and makes automatic changes during ozone generation. There should be a system of automatic maintenance of a given concentration and the output flow of ozone, because ozone therapy is a dose-dependent treatment.

Solenoid valves can be used to open or close the inflow of oxygen and / or the output of the O_2/O_3 mixture.

The MOG should be equipped with a catalytic ozone destructor built into or directly attached to the generator to eliminate ambient ozone leakage. This destructor may not use carbon as active agent, due to the risk of overheating, fire, and explosion. Some manufactures include active carbon and temperature sensors in order to avoid overheating, but combustion occurs in a very focal way and its progression is exponential. There is no system that can detect and stop this process in time. The catalysts must consist of an inert and totally inorganic medium. Ideally, the ozone catalyst destructor should be made from non-organic catalyst media.

2.2. Highly recommendable

The following resources and technical details may be considered **highly recommendable**:

Variable O_3 output flow adjustment. Low output flow should be useful in auricular application (3 L/h) (50 mL/min), flow of (6-12) L/h (100-200 mL/min) and vaginal insufflation in constant infusion. Flow of 20 L/h (333 mL/min) are used to fill a syringe or to generate Ozonized Saline Solution. Higher flow settings (50 L/h) (833 mL/min) are useful to fill bags.

Vacuum pump built into or directly attached to the generator, and connected directly to an ozone destructor, should be used to aspirate ozone/oxygen mixture from any closed compartment (e.g. “bagging” of external wounds with ozone). Such pump should have a gauge showing the actual vacuum strength (this is in cases of devises designing for bagging application).

Automatic power supply adjustment for 110 V or 220 V power input and for 50 Hz or 60 Hz alternate current input.

2.3 Optional

The following resources and technical details may be considered **purely optional**:

Attached or easily connectable system for the ozonation of water or oil (However, there is no medical generator able to manufacture a quality ozonated oil. The best option is to buy high quality commercially available ozonated oil).

Manometer attached to the vacuum pump mentioned under item 2.2 above, to measure the intensity of the vacuum produced.

Variable speed suction pump: This makes it possible to adjust the intensity of vacuum in certain would applications Alternatively, an external vacuum system with an ozone destructor can be used.

A timer, to switch off ozone generation after a preset time, might be useful for processes which require ozone generation for more than only a few minutes.

Foot pedal and/or Hand Switch Control 3-way solenoid valve (with 2 Luer Output) (In Devise for odontology use).

Touch Screen HMI (Human Machine Interface).

Remote Internet Diagnostics.

2.4. Ozone generators for dental applications

Even though most of the ozone generators used in dental research operate on air and are certified as CE MD, it is highly recommended that dentists use high purity medical grade oxygen to generate ozone gas.

Generators recommended for medical applications can also be used in dentistry.

Additional components are recommended to ensure safe ozone gas application in the oral cavity, especially when delivering ozone gas for extended period of times.
1- Ozone-resistant handpiece
2- Built-in vacuum pump / ozone gas destructor
3- Foot pedal control 3-way ozone-resistant solenoid valve

3. Other aspects

3.1 Easy maintenance

It is necessary that the manufacturer be able to provide technical assistance in a timely and geographically acceptable manner.

3.2 Calibration

Most professionals argue in favor, but many argue against the absolute necessity of regular, at least annual intervals for calibration of the ozone generators. Opinions are really very different or contradictory at times.

Many professionals argue that the simpler the generator's technical design and the less automatic and / or electronic circuitry devices it contains, the less maintenance and / or calibration it will require. There are already generators which include a direct LED photometric system *and* an indirect system in the same machine, thus offering highest quality level and reducing the frequency of necessary calibration.

Given the importance of doses in ozone therapy, it seems recommendable, however, to have the equipment checked periodically.

The use of a calibrated external spectrophotometer is a relatively simple method for calibration of the equipment *in loco*. Ideally, the manufacturer should supply the buyer a "Maintenance Book", containing instructions not only for the use but also for the adequate maintenance of the equipment, and in which any repair or calibration service made can be recorded.

3.3 Certification

There is an enormous number of technical norms and regulations established by public international Organization as the Council of the European Union or the European Parliament of the European Union,[†] private international organizations as the ISO, [‡] international quasi-governmental organizations as the

[†] Council Directive 93/42/EEC of 14 June 1993 concerning medical devices https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:1993L0042:20071011:EN:PDF
MEDDEV 2.7/1 revision 4. Medical Devices Directives Clinical Investigation - Clinical Evaluation: A Guide for Manufacturers And Notified Bodies Under Directives 93/42/EEC and 90/385/EEC
Council of the European Union: It is the "voice of EU member governments, adopting EU laws and coordinating EU policies (...) Together with the European Parliament, the Council is the main decision-making body of the EU." "Not to be confused with:
European Council - quarterly summits, where EU leaders meet to set the broad direction of EU policy making.
Council of Europe - not an EU body at all."
https://europa.eu/european-union/about-eu/institutions-bodies/council-eu_en
The main EU (European Union) institutions (Commission, Council, Parliament) issue different types of legal acts. Some are binding, others are not. Some apply to all EU countries, others to just a few.
Regulations. A "regulation" is a binding legislative act. It must be applied in its entirety across the EU.
Directives. A "directive" is a legislative act that sets out a goal that all EU countries must achieve. However, it is up to the individual countries to devise their own laws on how to reach these goals.
Decisions. A "decision" is binding on those to whom it is addressed (e.g. an EU country or an individual company) and is directly applicable.
Recommendations. A "recommendation" is not binding". It "allows the institutions to make their views known and to suggest a line of action without imposing any legal obligation on those to whom it is addressed."
Opinions. An "opinion" is an instrument that allows the institutions to make a statement in a non-binding fashion, in other words without imposing any legal obligation on those to whom it is addressed. An opinion is not binding.
https://europa.eu/european-union/eu-law/legal-acts_en

[‡] ISO: ISO 13485:2016, ISO 14903:2017, ISO 11135:2014, SO 11138-1:2017; ISO 11138-2:2017; ISO 11737-1:2018, ISO 19011:2018, ISO 17665-1:2006, ISO 11607-1:2019, ISO 11607-2:2019, ISO 10993-1:2018, ISO 10993-7, ISO 17665-1:2006
ISO (International Organization for Standardization) "is an independent, non-governmental international organization with a membership of 164 national standards bodies." https://www.iso.org/about-us.html

IEC,[§] public national organizations as the United Sates FDA,[**] and private national organizations as the German DIN.[††] All of them have issued guidelines, directives and other decisions for the necessary technical apparatus that may be applied to a medical ozone generator.

Manufacturing companies are advised to conform their medical ozone generators to the international standards that such devices should have, and for that reason should be aware of the different documents issued by the European Union, ISO, and the other recognized standardization organizations.

When buying a MOG, the practitioner should ask the sales person to see documentation demonstrating that the generator complies with the standards required by the country in which the device has been made and the requirements where the device is going to be used. Naturally, the criteria for equipment inspection, testing, and approval may vary from country to country.

3.3.1. Ozone generators made within the European Union

As per art. 9 of the Council Directive 93/42/EEC, medical devices are divided into Classes I, IIa, IIb and III and this "classification shall be carried out in accordance with Annex IX" of the same directive. **Ozone generators are medical devices falling within class IIb.**

The introduction of the Council Directive 93/42/EEC indicates that "as a general rule" medical devices should "bear the CE mark to indicate their conformity with the provisions of this Directive to enable them to move freely within the Community and to be put into service in accordance with their intended purpose".

As a consequence, it is highly recommended that the buyer verifies the "CE declaration of conformity".

3.3.2. Ozone generators made within the Commonwealth of Independent States (CIS)

The CIS, a regional intergovernmental organization, reunites the republics of the former Soviet Union, being currently Russia the most important in ozone therapy matters. The Russian certification is also said to obey rather strict rules, however, as far as we know, the Russian rules for MOG are only recognized in Russia and the CIS country members.

"Certification is the provision by an independent body of written assurance (a certificate) that the product, service or system in question meets specific requirements." https://www.iso.org/conformity-assessment.html

[§] IEC 60601-1-11:2015, IEC62366-1:2015.
IEC (International Electrotechnical Commission) "is a not-for-profit, quasi-governmental organization".
https://www.iec.ch/about/profile/?ref=menu

[**] FDA, Guidance for Industry1 Pyrogen and Endotoxins Testing — Questions and Answers - Contains Nonbinding Recommendations
https://www.fda.gov/media/83477/download

[††] DIN: DIN EN 980, DIN EN 556-1, DIN EN 15986, DIN EN 1041, DIN 58369:1996, DIN EN 868-2:2017-05, DIN EN 868-3, DIN EN 868-5.
DIN (German Institute for Standardization) "is the independent platform for standardization in Germany and worldwide (…) Anyone can use DIN Standards, and their use is voluntary. They only become mandatory if they are referred to in contracts, laws or regulations." https://www.din.de/en/about-standards/a-brief-introduction-to-standards . DIN is a "private sector organization." https://www.din.de/en/about-standards/benefits-for-the-public-sector

3.3.3. Ozone generators made in the United States of America and Canada

As to the United States of America and Canada, we understand that there are several brands of MOG being produced and sold for medical use, but there seems to be much disagreement as to the actual quality of such generators, especially because many contain cheap components.

The American Academy of Ozone Therapy advices its members that MOG should be "certified by an independent testing body for Electrical, Quality, Fire Safety and Proof of Professional Manufacturing and Quality by having one of these certifications: ETL, CSA, UL, QAI, or TUV." ⌗⌗ Products lacking a Quality and Safety Approval should be avoided.

At the national level the American government FDA has stated that there is no medical use for ozone. And as such, the American FDA does not authorize or certify parameters for medical ozone generators: "Ozone is a toxic gas with no known useful medical application in specific, adjunctive, or preventive therapy (…) c) A number of devices currently on the market generate ozone by design or as a byproduct. Since exposure to ozone above a certain concentration can be injurious to health, any such device will be considered adulterated and/or misbranded within the meaning of sections 501 and 502 of the act if it is used or intended for use under the following conditions: (…) (4) In any medical condition for which there is no proof of safety and effectiveness."

However, there are 15 states of the United States where is possible to practice ozone therapy. "No regulation in the fifteen states specified ozone therapy, but also did not list any unconventional therapy. However, it may be interpreted that ozone therapy may be used in 15 U.S. states" as a non-conventional therapy. For specified details of the US regulation on ozone therapy: Quintero et al, Ozone Therapy and Legislation – Analysis for its Regularization. http://xn--revistaespaoladeozonoterapia-7xc.es/index.php/reo/article/view/15/27. Regarding the other states of the United States, it seems that although there is no legislation on ozone therapy, its practice is widely tolerated as far as we know.

3.3.4. Ozone generators made in China

A number of manufacturers have started MOG production in China, and we understand that a Chinese ruling has been issued regarding the quality and safety standards for such equipment.

3.3.5. Ozone generators made in Latin America

There are several Latin America countries such as Argentina, Brazil, Colombia, Cuba, and México that are producing MOG. However, we know of no country, besides Cuba and Brazil, which have official approval and certification already established. Cuba, as far as we know, produces all MOG for its own use and does have a set of standards that must be locally followed.

3.3.6. To buy ozone generators from abroad

⌗⌗ American Academy of Ozonotherapy Guidelines for Ozone Generators Used in Medicine, Dentistry, and Veterinary Medicine. **https://aaot.us/page/GeneratorGuidleines?&hhsearchterms=%22devices%22**

As a general rule it is normally applied in the international exchange of commodities that the seller produces the "Free Sales Certificate" (FSC). It is a document which "certifies that a document required in certain countries or for certain commodities (such as pharmaceuticals), certifying that the specified imported goods are normally and freely sold in the exporting country's open markets and are approved for export." [§§] Even if this document is not mandatory by the authorities in the country of the buyer, the buyer might consider obtaining it from the vendor.

4. Concluding remarks

Understanding the machine
It is important that the buyer and future user of such equipment be well aware of the physical principles and technical details of the machine, as well as its natural limitations. Equally, the buyer needs to have very well-established goals / uses / purposes for which he or she wishes to use the equipment.

Technical support
When deciding for equipment, the buyer must also consider the availability and distance from technical a support facility in his geographical area.

Stay in touch!

It can be taken for granted that questions of technical or medical nature will arise during the use of such newly acquired equipment. Therefore, it is highly recommendable that the buyer pursuits a good relationship with the vendor.

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[§§] http://www.businessdictionary.com/definition/certificate-of-free-sale.html

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6. Change History

Effective Date	Significant Changes	Previous SOP no.
11/07/2017	Original version	First version
16/06/2019	Up-date of ISCO3/DEV/00/01. Was added: Disclaimer, checking list. Limit of O_3 concentration was extended from 1 to 80 µg/mL. It was declared that O_3 flow ranges interval need to be declared. Need of certification by an external company was introduced. Use of Hight grade ozone concentrator 95.5 % O_2 can be used for local application of ozone. The use of active carbon as catalytic destructor is not advisable. The presence of solenoid valve and catalytic destructor was moved to basic required. Categories to stablish the technical requirement was redefined ad basic required, highly recommendable and optional.	Draft 2
15/07/2019	Need of the medical quality cylinder is specified. Use of oxygen concentrator is approved in case of emergency, catastrophes or war condition and for topical-dermal application. The concept of Normalized ozone concentration was introduced. Grammatical correction by Dr. Frank Shallenberger**.**	Draft 3

7. Document Records

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Reviewer	Dr. Frank Shallenberger (Grammatical corrections)	ISCO3 Member		8/08/2019
Authoriser / Approved	ISCO3 Board and members 2015-2020	All members		23/09/2019

Attachment I. Check list.

Criteria of the MOG to be considering as: **Basic required**

- ✓ MOG must produce ozone exclusively from medicinal grade, at least 99,5% pure oxygen, coming from a medical quality certified container. Oxygen concentrator 95.5 % can be used as sources of ozone, for local application and in case of emergency, catastrophes or war conditions.
- ✓ All external and internal tubing, hard or flexible, as well as all external or internal connections and fittings must be made of ozone-resistant material.
- ✓ The MOG should be able to generate a homogeneous oxygen-ozone mixture with a range of ozone concentration between 1 (one) µg/mL and 80 (eighty) µg/mL.
- ✓ The user must be able to easily identify and adjust the desired ozone concentration in micrograms / milliliter. Step increments of 1 µg/mL are desirable. The error margin should not exceed ±10 %.
- ✓ The device should measure in real time the ozone concentration using a photometric method, algorithms calculation methods or both.
- ✓ The equipment must have a fully reliable internal cooling / ventilation system, switched in such manner as to interrupt the ozone generation when sufficient cooling is not present.
- ✓ The material of which the oxidation chamber is made must be of highest quality. The most recommended material is quartz glass.
- ✓ The exit nozzle must be protected against the flow into the generator of any unwanted or accidental solid or liquid contaminants when not in use. The exit nozzle must allow easy attachment and detachment of a syringe to be filled. The exit nozzle must not allow any ozone to escape from the generator into the ambient air. Such syringe port must be easily disinfected.
- ✓ Output flow of ozone must be adjustable between 3 L/h (50 mL/min) and 50 L/h (833 mL/min).
- ✓ Concentration and flow rate should be certified by an external laboratory and attached to the documents of the MOG.
- ✓ MOG should be certificated by a health authority according to the legal rules in the country in which the devise is used.
- ✓ MOG maintenance and calibration should be done in the intervals stablished by the manufacture or by the local law.
- ✓ Solenoid valves should be used to open or close the admission of oxygen and / or the output of the O_2/O_3 mixture.
- ✓ The generator should have a catalytic ozone destructor which is either built into or directly attached to the generator to eliminate the possibility of ozone escaping into the ambient air.
- ✓ The manufacturer must be able to provide technical assistance in a timely and geographically acceptable manner.
- ✓ The manufacturer should supply the buyer with a “Maintenance Book”, containing instructions not only for the use but also for the adequate maintenance of the equipment, and in which any repair or calibration service made can be recorded.

Criteria of the MOG to be considering as: **Highly recommendable**

- Variable O_3 output flow adjustment.
- Vacuum pump built into or directly attached to the generator, and connected directly to an ozone destructor.
- Automatic power supply adjustment for 110 V or 220 V power input and for 50 Hz or 60 Hz alternate current input.

Criteria of the MOG to be considering as: **Optional**

- ➢ Attached or easily connectable system for the ozonization of water or oil.
- ➢ Manometer attached to the vacuum pump. Possibility to adjust the intensity of vacuum.
- ➢ A timer, to switch off ozone generation after a preset time.
- ➢ Foot pedal and/or Hand Switch Control 3-way solenoid valve (with 2 Luer Output) (In Devise for odontology use).
- ➢ Touch screen HMI, Remote internet diagnostic

Attachment II. Medical Oxygen. Quality criteria and definition according the European Pharmacopoeia.

Medical Oxygen[6]		
Name		Oxygen
Reference		01/2010:0417
Chemical formula		O_2
Definition		Oxygen contains not less than 99.5% v/v of oxygen. It is produced by a purification process followed by a cryodistillation of the ambient air.
Identification		Complies with the assay
PRODUCTION		
Assay	Specification	≥ 99.5 % v/v oxygen
	Analytical method	Paramagnetic analyzer
IMPURITIES		
CO	Limit	≤ 5 ppm v/v
	Analytical method	Infrared analyzer
CO_2	Limit	≤ 300 ppm v/v
	Analytical method	Infrared analyzer
H_2O	Limit	≤ 67 ppm v/v
	Analytical method	Electrolytic hygrometer
TEST		
CO	Limit	≤ 5 ppm v/v
	Analytical method	Detector tube
CO_2	Limit	≤ 300 ppm v/v
	Analytical method	Detector tube
H_2O	Limit	≤ 67 ppm v/v
	Analytical method	Detector tube

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