

# Analysis of the Management of disposal of Antibiotics in Health Units in Amazonas

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**Abstract**— *The residues generated by the disposal of medicines are present, both in the terrestrial and in the aquatic environment, generating impacts, from the morphological alteration of fish to the appearance of bacteria super-resistant to antibiotics. In view of the social scenario, it is essential to implement an environmental education, through the adoption of public actions aimed at preserving the environment. In this work, the environmental impacts of drug disposal will be analyzed with the pharmacy and nursing professionals registered with the regional councils: Regional Pharmacy Council (CRF - AM) and Regional Nursing Council (COREN - AM), in December 2018 a January 2019. A survey carried out among the types of drugs most consumed and discarded by pharmacists and nurses registered with CRF - AM and COREN - AM. The effect of making the population aware of the disposal of medicines by pharmacists and nurses registered with their respective regional councils was evaluated in order to propose the environmental impact generated by the disposal of medicines in the environment. Finally, the socio-demographic profile of pharmacists and nurses registered with CRF - AM and COREN-AM was evaluated through interview questionnaire form.*

**Keywords**— *Disposal of Medicines; Disposal – Environment; Environmental Education, Environmental health.*

## I. INTRODUCTION

The presence of drugs in the environment is an emerging problem with regard to environmental impacts, as they compromise water quality, fauna, aquatic species and public health (Hubbard, 2007). Although advances in the field of drug discovery and chemical production of substances that make it possible to advance in the fight against various pathologies, few studies are published on the action of drugs in contact with the environment, and on the potential damage to public health. Studies by Ternesa et al (1999) in Germany, Canada and Brazil have shown that drug residues such as natural estrogen and estradiol are present in domestic sewage and its effluents from treatment and sewage plants (TEE). Impacts from the presence of estrogen in the aquatic environment were described by Sumpter (1998) in the finding of the feminization of male fish exposed to these effluents.

According to the Federal Pharmaceutical Council

(2010), Brazil ranks among the ten countries that most consume medicines in the world, with the finding that there is a pharmacy (or drugstore) for every 3,300 (three thousand and three hundred) inhabitants.

This scenario is worrisome when trying to understand the demand and supply, the relationship of consumption and disposal, a counterpoint, when considering that medicines are pharmaceutical substances technically obtained and elaborated for prophylactic purposes, in which pharmaceutical supplies and their correlates are regulated and previously established in the provisions of Law No. 5,991/73 by the National Health Surveillance Agency - ANVISA.

In the midst of so many changes in the health and disease process, a new conception is needed for professionals working in the health field, that new skills and capacities are developed to ensure the development of policies that support the government, society and health,

WHO (2016), such attitudes are foundations for actions that stimulate health promotion, that defend health at its different levels and, mainly, that health professionals are more involved in its promotion.

In view of the need to adopt more sustainable measures in daily life and which mainly aim to reduce the impacts on the environment, waste, whatever its origin, are the main targets of these concerns as they are by-products of contemporary life, highly consumerist and source of nature modification. Then, the concern arose as to the most correct destination for the disposal of medicines, since these are present in our daily lives. Faced with such questioning, the following questions emerge: “would these drugs, when disposed of incorrectly, cause damage to the environment?” and, “which public could disseminate measures that promote the disposal of correct medicines?”.

In Brazil, the regulation of medicines is carried out by the National Drug Policy, whose purpose is “to guarantee the necessary safety, efficacy and quality of medicines, the promotion of rational use and the population's access to those considered essential” (BRASIL, 2001, p. 9).

According to Melo et al. (2012, p. 2) antimicrobials can be defined as “substances that have the ability to inhibit growth and / or destroy microorganisms. They can be produced by bacteria, by fungi, and they can be totally or partially synthetic”. This class of drugs was discovered in 1982 by Alexander Fleming who found that the compound penicillin produced by fungi was able to inhibit bacterial growth. We also add that penicillin was the first type of antibiotic discovered by accident, being a bactericidal substance most used and recognized worldwide for years, Guimarães et al. (2010, p. 05).

Over the years, penicillin has been the subject of studies and contributed to the development of a series of drugs with bactericidal and bacteriostatic capacity, (MELO et al., 2012).

According to Guimarães *et al.*, (2010) there are several types, but for the purposes of understanding antibiotics, it is important to separate them into gram-positive, which dye color when exposed to violet crystal, and gram-negative, which dye red, this information is determinant for choosing the appropriate treatment. According to the same authors, there are several types of antibiotics, which are indicated according to the infection and the affected area, since there is an immense variety of these beings in nature.

The use of antibiotics has revolutionized healthcare, saving lives and preventing serious health complications, but overuse has serious adverse effects that can be reversible, debilitating or fatal to the health of people and communities. As an example, the harmful effects of a

person's healthy flora can be cited, resulting in opportunistic bacterial infections such as *Clostridium difficile*, which can be fatal.

The main concerns are the bacterial resistance this time to the choice of the medication will not have the desired clinical effect. Due to the overuse of antibiotics, resistant microorganisms entered the public's radar, posing a serious threat to the health of the population. Consequently, in May 2015, the World Health Organization endorsed a global action plan to combat this problem, with specific emphasis on antibiotic resistance (STEIN, *et al.*, 2018).

Antibiotic therapy has brought the most revolutionary change in the history of medicine to the field of infectious diseases. Over the years, due to negligence regarding the use of antimicrobials or at random, some bacteria have become resistant to the action of several antibiotics, especially vancomycin, which is considered the most potent. The most worrying microorganism in this respect is *Staphylococcus Aureus*, which has been resistant to several types of antimicrobials.

Another concern is with the group of antibiotics, according to Carvalho et al. (2009, p. 06), for their potential in promoting the development of bacterial resistance, and for being used in large quantities. A survey conducted in the United States, cited by Carvalho et al. (2009, p. 06), published in 2008 confirms that about 41 million American citizens from 24 metropolitan areas receive drinking water contaminated by a variety of pharmaceutical products, including antibiotics, which can enrich the environment with resistant bacteria capable of infecting man.

According to Storel *et al.*, (2014, p 33) Inadequate disposal is done by most people due to the lack of information and disclosure about the damage caused by medicines to the environment and the lack of collection points. To this end, the lack of information causes people to discard these drugs in the common garbage or in toilets, but according to Hope (2011), the Brazilian sewage system is not prepared to adequately treat toxic waste from medicines in the country. home environment. The classification of solid waste generated in health establishments is based mainly on nature and associated risks, as well as on the criteria established by the Ministry of Health.

Any material from the health facility should be considered waste from the moment it is rejected, because its usefulness or clinical management is considered complete and only then can you start talking about waste that has an associated risk.

Hospital Solid Waste is waste from health care activities, research in establishments such as hospitals,

clinics, gas stations, laboratories and others.

For Hope (2011, p. 23), the different types of industries, such as medicines, are great agents that cause environmental impact, in which they present different degrees of consumption of natural resources and also release pollutants, as industries often use techniques inadequate resources that help to degrade natural resources and threaten the life of the planet.

Hope (2011), the rational use of medicines is not an isolated attitude, but a joint action that should be exercised with the participation of patients, families, health professionals, legislators, public policy makers, industry, commerce and government policies, each adequately exercising the functions of its competence in the global process.

According to Storel et.al (2014), medicines are essential for maintaining the health of the population, however, the media gives a great incentive to excessive consumption of medicines and this increases the accumulation of unused medicines in homes. this, the subject of this research is the analysis of the management of antibiotic disposal in health units in Amazonas.

## II. MATERIALS AND METHODS

This research involves standardized techniques of data collection, questionnaires and observation, when carrying out surveys identifying the most used drugs, most consumed types, etc.

In this sense, this study adopted the descriptive model in which the facts are observed and recorded, classified, without interference from the researcher, involving the use of standardized techniques for data collection such as questionnaires, Pardanov and Freitas (2013).

In order to obtain information for data analysis, questionnaires were applied, which corroborate with that described by Cano (2012) where the strategies adopted for the production of scientific knowledge are based on the interest of the generation and validation of theories.

Cross-sectional studies are recommended when the objective is to study the frequency and associated factors of a given health event that manifests itself in a given population. It can be said that they are ideas to answer the following questions: "What are the frequencies of the risk factors and the outcome under study?". "Is there an association between the risk factor and the outcome in question?" (BASTOS AND DUQUIA, 2007).

In the first stage of this work, contact was made with the Regional Councils in order to present the research objectives and obtain authorization for its development. In

the second stage, the questionnaire was applied to the CRF-AM and COREN-AM, with the professionals duly enrolled in these. advice, to gather data on knowledge regarding the disposal of medicines in the environment, environmental education, and public health.

The third stage of the research consisted of analyzing the data and proposing measures to reduce the environmental impact generated by the disposal of medicines in the environment as forms of environmental education and promotion of public health.

The population that was studied is made up of professionals from the pharmacy and nursing fields, registered in their respective CRF – AM and COREN-AM.

Vieira (2011) defines population or universe as the set of units about which information is sought. Sample is any subset of units taken from a population to obtain the desired information.

Of this, the equation to determine the sample size (n) based on the estimate of the population proportion, as will be described in Equation 1 below, "Z" is the equivalence rate of the 95% confidence interval, which is 1,96, "e" is the sample error, which is 5%, "p" is the proportion of individuals in the population to be studied, which is 80%, while "q" is the proportion of the population that will not be studied, corresponds to 20%. Then we will have the proportion of 80% and 20% having as reference a homogeneous population, as they are professionals in Nursing and Pharmacy.

Equation 1 - Equation for sample calculation based on the estimation of the population proportion

$$n = \frac{Z^2 \cdot p \cdot q \cdot N}{e^2 \cdot (N - 1) + Z^2 \cdot p \cdot q}$$

Source: Falco, 2008

Thus, applying Equation 2 to COREN –AM:

$$n = \frac{1,96^2 \cdot 0,8 \cdot 0,2 \cdot 9,050}{0,05^2 \cdot (9,050 - 1) + 1,96^2 \cdot 0,8 \cdot 0,2}$$

$$n = 240$$

Equally applying Equation 3 to C. R. F - AM:

$$n = \frac{1,96^2 \cdot 0,8 \cdot 0,2 \cdot 5,696}{0,05^2 \cdot (5,696 - 1) + 1,96^2 \cdot 0,8 \cdot 0,2}$$

$$n = 236$$

The result of this sample calculation for the one studied at the Regional Pharmacy Council comprised 236 (two hundred and thirty-six) professionals and the Regional Nursing Council 240 (two hundred and forty)

professionals. Based on this equation, the number of questionnaires needed for the research was obtained from the respective councils. The data above were obtained from COREN - AM and CRF - AM.

The process of data collection used was the online questionnaire, self-applicable, objective questions and with the purpose of investigating the disposal of medicines, environmental education and the damage to public health with the Pharmacists and Nurses. The Web Survey questionnaire was made available on the Survey Monkey virtual platform. Data were collected from December 2018 to January 2019.

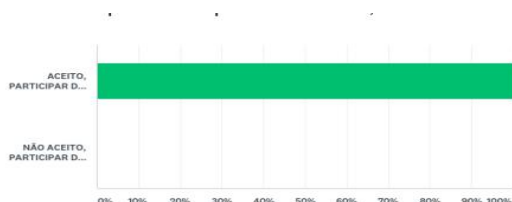
The inclusion criteria adopted in the research consisted of individuals of both sexes, aged eighteen or over; be enrolled in the Regional Pharmacy and Nursing Councils as a professional with a college degree and be working in the profession. Furthermore, it was necessary that he / she accepted to participate in the research, voluntarily and anonymously, signing the Informed Consent Form (ICF) on the study, before starting the questionnaire. Participants who did not meet the above criteria were excluded from the survey.

### III. RESULTS

Among the profile of these professionals interviewed, we have professionals aged mostly between 35-45 years old, female, with single marital status and who have a higher level of education, specialization and who exercise their profession mostly in private institutions. It is important to note that all respondents accepted to participate voluntarily in the research.

For the composition of the sample of this research, the participants should agree to voluntarily grant their data in order to make possible the ethical procedures and to proceed with the collection of information. The graph below shows 100% of the acceptance of the participants who composed the sample of this research.

Graph 1 - Acceptance of participation in the research



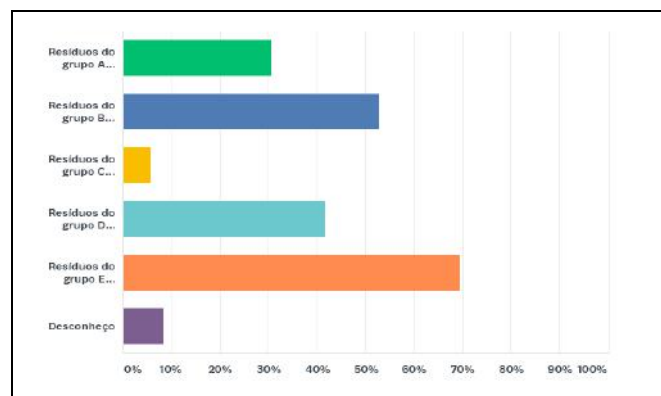
Source: Own authorship (2020)

After acceptance and due completion of the free and informed consent term, specific questions regarding the

composition of this research were applied. When questioned about age, most respondents were in the 31 to 45 age group, covering more than 70% of the participants, followed by the 18 to 30 age group with approximately 20%, as shown in the graph above.

When asked about the waste generated in their work environment, considering a sample composed of nurses, the graph below was obtained.

Graph 2 - Waste for hazardous work



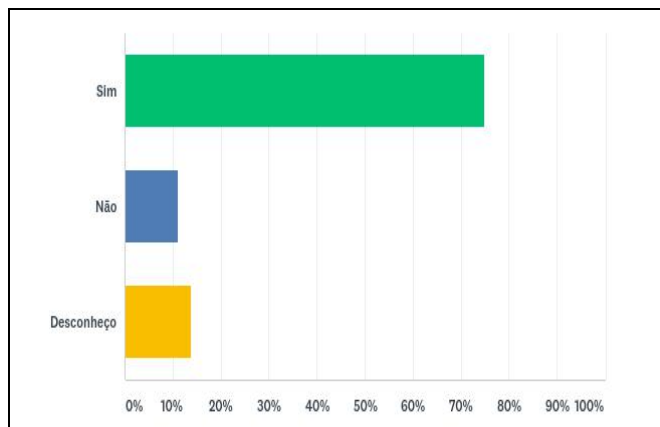
Source: Own authorship (2020)

These data point to a large amount of waste in group E (around 70%) and group B (over 50%) that refer to sharp cutting hospital materials with potential damage to health and chemicals that need special disposal, respectively. Residues in groups D and A also present significant portions of disposal (around 30-40%) which are equivalent to household and infectious ones, respectively, the latter needing special treatment for disposal.

According to Almeida *et al.*, (2016) a considerable portion of waste, including hazardous waste, is disposed of inappropriately, allowing contamination of the environment and resulting in risks to the population. According to the authors, the presence of drugs in the common garbage, although in a smaller amount than the other routes, also needs attention. These inputs are sent to landfills where they can come into contact with the population working in these places, as well as contaminate the soil.

The waste management plan in health services is essential to minimize the effects on the environment. When asked about the existence of this type of planning in the workplace, most participants (more than 70%) responded that there is a plan, as shown in the graph below. Professionals report that despite the large number of waste, there is, however, a waste management plan.

Graph 3 - Existence of a waste management plan in the workplace.

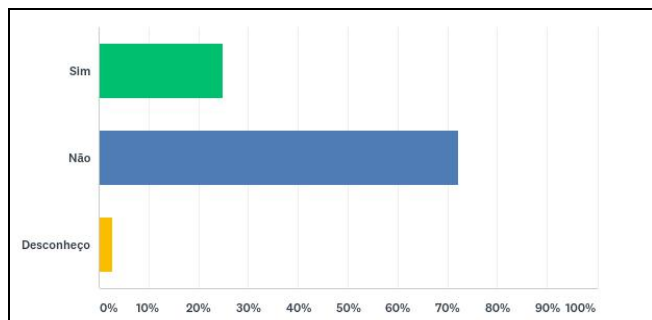


Source: Own authorship (2020)

It is interesting to note that a large portion of the interviewees reported that they were unaware of the procedures for separating waste according to dangerousness, adding up to around 15%.

Regarding training for the disposal of medicines, around 70% of respondents reported not having received any form of training or basic training for proper disposal, compared to 25% of respondents who said they had guidance for this, as shown in the graph below.

Graph 4 - Drug disposal training



Source: Own authorship (2020)

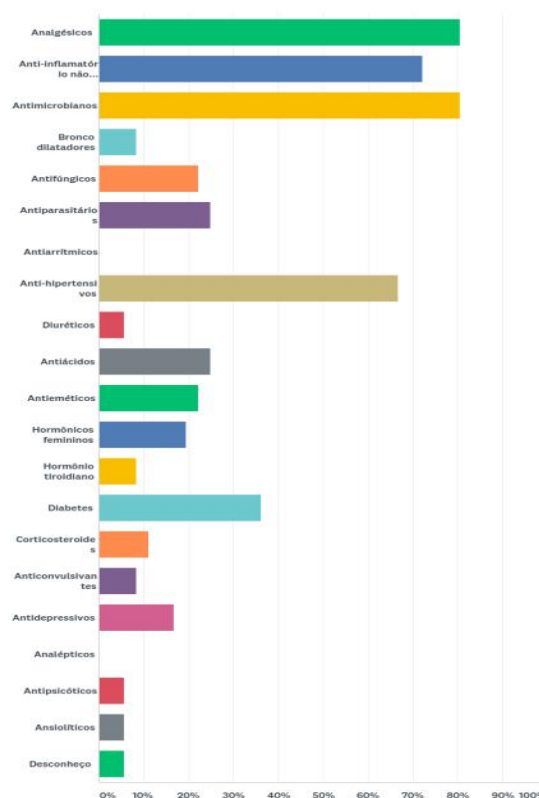
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Regarding the class of drugs most used in the workplace and separated for disposal by the interviewee, a large

amount of analgesics (80%), antimicrobials (80%), anti-inflammatory drugs (70%) and antihypertensive drugs (60%), which are the most used drugs in hospital settings. Antiarrhythmics and antiepileptics were not mentioned in the respondents' responses (Graph 5).

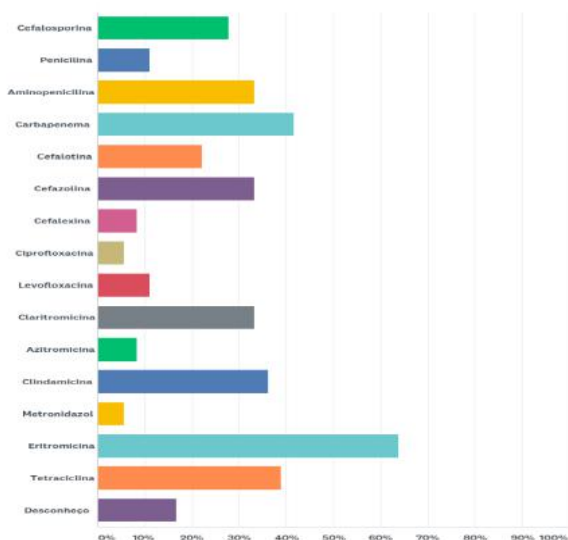
Graph 5 - Most consumed medications in the work environment



Source: Own authorship (2020)

With a focus on the antimicrobial classes, it was pointed out that erythromycin (64%), carbapenema (42%), tetracycline (38%), clindamycin (36%), aminopenicillin (32%), clarithromycin (32%) and cefazolin (32%) are the classes of antibiotics least consumed in hospital environments, as shown in the graph below.

Graph 6 - Antibiotics least consumed in hospitals

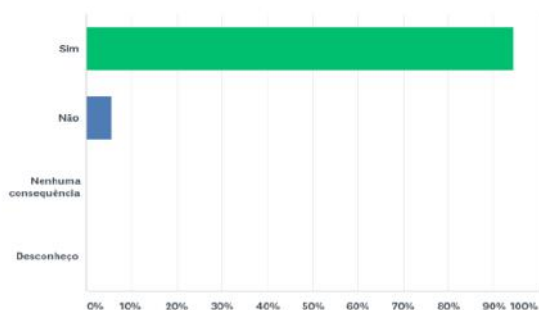


Source: Own authorship (2020)

These findings corroborate those shown by Guerra et al. (2020) when stating that Cefepime, piperacycline, meropenem, tazobactam and vancomycin are the most widely used antibiotics in the hospital environment, whereas erythromycin, carbapenema, tetracycline, clindamycin, aminopenicillin, clarithromycin and cefazoline are the least consumed and therefore generate smaller amounts of solid waste.

Participants were asked about their opinion on the possibility of inappropriate drug disposal causing damage to the environment. The vast majority (around 94%, stated that there is a possibility of improper disposal generating damage to the environment, as shown in the graph below.

Graph 7 - Disposal of medicines and damage to the environment

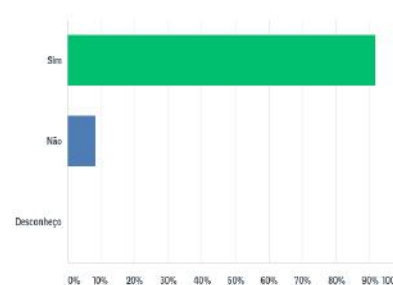


Source: Own authorship (2020)

Regarding the improper disposal of medicines, with the disposal of household waste and damage to public health,

the vast majority of respondents (92%) stated that there is an important and dangerous correlation, as noted below.

Graph 8 - Disposal of medicines and damage to public health

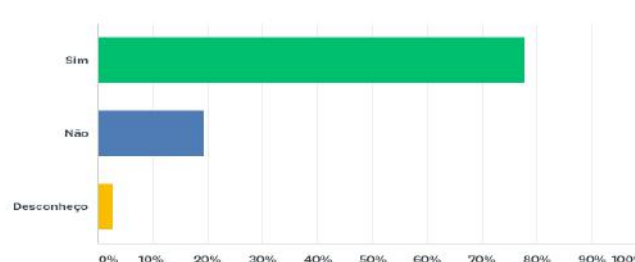


Source: Own authorship (2020)

The lack of training for the correct disposal of medicines can result in serious damage to the environment. According to the data presented, most of the professionals who perform the disposal do not have training, but they do it in the same way. One of the main damages to the environment was demonstrated by Al-Maadhed et al. (2019) by pointing out the presence of several types of antibiotics commonly used in hospitals in Qatar in effluents close to these places or even landfills. These authors also demonstrated how the removal of these antibiotics from water is complicated and, in the case of gentamicin, practically impossible.

Regarding the relationship between the inappropriate disposal of drugs and the appearance of super resistant bacteria, the majority of respondents (78%) stated that there was a positive relationship in their respective opinions. However, in relation to the proportions of responses in the previous questions, a small but significant group of respondents (approximately 20%) stated that they did not see this correlation, as shown in the graph below.

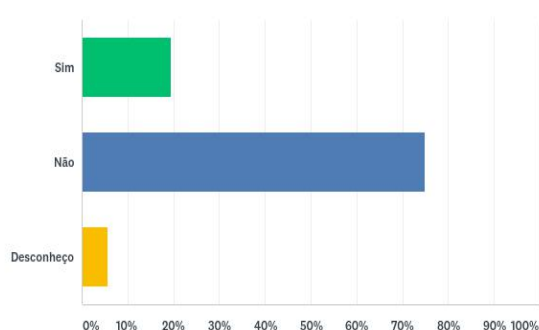
Graph 9 - Disposal of antibiotics and super resistant bacteria



Source: Own authorship (2020)

In this sense, the study by Irshad *et al.*, (2019) pointed out that there is a strong correlation between the increase in resistance and microbial pollution due to the inappropriate disposal of medicines. The explanation for this, according to the authors, would be that the presence of antibiotics in the environment would make it possible for bacteria to contact these compounds and induce changes in the survival mechanism to promote resistance, Chi *et al.*, (2020) reinforce these findings by pointing out that there is a greater presence of antibiotic resistance genes in bacteria from soils contaminated with hospital waste, which points to an important public health problem.

Graph 10 - Segregation of residues at home



Source: Own authorship (2020)

Based on these data, the vast majority of participants, that is, 75%, responded that they do not segregate residues from the residence, which makes up more than half of the answers obtained. What draws attention is that around 8% of the participants did not know the act of segregating waste, demonstrating a lack of information and even those who had it did not perform the act.

It is also necessary to make the population aware of the correct final destination of medicines and the problems that can be caused, if it is done incorrectly. Gondim (2012) adds that awareness can only be achieved through communication, through educational programs and campaigns to collect medicines in disuse.

#### IV. CONCLUSION

As a result of this research, it was possible to reveal the types of drugs most consumed and discarded by pharmacists and nurses registered with CRF/AM and COREN/AM, between December 2018 and January 2019, as well as by their users, which antibiotics stood out due to their potential risk. And also to unveil the impacts that this medication has on the environment and what its improper

disposal can cause. It was possible to find out how medication is disposed of in the places where these professionals work. And to identify the view of nursing and pharmacy professionals about the consequences of the disposal of medicines in relation to the environment. As well as the importance of the conscious performance of these professionals.

This survey showed that a large proportion of respondents have incorrect disposal habits, which, in turn, directly impact drug treatment and nature. Continuing education of health professionals and the population is necessary in order to make the population aware of the correct use and disposal of medicines. The frequency of inappropriate disposal, together with the scarcity of information on the subject, reinforces the real need for permanent education of health professionals and the population in general, to raise awareness of the correct use and disposal of medicines. In addition, stricter actions are needed to monitor compliance with national and state laws related to the reverse logistics of medicines, in order to minimize the potential clinical and environmental impacts caused by the incorrect disposal of medicines.

The findings of the present study revealed that although most professionals are aware that the correct disposal of medications is essential to avoid damage to the environment and increased bacterial resistance, few receive training and continuing education to perform such activity without equivocation.

As for the orientation of the population, there was a lack of policies and campaigns aimed at this in most of the cases addressed. This is worrying, as it may result in the disposal of antibiotics in household waste that is destined for landfills and open dumps, contaminating effluents and increasing bacterial resistance.

In general, this paper points to the need for a review of the solid waste management plan in hospitals in Amazonas, especially regarding the disposal of antibiotics. However, further studies are needed to build an intervention plan appropriate to each specific hospital.

#### REFERENCES

- [1] AL-MAADHED, *et al.* (2019) Antioxidant and antimicrobial activities of essential oil of *Skimmea laureola* growing wild in the State of Jammu and Kashmir Journal of Medicinal Plants Research Vol. 6(9), pp. 1680-1684, 9 March, 2019.
- [2] ALMEIDA, *et al.* (2016) ALMEIDA, Maria Angélica Randoli de, *et al.* Evaluation of drug waste disposal in pediatric units. Rev. esc. enferm. USP vol.50 no.6 São Paulo Nov./Dec. 2016

- [3] BASTOS E DUQUIA, 2007. BASTOS, L. J. D. e DUQUIA, R. P. One of the most used designs in epidemiology: cross-sectional study. *Scientia Medica*, Porto Alegre: v. 17, n° 4, p. 229-232, out / dez. 2013.
- [4] BRASIL. Lei n° 5.991, de 17 de dezembro de 1973. Provides the Sanitary Control of the Trade of Drugs, Medicines, Pharmaceutical Inputs and Related, and provides other measures. *Diário Oficial da União*, Brasília, DF, 19 de dezembro de 1973. Disponível em: [http://www.planalto.gov.br/ccivil\\_03/leis/L5991.htm](http://www.planalto.gov.br/ccivil_03/leis/L5991.htm) Acessado em: 10 maio 2018.
- [5] BRASIL. Ministry of Education National Education Council (MEC). Resolution No. 3, of November 7, 2001. Establishes National Curriculum Guidelines for the Undergraduate Nursing Course. *Official Gazette of the Union*, Brasília, DF, 9 de novembro de 2001. Disponível em <http://portal.mec.gov.br/cne/arquivos/pdf/CES03.pdf> Acessado em: 10 de maio de 2018.
- [6] CANO (2012) CANO, I. In the trenches of the method: teaching the methodology of social sciences in Brazil. *Sociologies*, Porto Alegre: ano 14, n° 31, set /dez. 2012, p. 94-119.
- [7] CARVALHO, *et al.* (2009, p. 06) CARVALHO, V. E., FERREIRA, E. *et al.* Legal and toxicological aspects of drug disposal. *Brazilian Journal of Toxicology*, v. 22, n° 1-2, p. 1-8, 2009.
- [8] CHI, *et al.* (2020) Chang S, Sievert DM, Hageman JC, Boulton ML, Tenover FC, Downes FP, *et al.* Infection with vancomycin-resistant *Staphylococcus aureus* containing the vanA resistance gene. *N Engl J Med*. 2003; 348(14):1342-7.
- [9] Federal Pharmaceutical Council (2010) NATIONAL HEALTH COUNCIL. Federal Pharmacy Council (2010). Disponível em: [http://www.conselho.saude.gov.br/ultimas\\_noticias/2010/medicamentos.htm](http://www.conselho.saude.gov.br/ultimas_noticias/2010/medicamentos.htm). Acessado em: 20 de Junho de 2018.
- [10] Fonte: Falco, 2008 FALCO, J. G. *Applied statistics* Cuiabá - Curitiba: Ed UFMT / UFPR, 2008.
- [11] Gondim (2012) GONDIM, Veruska Narikawa. Communication as a transformation agent: The role of the Federal Pharmacy Council in providing guidance on expired or unused drugs. Brasília, 2012. Disponível em: <<<https://repositorio.uniceub.br/jspui/bitstream/235/7881/1/50907000.pdf>>> Acessado em: setembro de 2020.
- [12] GUIMARÃES; *et al.* (2010) Guimarães, Denise Oliveira, Luciano da Silva Momesso, Mônica Tallarico Pupo. "Antibiotics: therapeutic importance and perspectives for the discovery and development of new agents." *Química Nova* 33.3 (2010): 667-679.
- [13] HOPPE, Taíse Raquel Grings. Contamination of the environment by improper disposal of expired or unused drugs. Agudo – RS, 2011.
- [14] Hubbard, 2007. HUBBARD, M. L. Analysis of the Oregon Stakeholder Drug Take Back Policy Process to Reduce Pharmaceutical Pollution in Oregon's Water Resources. Analysis of the Oregon Stakeholder Drug Take Back Public Policy Process to Reduce. 2007.
- [15] MELO, Vivianne Vieira; DUARTE, Izabel de Paula; SOARES, Amanda Queiroz **Guia Antimicrobianos**, 1.ed. - Goiânia, 2012.
- [16] OMS (2016), WORLD HEALTH ORGANIZATION. The Sustainable Development: Na agenda for transformation. Disponível em: <http://www.who.int/healthpromotion/conferences/9gchp/shanghai-declaration-zero-draft.pdf> Acesso em: 26 de junho de 2018.
- [17] PARDANOV E FREITAS (2013) PRODANOV, C.C. e FREITAS, E.C. *Methodology of scientific work: methods and techniques of research and academic work*, 2° ed. Novo Hamburgo – RS, Feevale, 2013.
- [18] STEIN *et al.*, 2018 STEIN, Kelli, *et al.* The use and misuse of antibiotics in dentistry: A scoping review. *The Journal of the American Dental Association*, 2018, 149.10: 869-884. e5.
- [19] STOREL *et al.*, (2014, p 33) STOREL, Ilse de Lima Arruda. Inadequate drug disposal: negative impacts on the environment and public health. X Alta Paulista Environmental Forum, v. 10, n. 12, 2014, pp.104-111. São Paulo, 2014.
- [20] SUMPTER (1998) SUMPTER, J. P. Xenoendocrine disrupters: Environmental impacts *Toxicology Letters*, v. 102-103, p. 337-342, dec. 1998.
- [21] Ternesa *et al* (1999) TERNESA, T.A.; STUMPF, U.M., MUELLER, J. Behavior and occurrence of strogens in municipal sewage treatment plants – I. Investigations in Germany, Canada and Brazil. *The Science of the total environment*, v. 225, p. 81-90, 1999.