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ANVISA
Agência Nacional de Vigilância Sanitária

PESQUISA CLÍNICA

RELATÓRIO ANUAL

2023

COORDENAÇÃO DE PESQUISA CLÍNICA (COPEC)

SEGUNDA DIRETORIA

7ª EDIÇÃO

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summary

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1. INTRODUCTION

Clinical research is a part essential for the development and registration of medicines and the arrival of new alternatives therapies on the market. Rehearsal clinical and clinical study are others terms used to name an investigation process scientific study involving human beings. The knowledge obtained through clinical research allows new and better therapeutic options are offered to the population, in addition to generate scientific innovation and technology in the country's health sector.

Clinical trials that will have all or part of its development clinic carried out in Brazil, with the purpose of supporting the registration of medicines and biological products, before being started, they must be authorized by the National Agency for Health Surveillance (Anvisa) and approved by the National Commission for Research Ethics (CONEP) or by Research Ethics Committees (CEPs), according to Resolution No. 466 of 12 December 2012. The analysis and approval of clinical trials by Anvisa and CONEP may occur in parallel.

Endless academic research of subsidiary o register of medicines, called scientific or technological research, are not subject to evaluation and regulatory consent from Anvisa, but for the import of medicines or inputs to be used, there must be authorization from the Anvisa, prior to its clearance in the national territory, compliant RDC nº 172, from 08 from September 2017.

The regulation of clinical research with medicines and biological products is RDC nº 9, of 20 February 2015. This Resolution is applicable to all clinical trials with medicines that will have all or part of its clinical development in Brazil for registration purposes. That DRC is aligned with international regulations and guidelines for the clinical development of medicines and biological products, in particular to the guides of the Advice International for

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Harmonization of Technical Requirements for Pharmaceuticals for Human Use Products (I).

The ICH is made up of main regulatory authorities and by industry representatives international pharmaceutical companies, such as Foodand Drug Administration (FDA), United States, to European MedicinesAgency (EMA), Europa, a Pharmaceuticals and Medical Devices Agency (PMDA), Japan and the permanent members Health Canada, Canada and Swissmedic, Switzerland. Including members regulators, such as Anvisa, Brazil, HSA, Singapore, MFDS, Korea do South of the NMPA, China. The objective do advice is to discuss and harmonize the scientific and technical aspects of development and registration of medicines. Anvisa is a member I have been here since 2016.

It is the responsibility of the Coordination of Search Clinic in Medicines and Biological Products (COPEC), linked to Second Anvisa Board (DIRE2), evaluate Dossier consent petitions of Clinical Development Medicines (DDCMs), from Dossiers Clinical Trial Specifics (DEECs) and related petitions, in addition to carrying out Goods inspections Clinical Practices (GCP) and evaluate requests of the Software Expanded Access assistance (AE), Compassionate Use (UC) and the Post-study Medication Supply program (FMPE).

This is the 7th edition of the report annual number of activities carried out by COPEC. The objective of this report is publicize widely and detailed information on all activities carried out throughout the year by the area technique. The first report was published in 2017, and since then the area annually updates the information and data about the consent to clinical trials for registration purposes, and activities related.

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2. CLINICAL DRUG DEVELOPMENT DOSSIER - DDCM

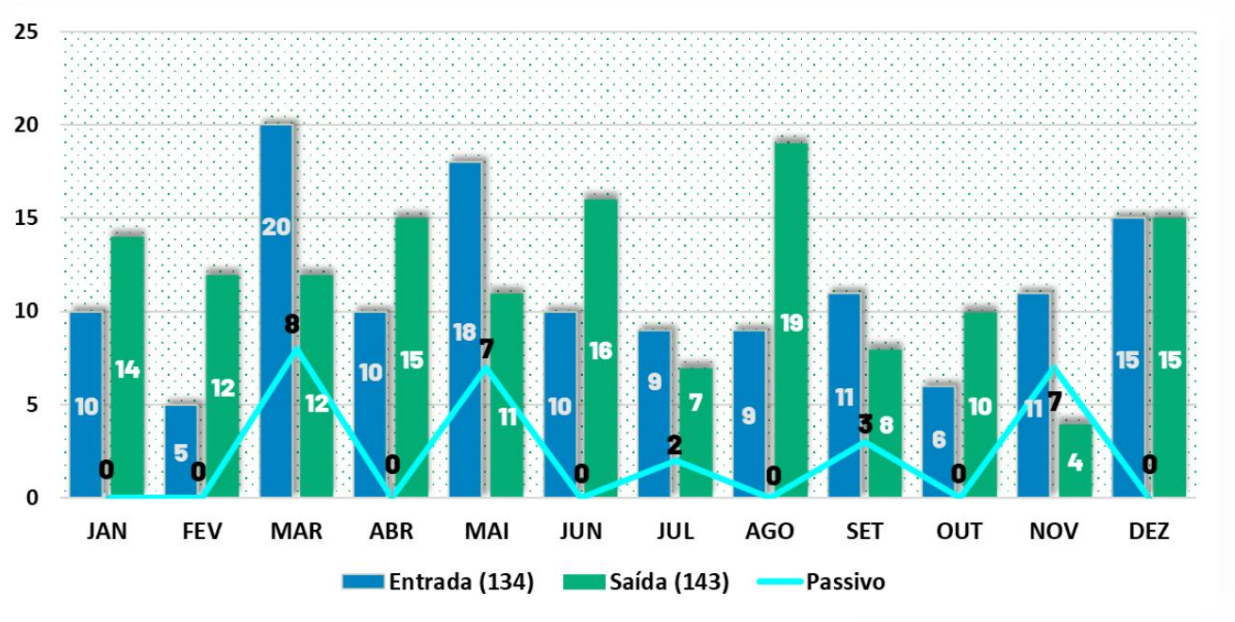

Figure 1 – *Monthly Input and Output of DDCMs in 2023.*

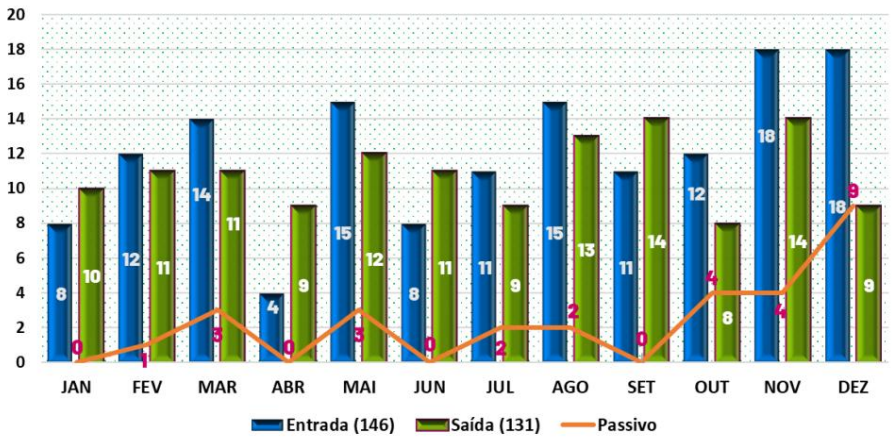

Figura 1a

Entrance and exit Monthly DDCMs in 2022.

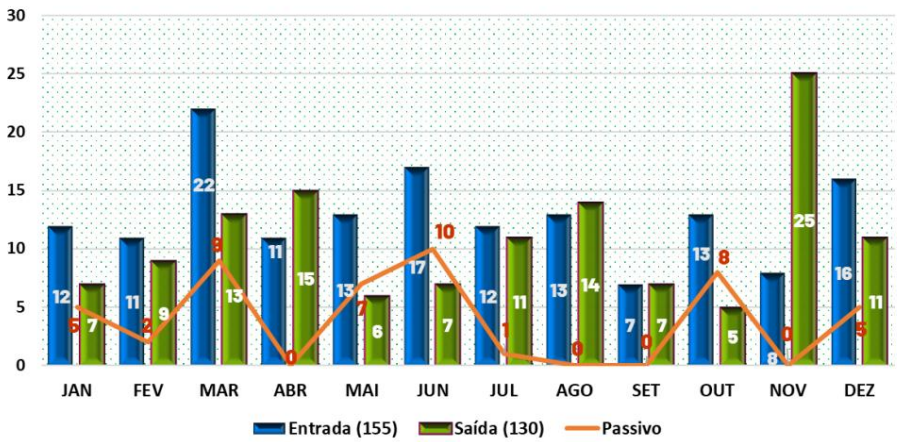

Figura 1b

Entrance and exit Monthly DDCMs in 2021.

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The main documents technicians required for instruction and DDCM submission are: drug development, Investigator Brochure (BI), which brings together clinical and non-clinical data relevant information about the medicine experimental to be studied, the Dossier do Medicine Experiment with information about the production process and quality control, the Summary of Safety Aspects of the Experimental Medicine and the Specific Clinical Trial Dossier (DEEC).

As of the validity of *RDC no. 09/2015,* it was established that each investigational medicinal product must have a DDCM to which linked all protocols clinical trials (Specific Dossiers of Clinical Trials – DEECs) to be conducted with the medication to experimental.

Thus, the number of DDCMs submitted for evaluation by the agency cia corresponds to the amount of new molecules in development clinical, or, to a lesser extent, molecules already registered in Brazil or abroad or both, investigated for other indications therapies, for example.

RDC *nº 09/2015* establishes that each investigational drug must have a DDCM to which they must be linked to all clinical trial protocols (DEEC). Therefore, each DDCM refers to a new medicine.

For the purposes of this report, I considered was considered a completed petition when there was any decision conclusive regulatory, as I deferred ment or denial, release due to the expiration of a deadline, withdrawal or cancellation.

Figures **1, 1a and 1b** refer the number of DDCMs received and concluded by Anvisa, in the years 2021, 2022 and 2023.

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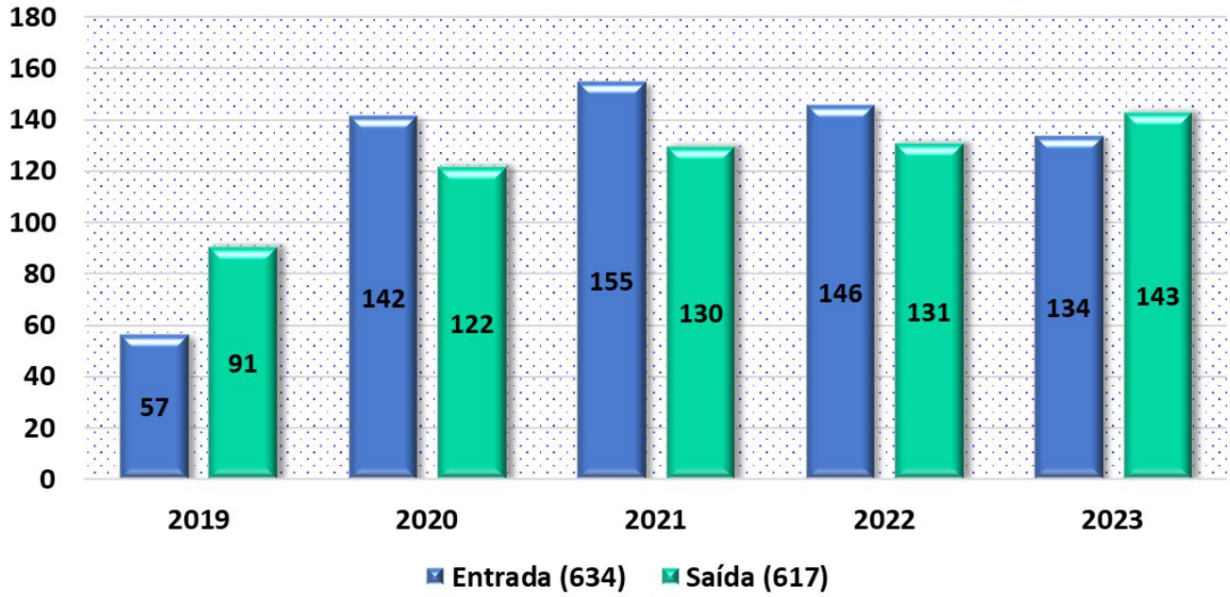

Figure 2 – *Entry and Exit of DDCMs between 2019 and 2023 (History)*

Over the last few years (2019 to 2023), the most significant change observed in relation to the entry of new DDCMs occurred between the years from 2019 to 2020 and 2021, in which there was an increase of 2.5 times (from 57 for 142 DDCMs) of 2019 for 2020 and 2.7 times (57 to 155 DDCMs) from 2019 to 2021.

Although the observed increases can be attributed to new medicines and vaccines for Covid-19, the entry of new DDCMs if maintained at a similar level, in the following years. In 2022 and 2023 146 and 134 DDCMs were submitted, respectively.

In 2020 and 2021, of the 252 petitions of DDCMs completed, 41 (16%) were related to development medicines and vaccines clinic for Covid-19. As already mentioned, each DDCM corresponds to a medicine, but several trials clinics can be carried out with the same medicine. Therefore, the despite having been subjected to 41 DDCMs in 2020 and 2021, in this same period, 134 were evaluated clinical trials for Covid-19.

Finally, in comparative terms, the number of DDCMs submitted, in average, prevails greater than the number of DDCMS evaluated over a period of 5 years **(Figure** 2).

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2.1 DDCMs - Experimental Medicines: Categories

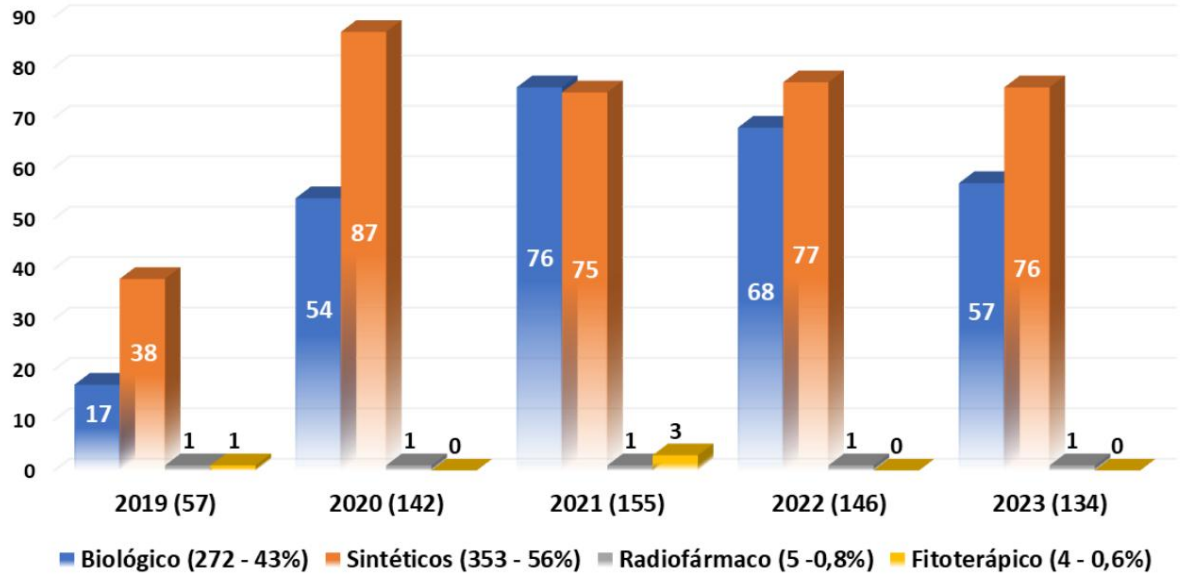

Figure 3 – *Categories of Experimental Medicines (DDCMs submitted between 2019 and 2023).*

The category of the medicine experimental is one of characteristics that determine the level of complexity and time necessary for analysis of the respective DDCM. There are four main categories of medicines experimental or products under research, namely: Biologicals, including vaccines, synthetics or Semisynthetics Phytotherapeutics and Radiopharmaceuticals Over the last few 5 years, synthetic medicines represented the largest number of DDCMs submitted, achieving 56% (353) of the 634 DDCMs submitted during the period. In second place, organic products corresponded to 43% (272) of the DDCMs submitted in the last 5 years.

It is not uncommon for medication nts already registered in Brazil and/or in other countries are studied for other therapeutic indications, new pharmaceutical forms or new populations, renewal of registration of medicine, among others. In 20 23, of the 134 DDCMs submitted, 23 (17%) were related to medicine ments registered in Brazil and/or not external.

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3. SPECIFIC CLINICAL TRIAL DOSSIER (DEEC)

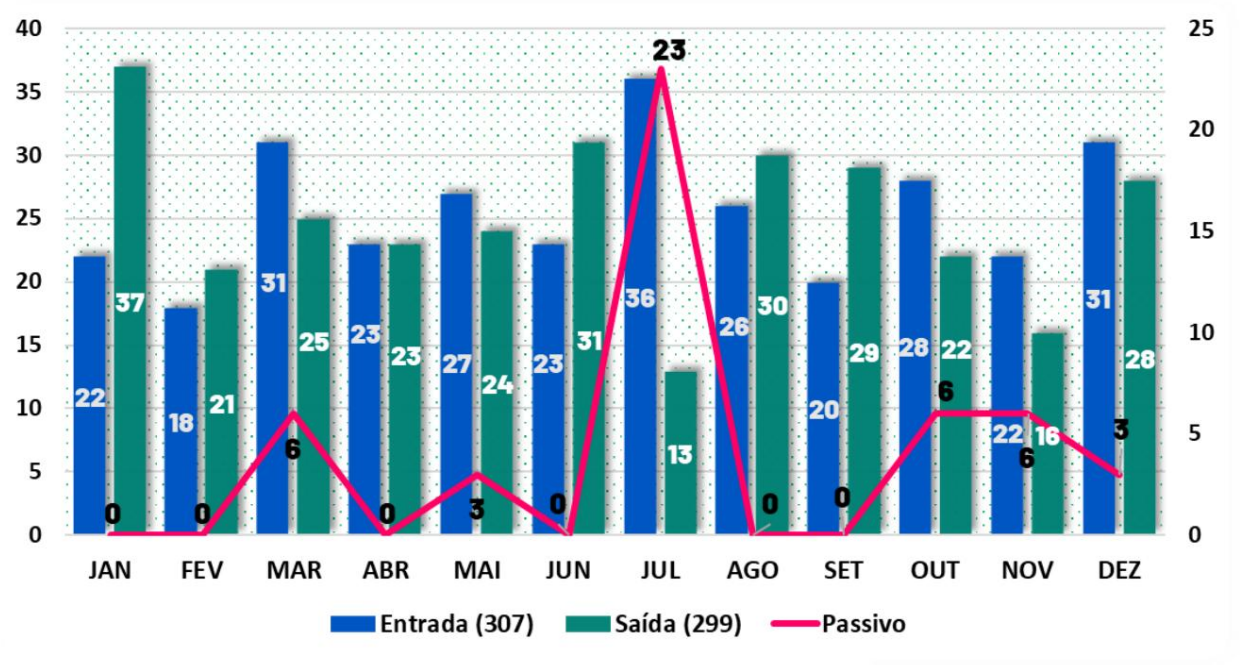

Figure 4 – *Monthly Input and Output of DEECs in 2023.*

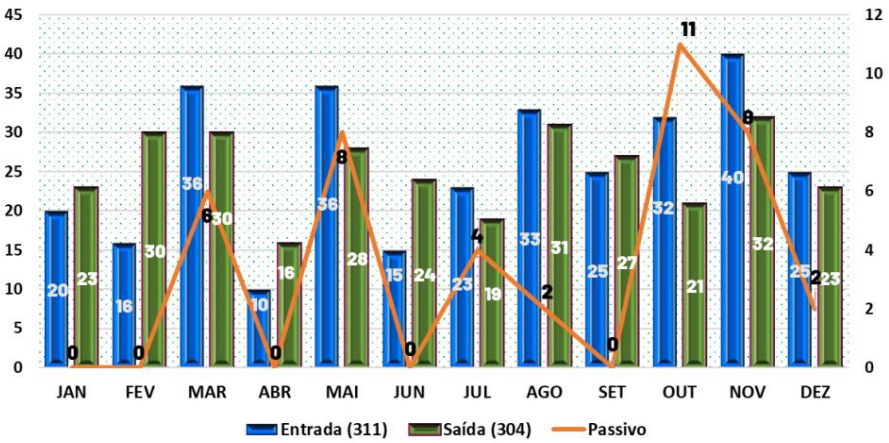

Figure 4a

Entrance and exit Monthly DEECs in 2022.

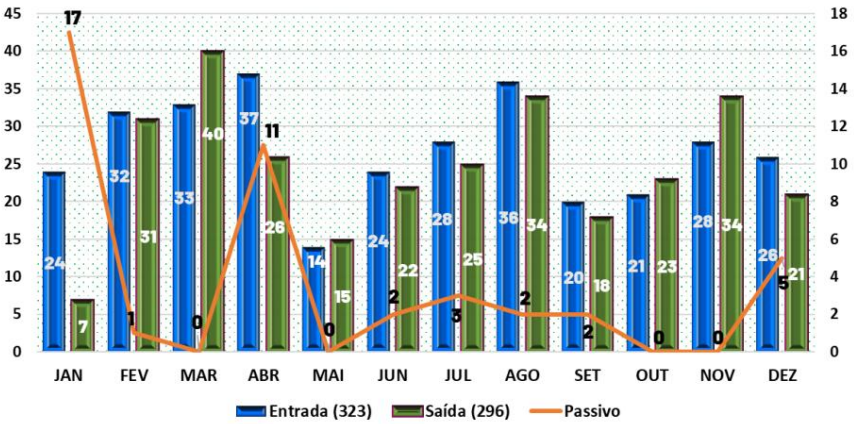

Figure 4b

Monthly Entry and Exit of DEECs in 2021.

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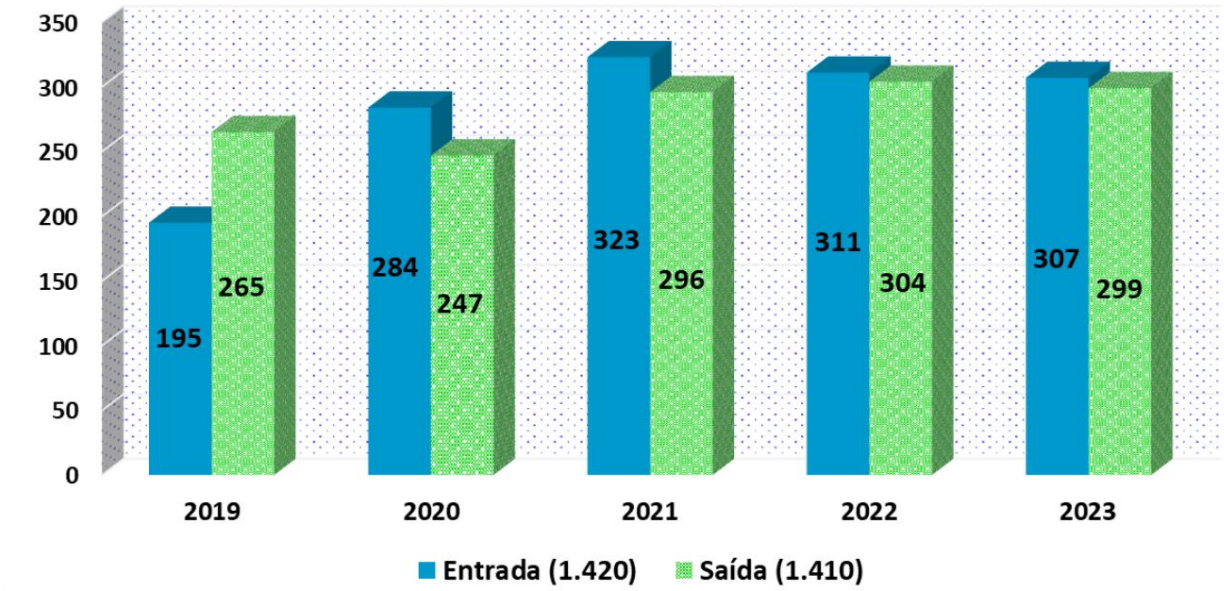

Figure 5 – *Entry and exit of DEECs between 2019 and 2023 (history).*

Over the last few years (2019 to 2023), as observed in Regarding DDCMs, there was a significant increase in the number of new DEECs submitted; there was a 1.5 times increase (from 195 to 284) in the number of DEECs submitted 2019 to 2020 and almost 2 times (195 to 323 DDCMs), from 2019 to 2021.

Thus, as mentioned in in relation to DDCMs, even though the increase in DEECs has occurred as a result of the pandemic Covid-19, in the following years of 2022 and 2023, the number of new DEECs submitted remained in high. Of the 543 DEEC petitions completed in 2020 and 2021, 134 (25%) were related to trials clinics for Covid-19.

In comparative terms, the number of DEECs submitted, prevails greater than the number of DEECs evaluated (1,420 *vs* 1,410), in period of 5 years **(Figure** 5). It is important to highlight that during the Covid-19 pandemic period, technical team directed all efforts to quickly analyze clinical trials for Covid-19. These clinical trials were prioritized, while time than other clinical trials remained waiting for the start of technical analysis for longer than expected.

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3.1 Clinical Trials (DEECs): National and Foreign Sponsors and ORPCs

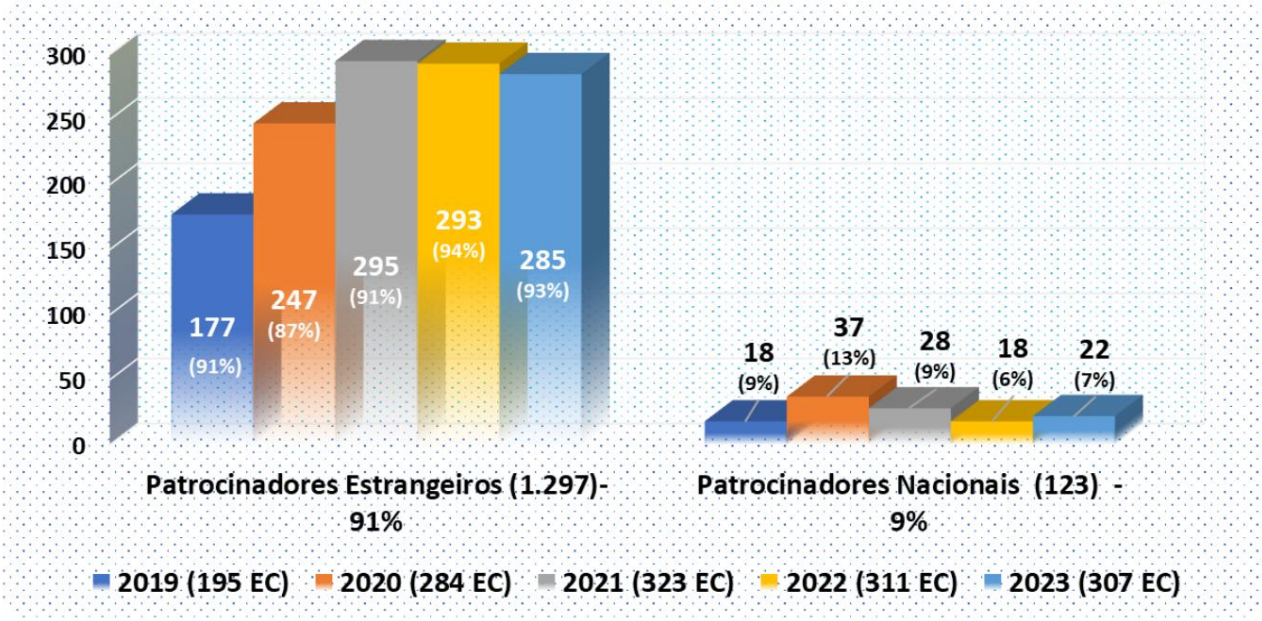

Figure 6 – *DEECs submitted between 2019 and 2023 (history) – foreign cooperation and national capital sponsor.*

The submission of DDCMs, DEECs and of secondary petitions is responsibility of the sponsor or designated ORPC. The sponsor is person, company, institution or organization responsible for initiating, manage, control and/or finance a clinical study. RDC *nº 09/2015* allows the sponsor who does not has headquarters or branch in Brazil, hire a Represent Organization tative Clinical Research (ORPC) that can represent you before the agency.

In 2023 the sponsors were responsible for the submission of 63% (194) of the 307 DEEC petitions submitted in the year, while 37% (114) were submitted by ORPCs.

Of the 1,420 DEEC petitions submitted over the last 5 years, 1,297 (91%) were sponsored with foreign cooperation and 123 (9%) were sponsored by national capital companies **(Figure** 6).

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3.2 Clinical Trials (DEECs): Regulatory Status

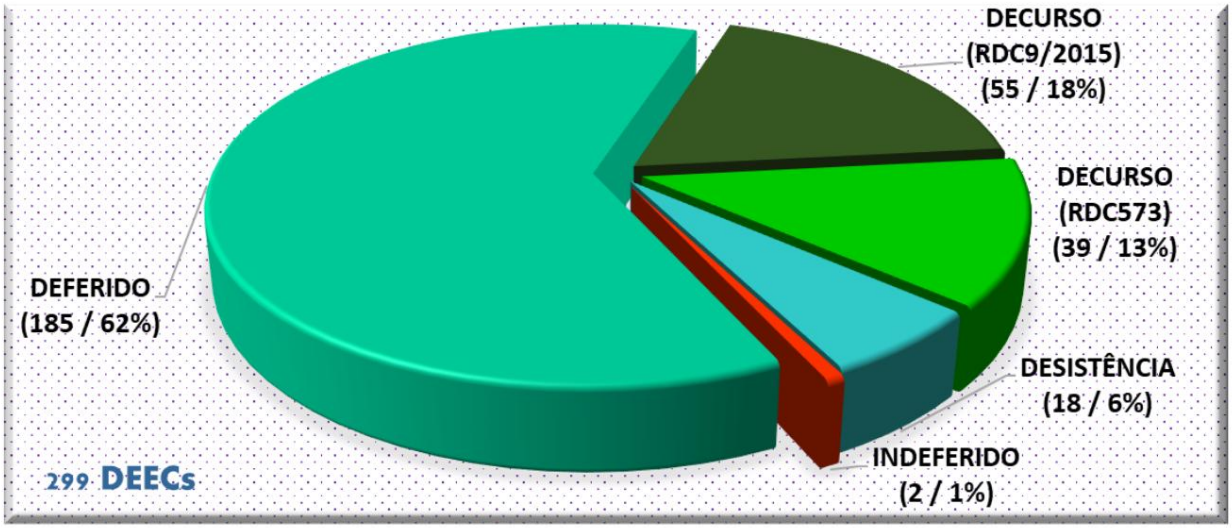

Figure 7 – *DEECs completed in 2023 – Regulatory status.*

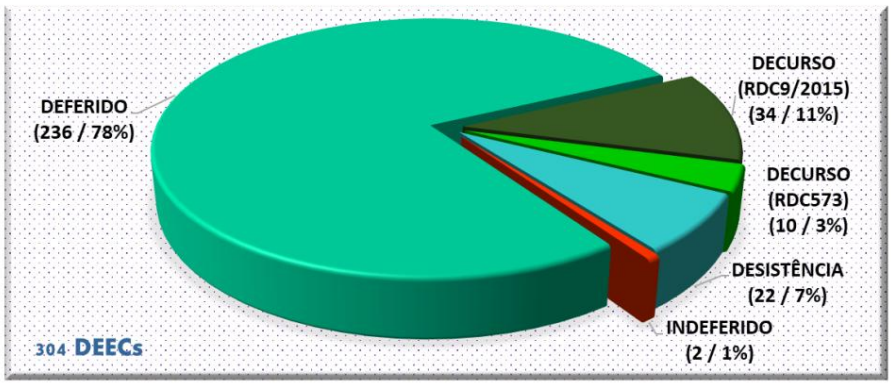

Figura 7a

DEECs completed in 2022 – Regulatory status.

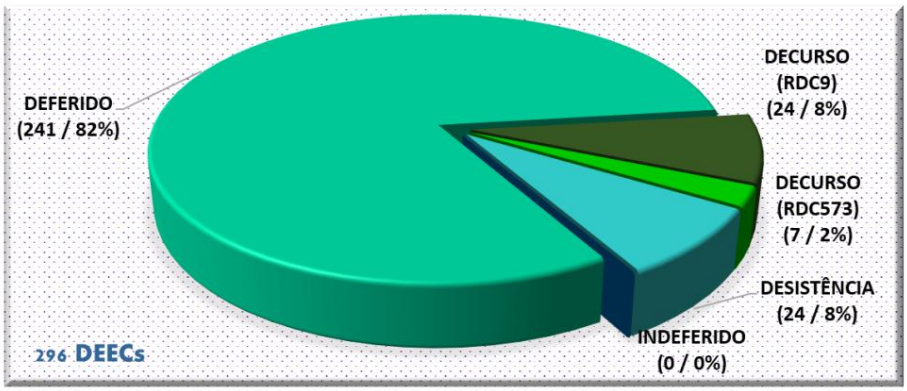

Figura 7b

DEECs completed in 2021 – Regulatory status.

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As recommended by *RDC no. 204, of July 6, 2005,* after technical analysis of a petition for DDCM, DEEC or secondary petition, the conclusion could be Grant or Rejection. A at any time the sponsor or ORPC may withdraw the petitions in the if they have not yet been completed, or cancel, in cases where that the petitions were granted and published in the Official Gazette of the Union (DOU).

RDC *nº 9/2015* establishes that the Anvisa must respond within 90 days in relation to primary petitions and secondary clinical trials. No there is a manifestation within this term, the clinical trial may be initiated, as long as authorized by the ethical instance. In this case, the petitions are released during term, without technical analysis, and published in the DOU.

For some types of tests clinicians the deadline for manifestation of the Anvisa is 120 days, but it is not a tacit deadline, that is, these tests clinicians cannot be released by expiry of the period, unless they have already been approved by authorities foreign regulatory members founders or permanent members of ICH, according to the criteria described in *RDC nº 573, of October 29, 2021,* based on trust regulatory *(Reliance).*

Therefore, test requests clinicians may be granted or rejected, after technical analysis, or may be released during term, based on *RDC nº 9/2015 or DRC nº 573/2021.*

In this context, it is observed that the number of petitions released per period has been increasing significantly over the last few years: 31 (10%) in 2021, 44 (14%) in 2022 and 94 (31%) in 2023 **(Figures 7, 7a and 7b,** respectively). This increase is primarily due to the gradual increase in the number of clinical trials throughout these recent years and other demands, without proportional recomposition of the number of servers in the technical area.

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3.3 Clinical Trials (DEECs): Prioritized analysis

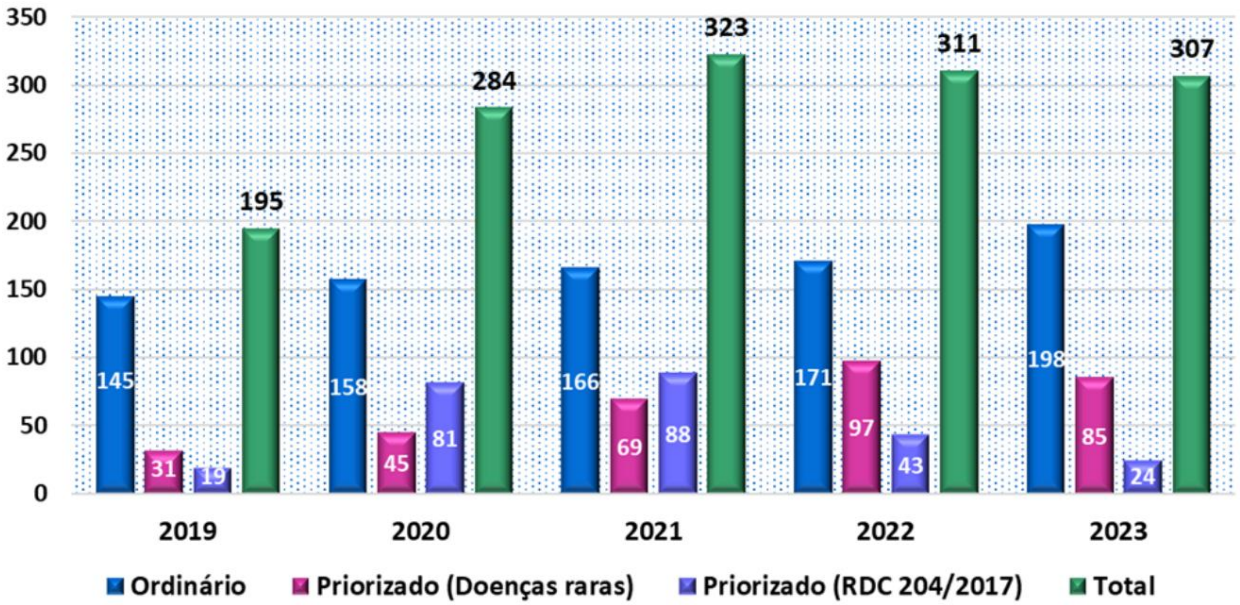

Figure 8 – *DEECs submitted – Analysis prioritization (2019 to 2023).*

RDC nº 204, of December 27th 2017 establishes the criteria for the framing of petitions for simplified analysis, among which stand out: clinical trials involving neglected disease, emergent or reemerging, medical health emergencies public or serious conditions debilitating, pediatric population and Phase 1 clinical trials conducted exclusively in Brazil. Other situation in which it applies to prioritization of technical analysis by Anvisa is when it comes to petitions of consent for clinical trials for rare diseases (up to 65 cases per 100 thousand inhabitants) or ultra-rare (one case for every 50,000 inhabitants, according to CNS Resolution No. 563, of 12 November 2017. The DRC no 205, of December 28, 2017, establishes the criteria for prioritization of the analysis of petitions for clinical trials for rare diseases, whose deadline for completing the analysis is 30 days.

Over the last few years It is observed that the number of petitions prioritized has been gradually growing mind: 50 (26%) petitions in 2019, 126 (44%) children 2020, 157 (49%) children 2021, 140 (45%) in 2022 and 109 (36%) in 2023, respectively **(Figure** 8).

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3.3 Clinical Trials (DEECs): Regulatory Times

Clinical Trials (299)	Regulatory Times (Median – Days/Months) Line	Analysis	TOTAL company	
PRIORITIZED				
Rare deseases DRC nº 205/2017 petitions – 7.8%] [23	61d (2,0M)	36d (1,2M)	23d (0,8M)	103d (3.4M)
Rare deseases DRC nº 205/2017 “Reliance” Simplified Analysis [58 petitions – 19%]	44d (1.5M)	7d (0,3M)	0 d (0,0M)	60d (2,0M) ↓ 42%
DRC nº 204/2017 (11 petitions – 3.7%)	55d (1,8M)	62d (2,0M)	25d (0,8M)	126d (4,2M)
DRC nº 204/2017 “Reliance” Simplified Analysis [11 petitions – 3.7%]	60d (2,0M)	6d (0,2M)	2d (0.1M)	67d (2,2M) ↓ 47%
NOT PRIORITIZED				
Ordinary analysis petitions - 4.7%] [14	186d (6,2M)	233d (7,8M)	77d (2.6M)	468d (15,6) ↓ 71%
Simplified Analysis “ (60 Relianceclinical trials – 20%)	127d (4,2M)	7d (0,2M)	0 d (0,0M)	138d (4.6M)
RELEASED DUE TO DEADLINE				
DRC nº 9/2015 clinical trials – 18%] [55	97d (3,0M)	2d (0.1M)	0 d (0,0M)	99d (3,3M)
DRC nº 573/2021 – “ Reliance clinical trials – 13%] [39	129d (4,3M)	2d (0.1M)	0 d (0,0M)	134d (4.5M)
NOTIFICATIONS				
Phase IV/Observational [11 clinical trials – 3.4%]	2d (0.1M)	3d (0.1M)	0 d (0,0M)	8d (0,3M)
Total (output): 299 petitions Include 17 (6%) dropouts				

Table 1 – *Regulatory times - DEECs completed in 2023.*

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Case during the analysis of DDCMs/DEECs petitions and petitions related to need of information additional information or clarifications regarding the documentation presented by the sponsor, the agency may issue a technical requirement, which must be fulfilled within 120 calendar days *(RDC nº 23, of June 5, 2015),* identified in the table as company time **(Table** 1).

In addition to the adoption of the mechanism regulatory trust Reliance, the RDC nº 573/2021, changed the deadline from 180 days to 120 days, for the Anvisa's first manifestation, in relation to the petitions considered as exceptions. Thus, there was a expansion of the scope of petitions for Initial DDCMs and DEECs with deadline tacit for Anvisa's manifestation. A standard establishes that if there is no Anvisa's statement on these petitions within 120 days, the trials corresponding clinicians may be initiated, after authorization from the ethical instance. In these cases, the petitions are released during deadline and published in the DOU.

In 2023, of the 299 petitions for clinical trials completed, 103 (34%) were prioritized (81 petitions referring to rare diseases) and of these, 69 (79%) petitions met in the simplified analysis criteria. The median analysis time for these petitions was 7 days. Already at 34 prioritized and ineligible petitions for the simplified analysis, the time median analysis was 36 days (rare diseases) and 62 days for other petitions *(RDC nº 204/2017).* Therefore, the median analysis time of prioritized petitions and frames given in the simple analysis criteria was 80% lower than that of petitions not classified **(Table** 1).

Regarding the 74 petitions ordinary, 60 were framed us criteria for analysis simplified, whose median time of analysis was 7 days, while the median time for analyzing the 14 petitions not ordinary meeting the criteria for simplified analysis was 233 days. The petitions released by expiry of the period, corresponded to 31% (94) of the 299 petitions completed in 2023 **(Table** 1).

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3.5 Clinical Trials (DEECs): Development Phases

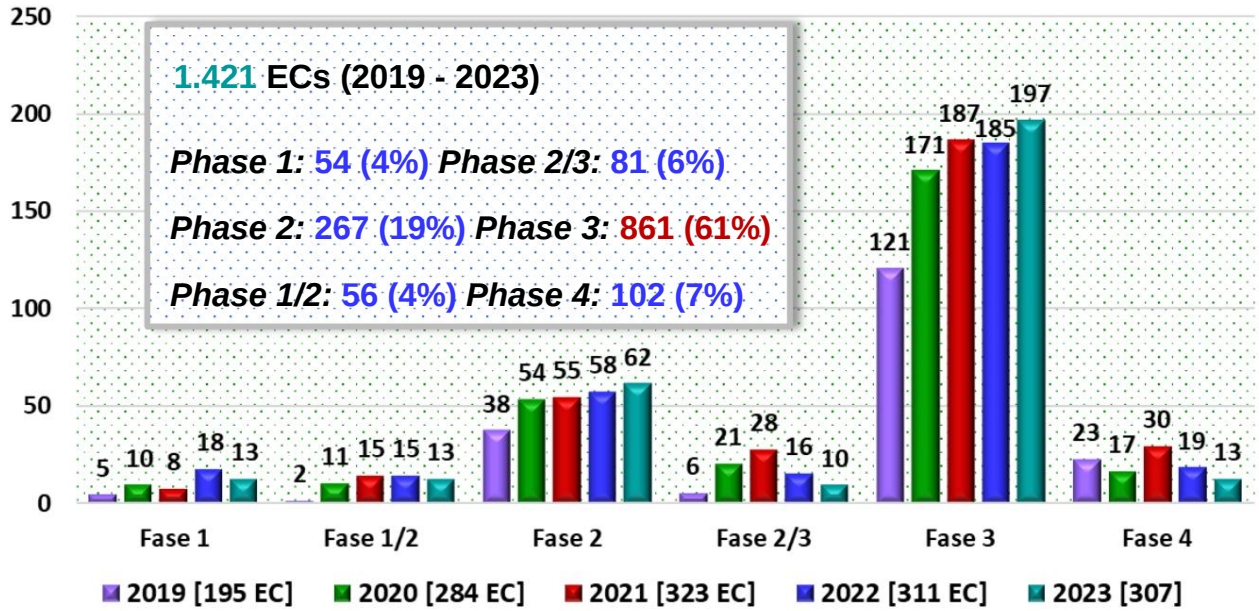

Figure 9 – *DEECs submitted (2019 – 2023) - Development Phases.*

Phase 1 is considered to be the first clinical trials in human beings human (security initials), mainly comprising the administration of the medication in few participants. The tests Phase 2 clinical trials are carried out in a greater number of participants with the disease you want to study (100 – 300 patients), whose objective The main thing is to evaluate the safety in short term, dose-response relationship and the preliminary efficacy of the drug experimental. The clinical trials of Phase 3 or comparative effectiveness are those in which the medicine experimental is administered to a much larger patient population than in the previous phases and generally has the aim of confirm efficacy results and security and demonstrate the relationship benefit/risk of the medicine experimental.

In 2023, as well as in years previous clinical trials of Phase 3 were predominant and corresponded to 64% (197) of the 307 DEEC petitions submitted in 2023 **(Figure 9).**

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3.6 Clinical Trials (DEECs): Therapeutic Areas

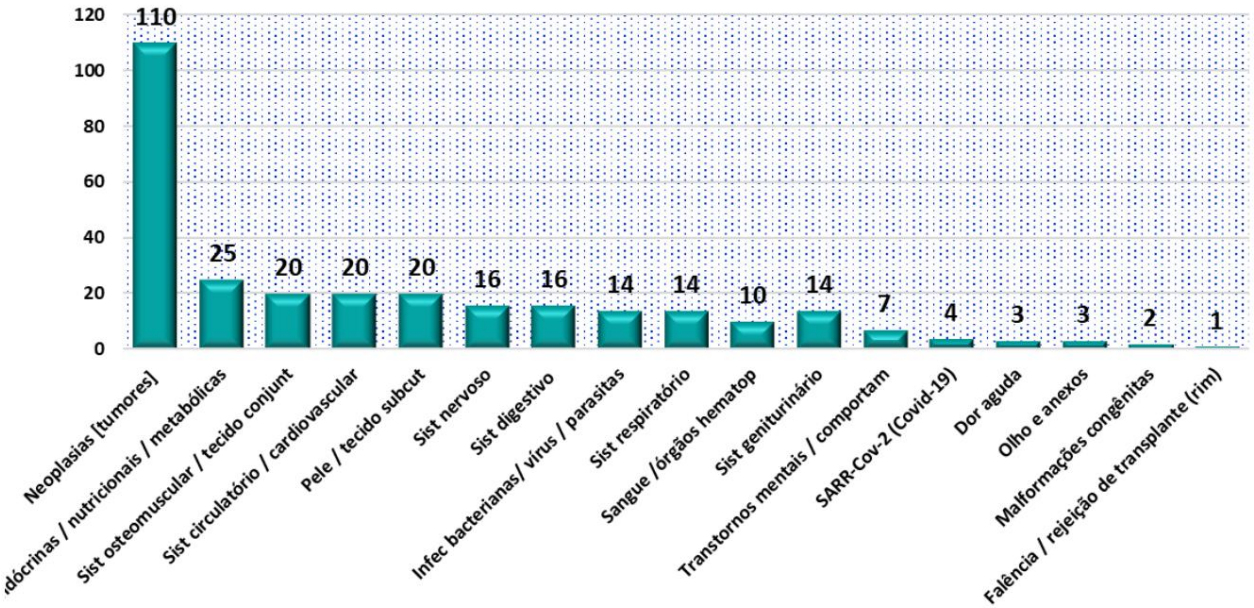

Figure 10 – *Therapeutic areas – 299 DEEC petitions completed in 2023.*

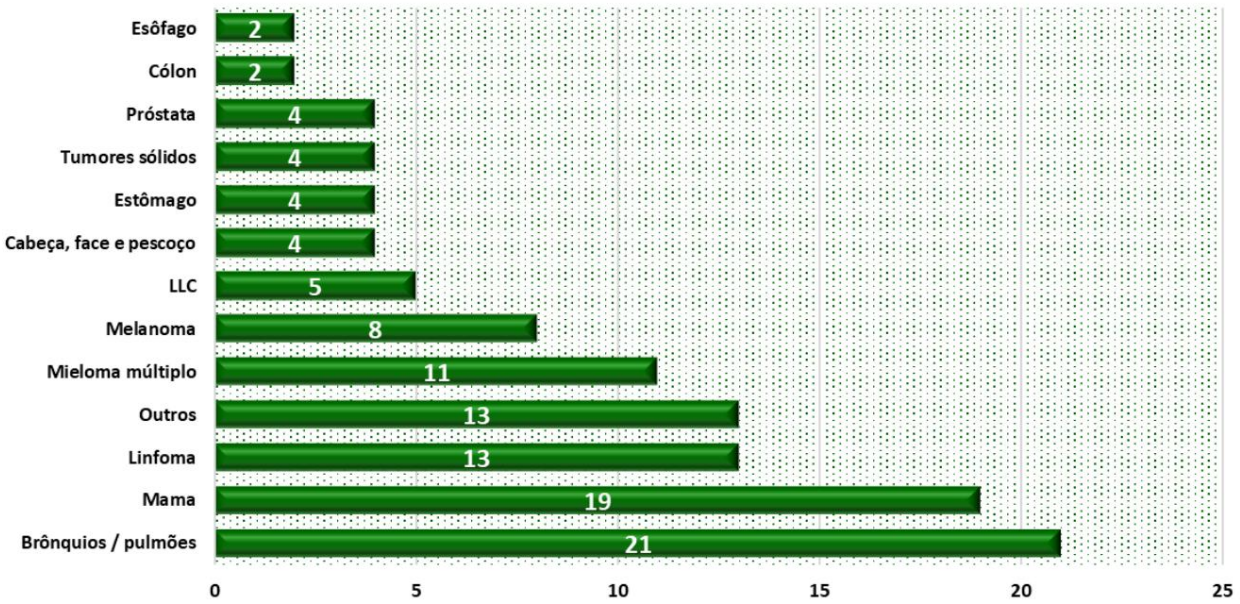

Figure 10a – *Therapeutic areas – 110 DEECs petitions completed for neoplasms.*

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Over the past few years, clinical trials for neoplasms have been prevalent; in 2021 corresponded to 24% (72) of the 296 essay requests clinicians completed; in 2022 it was 37% (112) of the 304 completed petitions and in 2023 were also 37% (110) of the 299 petitions completed **(Figure 10 and 10a).** It is important to highlight, as already mentioned, that in 2021 there was a increase in clinical trials for Covid-19, which justifies there being fewer clinical trials for neoplasms this year.

Among the neoplasms, lung cancer stands out, which corresponded to 19% (21) of the 110 clinical trials for neoplasms, followed by breast cancer, 17% (19) and lymphoma 12% (13). Others neoplasms, together, corresponded to 12% (13) of the total and include: cervix, liver and biliary tract, tissues moles, endometrium, nasopharynx, ovary, kidney, CNS and mesothelioma, corresponding to a clinical trial for each one.

After neoplasms, if highlighted endocrine diseases and metabolic processes, which corresponded to 8% (25) of 299 test requests completed clinics, highlighting for diabetes (4) and obesity (5), followed by clinical trials to musculoskeletal diseases and tissue connective system circulatory system/vas cular, skin and subcutaneous tissue, which corresponded to 7% (20) each **(Figure** 10).

Among the 20 clinical trials for diseases of the circulatory system or cardiovascular, with highlight: arterial hypertension (5) and congestive heart failure (3). And from 20 clinical trial petitions for diseases of the skin and subcutaneous tissue, atopic dermatitis (8) and psoriasis (3)

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4. TIME BETWEEN AUTHORIZATION BY ANVISA AND THE START OF CLINICAL TRIALS

Time between authorization and start of EC (days)	Number of clinical trials started
1 a 60	10 (4%) [4 had the analysis prioritized]
61 a 90	18 (8%) [5 had the analysis prioritized]
91 a 120	24 (10%) [9 had the analysis prioritized]
121 a 150	31 (13%) [12 had the analysis prioritized]
151 a 180	15 (6%) [6 had the analysis prioritized]
>180	142 (59%) [54 had the analysis prioritized]
Total	240 Clinical Trials

Table 1 – *Time between authorization from Anvisa and the start of clinical trials (2023).*

According to RDC no. 09/2015, the start date of the trial clinical corresponds to the date of inclusion of the first participant in clinical trial in Brazil, and the date end of clinical trial corresponds to the date of the last visit of the last trial participant clinician in Brazil or another definition do sponsor, determined expressly, no protocol specific clinical trial. You sponsors or ORPCs must inform the start and end date of the clinical trial to Anvisa, within 30 (thirty) calendar days after each date start and end.

Deadlines for starting rehearsals clinics after authorization from Anvisa may vary depending on other factors and measures that need be taken by sponsors, to create the necessary conditions to begin recruiting clinical trial participants. Furthermore, even after authorization from Anvisa, the tests clinics can only be started after authorization from the ethical body. It is observed that 60% of the tests clinicians authorized by Anvisa only were actually started after 6 months from the authorization date **(Table** 1).

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5. JUSTIFICATIONS FOR CANCELLATIONS AND WITHDRAWAL OF CLINICAL TRIALS

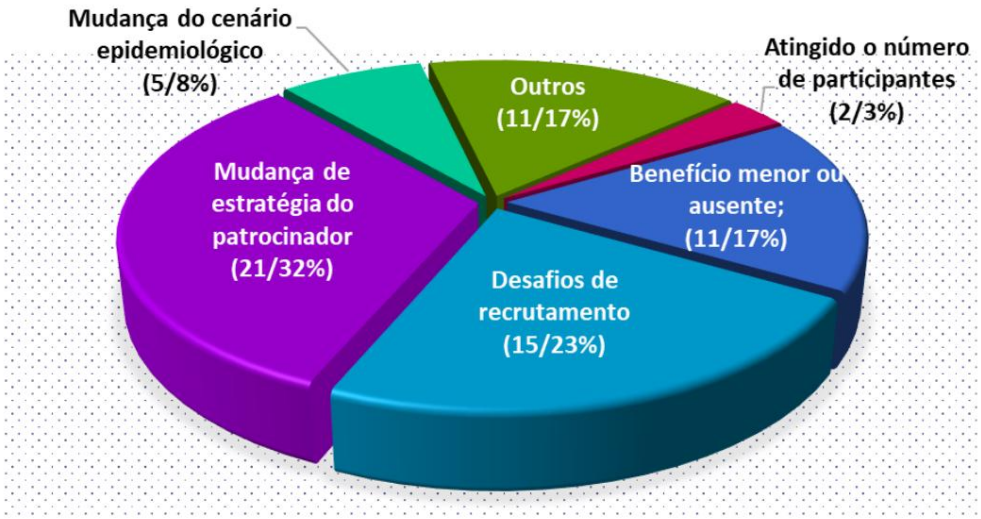

Figure 11 – *Justifications for clinical trial cancellations (2023).*

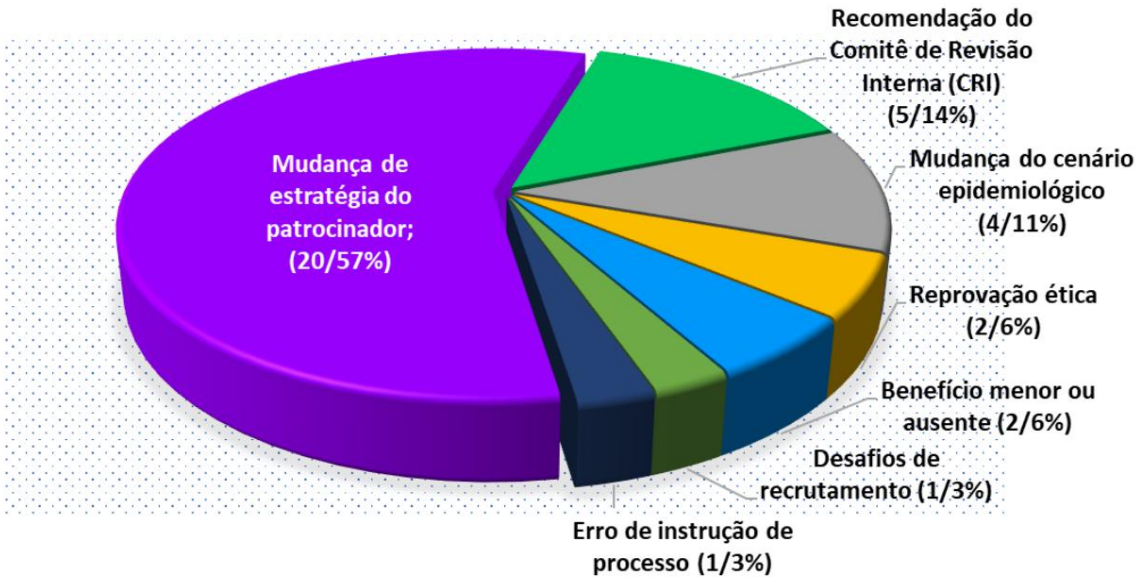

Figure 11a – *Justifications for withdrawals from clinical trials (2023).*

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RDC *nº 9/2015* recommends that the sponsor may withdraw, cancel or suspend a DDCM petition or clinical trial (DEEC) and petitions secondary, at any time, provided that the appropriate technical-scientific justifications, as well as as a follow-up plan of participants in clinical trials that may have already started. The request for withdrawal must be made before conclusive decision on the petition and publication in DOU. The request for cancellation applies when already the petition was published in DOU.

Furthermore, Anvisa may, at at any time, cancel or suspend the DDCM or any linked clinical trial, if it is judged that the approval conditions were not met or if there are reports of safety or efficacy that affect significantly the participants of the clinical trial or affect the validity scientific data obtained, information Give the reasons to the sponsor.

The largest number of requests for clinical trial cancellations was motivated by the change of sponsor strategy (32%), followed by challenges related to recruitment (23%), lower than expected or absent benefits (17%) and other reasons (17%) **(Figure** 11).

In the case of withdrawals, observe if the largest number of requests was also motivated by a change in sponsor strategy (57%), followed by internal committee recommendation (14%) and change in scenario epidemiological (11%) **(Figure 11a).**

It is important to highlight that the withdrawal and cancellation notices to submitted in 2023 refer also authorizes clinical trials in previous years and do not need to sarily to clinical trials rized in 2023.

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6. SUBSTANTIAL CHANGES TO THE DDCM

The modifications to the DDCM, in context of RDC nº 09/2015, are defined as any changes carried out in the global context of DDCM, especially regarding those related to the quality of investigational product or administrative changes, such as form updates, for example.

6.1 Changes that potentially impact the quality or safety of the experimental medicine, active comparator or placebo

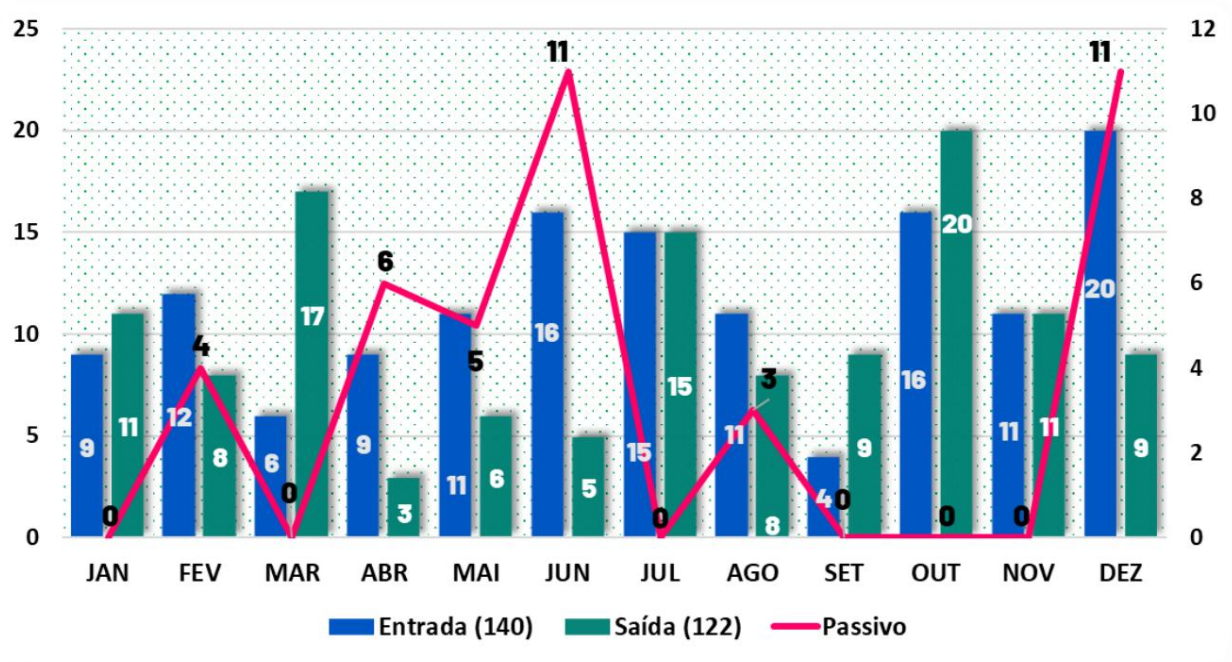

Figure 12 – *Monthly Input and Output of quality change petitions in 2023.*

Substantial changes can be protocolized a any time, including before of Anvisa's final demonstration about DDCM. All modifications must be presented has Anvisa. The modifications substantial must to be registered and the sponsor must wait for Anvisa approval to implement them. The changes no substantial must be presented as part of the security update report for the drug development experimental.

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Quality changes (122)	Regulatory Times (Median – Days/Months) Line	Analysis	Company	TOTAL
PRIORITIZED				
Rare deseases DRC nº 205/2017 petitions – 12%] [15	37d (1,2M)	18d (0.6M)	0 d (0,0M)	69d (2,3M)
Rare deseases DRC nº 205/2017 "Reliance" Simplified Analysis petitions – 10%] [12	26d (0.9M)	8d (0,3M)	0 d (0,0M)	38d (1,3M)
DRC nº 204/2017 (1 petition – 0.8%)	55d (1,8M)	18d (0.6M)	118d (4,0M)	191d (6.4M)
DRC nº 204/2017 "Reliance" Simplified Analysis petitions – 2.5%] [3	20d (0.7M)	9d (0,3M)	0 d (0,0M)	56 d (1.9M)
NOT PRIORITIZED				
Ordinary analysis petitions - 16%] [19	140d (5,0M)	12 d (0.4M)	0 d (0,0M)	156d (5,2)
Simplified Analysis " (39 Relianceclinical trials – 32%)	112d (3.7M)	6d (0,2M)	0 d (0,0M)	120d (4,0M)
RELEASED DUE TO DEADLINE				
DRC nº 9/2015 clinical trials – 23%] [28	96d (3,2M)	2d (0.1M)	0 d (0,0M)	98d (3,3M)
Total (output): 122 petitions				
Include 5 (4%) dropouts				

Table 2 – *Regulatory times – Quality Alt Petitions completed in 2023.*

The substantial changes to quality may also be fit into the prioritization criteria of analysis, under the terms of RDC no. 204/2017 and 205/2017, as well as can be analyzed in a simplified, under the terms of RDC no. 601, of February 16, 2022, which establishes utilization criteria of analysis by authority equivalent foreign regulatory, by the Reliance mechanism.

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7. AMENDMENTS TO CLINICAL PROTOCOLS

All substantial amendments to a clinical trial protocol should be presented to Anvisa in the form secondary petition, and should only be implemented after approval of the Anvisa and ethical bodies, of in accordance with current legislation.

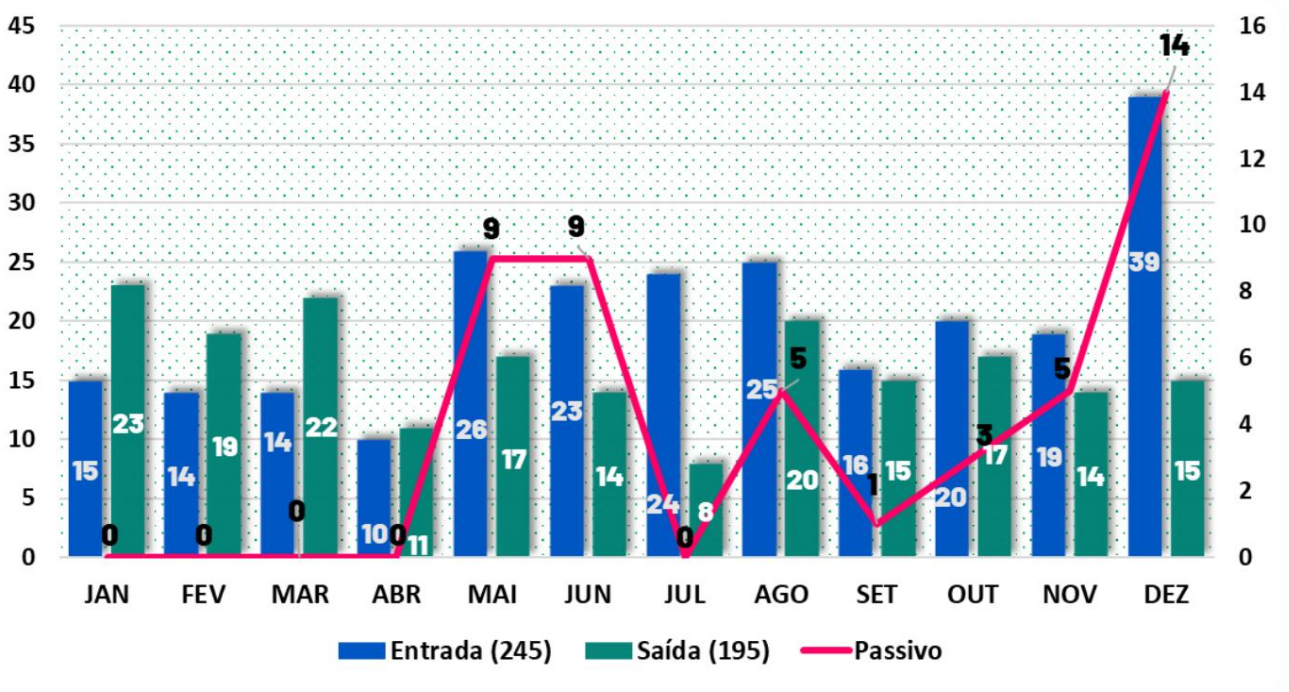

Figure 13 – *Monthly Input and Output of Amendments in 2023.*

An amendment is considered substantial when the change in clinical trial protocol interfere security or physical integrity or mental of the participants and/or change the scientific value of the protocol of clinical trial.

Amendments to the test protocol non-substantial clinical presented to Anvisa as part of the annual monitoring report clinical trial protocol. Per Therefore, the amendments related to the **Figure 13** refer only to substantial amendments.

It is observed that in 2023 there were submitted, on average, 20 amendments to the protocol per month, and were completed an average of 16 petitions/month.

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Amendments to clinical protocol (195)	Regulatory Times (Median – Days/Months)			
	Line	Company Analysis		TOTAL
PRIORITIZED				
Rare deseases DRC nº 205/2017 petitions – 16%] [31	53d (1,8M)	16d (0.5M)	0 d (0,0M)	78d (2.6M)
Rare deseases DRC nº 205/2017 "Reliance" Simplified Analysis [43 petitions – 22%]	35d (1.1M)	8d (0,3M)	0 d (0,0M)	56 d (1.9M)
DRC nº 204/2017 (9 petitions – 3.6%)	27d (0.9M)	9d (0,3M)	0 d (0,0M)	50d (1.7M)
DRC nº 204/2017 "Reliance" Simplified Analysis petitions – 4.1%] [6	47d (1.7M)	6d (0,2M)	0 d (0,0M)	53d (1,8M)
NOT PRIORITIZED				
Ordinary analysis [15 petitions – 7.7%]	138d (4.6M)	20d (0.7M)	0 d (0,0M)	177d (5,9)
Simplified Analysis " Reliance(63 clinical trials – 32%)	92d (3,0M)	6d (0,2M)	0 d (0,0M)	98d (3,3M)
RELEASED DUE TO DEADLINE				
DRC nº 9/2015 clinical trials – 12%] [24	96d (3,2M)	3d (0.1M)	0 d (0,0M)	99d (3,3M)
Total (output): 195 petitions				
Include 4 (2%) dropouts				

Table 3 – *Regulatory times – Quality Alt Petitions completed in 2023.*

Deadlines for analyzing petitions of substantial amendments to the protocol are the same deadlines established for the respective petitions of DEECs that gave rise to them, according to *RDC nº 09/2015.* Apply-whether to these petitions the same prioritization criteria described in *RDCs nº 204 and 205/2017,* in addition to *DRC nº 601/2022.*

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8. CLINICAL TRIALS IN RARE DISEASES

In DRC nº 205/2017, mentioned previously, established special procedure to reduce analysis deadlines consent to clinical trials, to rare diseases, in addition to certification of Good Manufacturing Practices (CBPF) and registration of medicines for treatment, diagnosis or prevention of rare diseases. In 2023 there were 81 petitions relating to clinical trials for rare diseases **(Table 2).**

Rare disease	Experimental Medicines
Cerebral adrenoleukodystrophy (cALD)	Leriglitazona (MIN-102)
Autoimmune hemolytic anemia	Nipocalimabe / JNJ-80202135 / M281 / N027
Colorectal cancer	Botensilimabe (AGEN1181) - Balstilimabe (AGEN2034)
Breast cancer	Inavolisibe (GDC-0077, RO7113755) / RO7247669 / Giredestrant tartrate
Amyloidotic cardiomyopathy mediated by transthyretin	Carlsbad (CA)
Lung Cancer (with characteristics)	Tarlatamabe (AMG 757) / Sotorasibe (AMG 510) / BI 1810631
Biliary Tract Cancer	Rilvegostomy
Nasopharyngeal Carcinoma / Hepatocellular Carcinoma	Pempulimabe (AK105) / Tiragolumab
Crohn's disease	Adipato (VTX958; VTX958)
Dermatomiosite / Polimiosite	Daxdilimab/Daxdilimabe/HZN-7734 / Anifrolumab
Liver Disease Associated with Alpha-1 Deficiency Antitripsina.	Fazirsiran (TAK-999)
Interstitial Lung Disease	Belimumabe (GSK1550188)
Anti-n-methyl-d-aspartic acid receptor encephalitis (NMDAR)	Satralizumabe
Epileptic and developmental encephalopathy (DEED)	PRACTICE-222
Multiple sclerosis	Tolebrutinibe
Eosinophilic esophagitis	Dupilumabe (SAR231893)
Fibrodysplasia Ossificans Progressive	Garetosmabe (REGN2477)
Idiopathic Pulmonary Fibrose	Vixarelimab (RO7622888/ KPL-716)

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GM2 Gangliosides and Niemann-Pick Doença Type C. AZ-3102	
Classic congenital adrenal hyperplasia (CAH).	Tildacerfont (SPN001) / CRN04894 Maleate
Glomerulopathy	Pegcetacoplan (APL-2) / LNP023
Pulmonary arterial hypertension (PAH)	Seralutinib / Imatinib (AV-101)
Autosomal Dominant Hypocalcemia Type 1 (ADH1) CLTX-305 - Encalerete	
Neurogenic orthostatic hypotension;	Ampreloxetina (TD-9855)
Acute Kidney Injury	Ravulizumab (ALXN1210)
Chronic lymphocytic leukemia	BGB-11417
Acute myeloid leukemia (AML)	Mocravimod (KRP203 HCl)
Lymphoma	Pirtobrutinibe (LOXO-305) / BGB-11417 / BI-1206/ Zanubrutinibe (BGB-3111) / Glofitamabe / BGB-16673 / Acalabrutinibe
Partial lipodystrophy	Metreleptina
Dedifferentiated liposarcoma	Brigimadlina
Primary Discoid Lupus Erythematosus	Daxdilimabe (HZN-7734) / Upadacitinib (ABT-494)
Skin melanoma, head and neck cancer	VSV-hIFNÿ-NIS Encorafenibe – Binimetinibe
Mesothelioma	Volrustomig
Generalized Myasthenia Gravis	Batoclimabe / Pozelimabe - Cemdisiran
Multiple Myeloma	SAR650984 (Isatuximabe) / Belantamabe (GSK2857914) / RO7425781 (Gpcr5d Cd3 Tcb) / BGB-11417 / Forimtamig / Talquetamab- Teclistamab / Lenalidomide
Nephropathy / Nephritis lupica	RO7434656 (ISIS 696844) Zanubrutinib/Zigakibart/Atacicept (VT-001)/Maleato de zetomipzomib (KZR-616)
Osteogenesis Imperfecta	UX143 - Setrusumabe
Bullous pemphigoid	Nipocalimabe / JNJ-80202135 / M281 / N027
polineuropatia	batoclimab
Generalized Pustular Psoriasis (GPP)	Espesolimabe
Lung Sarcoidosis	Efzofitimode (ATYR1923)
Treatment of leg ulcers	Voxelotor
Hematopoietic Stem Cell Transplant	GBT021601
Gastrointestinal tumors (GIST)	Bezuclastinibe (CGT9486)
Solid tumors	Atezolizumab
Central Nervous System Tumors	Alectinib

Table 2 – *Clinical Trial Petitions completed in 2023 for Rare Diseases.*

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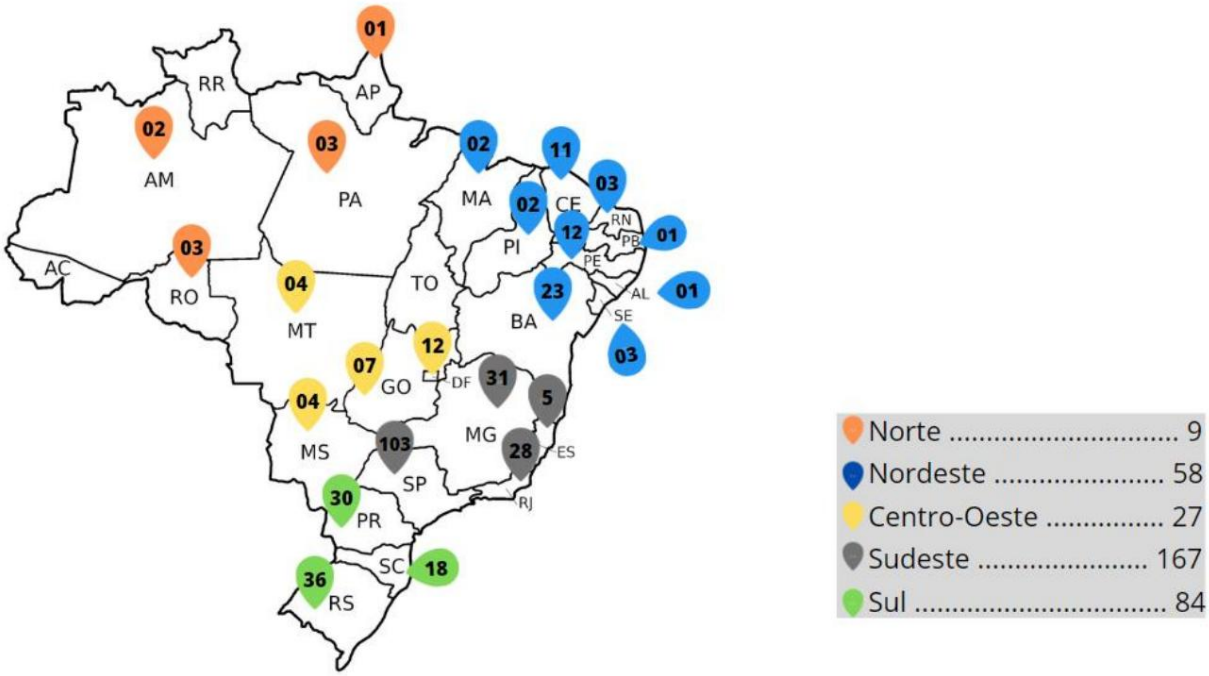
9. CENTERS AND INVESTIGATORS IN CLINICAL TRIALS

Clinical trial centers are public or private organizations, legitimately constituted, properly registered in the National Registry of Health Establishments (CNES), where the clinical trials. There is no interference of Anvisa in relation to the choice of clinical centers and researchers, but sponsors and ORPCs need to present the list to the agency with the names of these centers and investigators for each trial clinician and ensure that both are qualified to conduct clinical trials.

Figure 14 – *Distribution by state of indicated clinical centers (2023).*



In 2023, 299 were completed clinical trial petitions (DEECs) and to carry out these tests 345 clinical centers were indicated candidates across Brazil. The South and Southeast were the regions that had the highest frequency of indication of centers for carrying out tests authorized clinicians. In the region Southeast, 167 were nominated (56%) centers, followed by the South region with 84 (28%) centers and the Northeast region,

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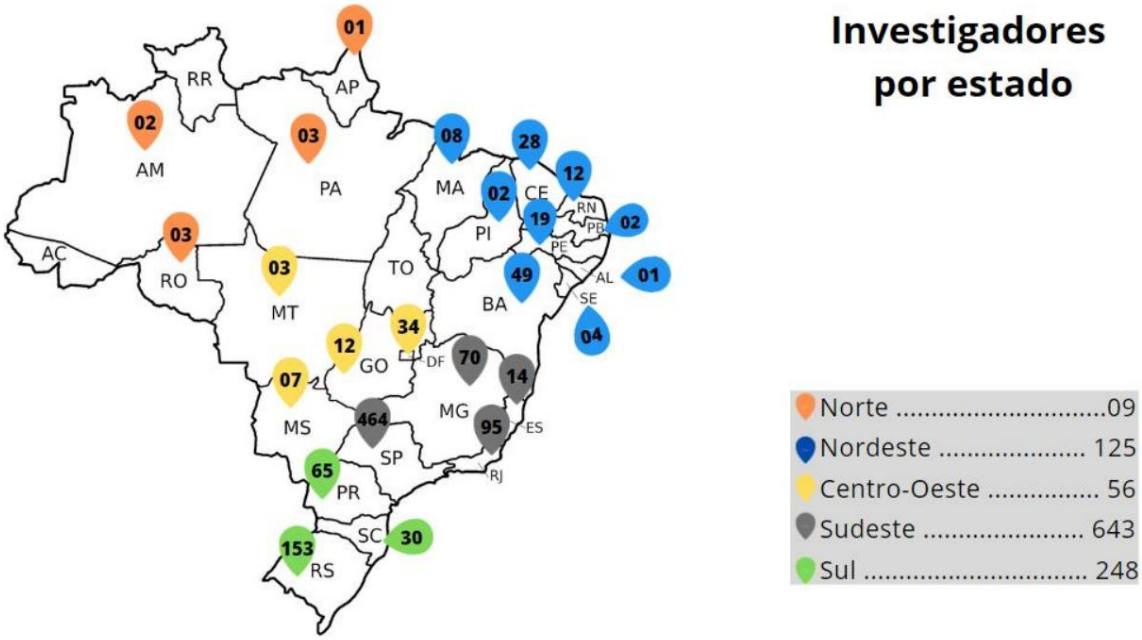
with 58 (19%) centers indicated **(Figure** 14).

In the last 4 years it has not been No change observed significant in the distribution of centers in the regions Brazilians. In 2020 they were nominated of 238 (51%) centers in the southeast region, 214 (54%) in 2021 and 169 (50%) in 2022. The proportions of centers indicated in the other regions in the years 2020, 2021 and 2022 remained similar to the year of 2023.

Figure 15 – *Distribution by state of nominated Researchers (2023).*



The number of researchers in tips was proportional to the number and the distribution of listed centers by sponsors or ORPCs in the Brazil, and resulted in 1,081 investments farmers in 2023, with a greater number in the states of São Paulo and Rio Grande do Sul, with 464 (43%) and 153 (14%), respectively, **(Figure** 15).

The numbers presented above represent the total amount of centers and researchers **(Figures 14 and 15)** nominated by sponsors and informed to Anvisa, as a candidate to conduct the tests clinicians authorized in 2023.

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10. CARE ACCESS TO EXPERIMENTAL MEDICINES

The development of a new medicine must comply with a complex and time-consuming process that ensure that the medicine is safe, effective and quality for intended therapeutic use, until be registered and authorized to commercialization. In this context, as an alternative to the long wait for access to new medicines, new possibilities for special access to medicines still under investigation, through assistance programs, such as the use compassionate or expanded access, for patients with diseases severe debilitating and/or threaten life and do not have access to therapeutic alternative satisfactory with registered products.

Additionally, according to the CNS/MS Resolution No. 466, dated 12th December 2012, which approves the regulatory guidelines and standards of research involving beings humans in Brazil, the research that use experimental methodologies in the biomedical area, involving human beings, must ensure that everyone participants at the end of the study, by the sponsor, access free of charge and for an indefinite period, to the best prophylactic, diagnostic and therapeutic methods available demonstrated to be effective. In that sense, the supply program of post-study medication was included in the regulation of assistance program, *DRC no 38, of August 12, 2013.* No case of ultra-rare diseases, the *Resolution CNS/MS nº 563/2017,* access must be for a period of five years after obtaining registration with the Agency National Health Surveillance (Anvisa). RDC *nº 38/2013,* establishes provides the criteria and procedures for conducting these programs.

According to RDC nº 38/2013, The following are the characteristics of each of the assistance programs **(Table** 3).

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	Post-delivery study	Expanded Access	Compassionate Use
Phase do Development Clinical do Medicine	Clinical trial closed or early departure from participant.	At least one clinical trial of Phase III in progress or concluded in the indication in that is intended to be used.	Clinical trial at any stage with promising initial data or scientific evidence for the indication in which it is intended to use.
Who he can to participate	Survey participants clinic.	Group of patients.	For personal (Individual) use not access participants expanded or clinical research
When to use	As long as there is benefit, at medical discretion.	Lack of alternative satisfactory therapy with registered products.	Lack of alternative satisfactory therapy with registered products.
Condition for use	In therapeutic indication studied.	Severe debilitating illnesses and/or that threaten life without therapeutic alternatives.	Severe debilitating illnesses and/or that threaten life without therapeutic alternatives.
Situation regulatory medicine	Medication with or without record	Unregistered medicine in Brazil in the indication intended	Medicine not registered in Brazil in the intended indication

Table 3 – *Characteristics of assistance programs.*

Requests for consent from expanded access and use programs compassionate must meet some criteria, as mentioned in **Table** 3. Request for program authorization assistance must be carried out by sponsor or ORPC, taking into account the request from an attending physician, with the patient's consent. You program authorization requests assistance received by COPEC in 2023 are described below, **(Panel 4 and Figure** 16).

Figure 16 – Authorized Assistance Programs (2023).

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In the year 2023, they were submitted 172 requests for authorization to supply of medicine in compassionate use program. You therapeutic uses and medicines of these requests are described I don't want to follow.

In the same period there were 6 program requests approved assistance in expanded access and 66 supply of post-study.

Table 4 – *Compassionate Use, Expanded Access and Authorized Post-Study Supply Programs: Medications and therapeutic indications (2023).*

THERAPEUTIC INDICATION	QTY	ACTIVE SUBSTANCE / NAME COMMERCIAL
COMPASSIONATE USE		
Rheumatoid arthritis (RA)	1	Tofacitinibe (Xeljanz®)
Unresectable or metastatic triple-negative breast cancer (CMTNM)	3	Sacituzumabe Govitecana (Trodelvy™)
Advanced Breast Cancer	1	Palbociclibe (Ibrance®)
Non-small cell lung cancer (NSCLC)	1	Lorlatinibe (Lorbrena®)
Metastatic non-small cell lung cancer (NSCLC)	5	Mobocertinib (Exkivity®)
Rectal cancer (RC)	7	Dostarlimab (Jemperli®)
Amyloidosis cardiomyopathy	1	Patisiran Sodium (Onpattro®)
macular degeneration Age-related (AMD)	2	Pegcetacoplana (Empaveli®)
Amyotrophic Lateral Sclerosis (ALS)	5	Tofersena (Qalsody)
Low Grade Glioma/Xanthoastrocytoma Pleomorphic	17	Trametinibe + Dabrafenib (Mekinist® E Taffins®)
Chronic Myeloid Leukemia (CML)	30	Asciminibe (Scemblix®)
Diffuse large B cell lymphoma	14	Epcoritamabe (Epkinly)
Melanoma	21	Nivolumabe + Relatlimabe (Opdualag®)
Relapsed/Refractory Triple Refractory Multiple Myeloma	11	Elrantamabe (Elrexfio®)
Neuroblastoma of high Risk or refractory	7	Naxitamabe (Danyelza®)
Generalized pustular psoriasis (gpp)	7	Spesolimabe (Spevigo™)
Hutchinson-Gilford progeria syndrome (HGPS)	2	Lonafarnibe (Zokinvy®)
Advanced or metastatic solid tumors with rearranged activation during transfection (RET)	20	Selpercatinib (Retevmo®)
Human Immunodeficiency Virus (HIV-1)	5	Fostemsavir (Rukobia®)

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EXPANDED ACCESS		
Non-small cell lung cancer (NSCLC)	2	Tarlatamabe
Endometrial cancer (EC)	1	Dostarlimab (Jemperli®)
Advanced Esophageal Squamous Carcinoma	1	Tislelizumab
Hidradenitis suppurativa	1	Secuquinumabe
Relapsed or refractory multiple myeloma	1	Talquetamabe
Human Immunodeficiency Virus (HIV-1)	1	Fostemsavir (Rukobia®)
POST-STUDY MEDICATION SUPPLY		
Gastric adenocarcinoma	1	Trastuzumabe
Acromegaly	1	Pasireotide Pamoate
Leber's congenital amaurosis (LCA)	1	Sepofarsen (QR-110)
Juvenile idiopathic arthritis (JOART)	1	Tofacitinib Citrate
Moderate to severe active polyarticular juvenile idiopathic arthritis	1	Certolizumabe-Pegol
Psoriatic arthritis	1	Upadacitinibe (ABT-494)
Rheumatoid arthritis/atopic dermatitis	1	Baricitinibe (LY3009104)
Asthma	2	Fluticasone Propionate/Fumarate Formoterol
Secondary geographic atrophy (GA) (AMD)	1	Pegcetacoplan (APL-2)
Non-cystic fibrosis bronchiectasis	1	Brensocatib
PD-L1 positive metastatic and/or recurrent cervical cancer	1	Atezolizumab
Refractory metastatic colorectal cancer	1	Bevacizumabe
Refractory metastatic colorectal cancer	1	Trifluridine / Tipiracil Hydrochloride (S95005)
ER (+) and HER2 (-) breast cancer	1	1-Amcenestrant 2-Letrozol 3-Palbociclib 4-Gosserrelin
Non-small cell lung cancer (NSCLC)	1	Brigatinib
Non-small cell lung cancer (NSCLC)	1	Tislelizumab
Non-small cell lung cancer (NSCLC)	1	Irinotecan hydrochloride trihydrate
Gastrointestinal, pancreatic or colorectal cancer	1	Romiplostim (AMG 531)
Advanced urothelial cancer and selected FGFR genetic aberrations	1	Erdafitinibe
Recurrent or metastatic cervical carcinoma	1	RAIN2810
Solid carcinoma SOE	1	Erdafitinibe
Untreated metastatic or locally advanced urothelial carcinoma	1	Atezolizumab
Ulcerative Colitis and Crohn's Disease	1	Vedolizumabe
Pyruvate kinase deficiency	1	Mitapivate Sulfate (Ag-348 Sulfate Hydrated/ Mitapivate)

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Acid Sphingomyelinase Deficiency	1	GZ402665 - Olipudase alfa
Neovascular age-related macular degeneration	1	RO6867461 (Faricimab)
Established Cardiovascular Disease and Overweight or Obesity	1	Semaglutida
Moderate to Severe Crohn's Disease	1	a. Risanquizumabe b. Ustequinumabe
Sickle cell disease (prior use of crizanlizumab sponsored by Novartis	1	SEG101 (Crizanlizumab)
Diabetic or non-diabetic chronic kidney disease	1	1 - BI 690517 2 - Empaglifozin / BI 10773
Macular Edema (primary and secondary)	4	RO6867461 (Faricimab)
Important cardiovascular events	1	Bempedoic acid (ETC-1002)
Multiple sclerosis	4	Ocrelizumabe (RO4964913)
Heart failure with preserved ejection fraction (HFpEF) deliver	1	Dapagliflozina propanediol
Mantle Cell Lymphoma Relapsed/Refractory	1	Ibrutinibe
Systemic lupus erythematosus	1	Deucravacitinib
Lymphoid Malignancies Associated with Epstein-Barr Virus	1	Nanatinostat (VRx-3996) Valganciclovir hydrochloride
BRAF V600 metastatic melanoma.	1	Trametinib (TMT212) Dabrafenib (DRB436)
Multiple Myeloma	1	Daratumumabe
Mucopolysaccharidosis (MPS) type VI (Mucopolysaccharidosis Syndrome) Maroteaux-Lamy)	1	Pentosan Sodium Polysulfate
Mucopolyssacaridose type II	1	alfapabinafuspe (JR-141)
BRAF v600 mutation /no Melanoma	1	1 - Atezolizumabe 2 - Hemifumarato de Cobimetinib 3 - Vemurafenib
Mama malignant neoplasm	1	Trastuzumabe entansina
Obesity and Overweight	2	in Tirzepati
Patients with Spinal Muscular Atrophy Type 1 (AME)	2	Risdiplam
Schizophrenia	1	Iclepertina
Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP).	1	Human Recombinant Hyaluronidase
Reduced intraocular pressure/glaucoma	1	Brimonidine tartrate timolol maleate
Endogenous Cushing's syndrome in adults.	1	Osilodrostat phosphate
Atypical Hemolytic-Uremic Syndrome (aHUS)	1	LNP023
Targeted therapy or immunotherapy for cancer guided by genomic profiling	1	Atezolizumab
Major depressive disorder (MDD)	1	Aticapranto
Treatment of Virologically Suppressed HIV-1 Positive Patients	1	Dolutegravir / Lamivudine 300mg
Advanced solid tumors	1	AMG 404
Cerebrotendinous Xanthomatose	1	Chenodeoxycholic Acid (CDCA)

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11. INSPECTIONS IN GOOD CLINICAL PRACTICES (GCP)

With the aim of ensuring the protection of rights, security and well-being of trial participants clinical, as well as the precision and con reliability of the data to be obtained or submitted for health registration rio, Anvisa will be able to carry out inspection ctions in GPC in testing centers clinicians, sponsor, ORPC, labor tories and other institutions involved in the development of my dicamento experimental.

The objective of the inspections is to verify the degree of adherence to current Brazilian legislation and compliance of BPC, in addition to ensuring the rights and duties that concern to the scientific community and the State.

Depending on the inspection result in BPC, Anvisa may determine:

I- temporary interruption of the test clinical;
II- the definitive cancellation of the trial clinician at the center in question;
III- the definitive cancellation of the trial clinical in all centers in Brazil;
or IV- invalidation of the data from centers and trials non-compliant clinicians com as BPC.

The *Normative Instruction – IN nº 122, of March 9, 2022* provides for inspection procedures in BPC for clinical trials in me dications and stratifies the findings or observations noted in the inspection as follows:

I - "C" criticism: related findings directly to the security of research participant, being able to result in death, risk of death or unsafe conditions and when related to study data, may compromise its validity, example of studies conducted without authorization, tampering, lack of information or falsification;
II - major "M": findings that can result in a risk to the health of research participant or invalidation of data;
III - "Me" minors: findings that are not frame critical observations or larger, but which indicate deficiency and/or diversion;
IV - "INF" information: findings descriptive and/or complementary; It is
V - nothing appears/does not apply "NC/NA": means the item was not checked or not applicable.

Additionally, *Guides nº 35/ 2020 and nº 36/2020, version 2, of 01/26/2022,* describe the procedures

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ments for conducting a
GPC inspection in centers and in
clinical trial sponsors,
respectively. In general, in addition
procedures, scope, steps,
center selection criteria,
sponsors and clinical trials, the
Guides describe the items that should
be checked during inspection,
as listed below:

> "8. ITEMS TO BE CHECKED
> IN CLINICAL TRIAL CENTERS
> 8.1. APPROVALS AND
> AGREEMENTS/CONTRACTS
> 8.1.1. Regulatory approval
> 8.1.2. Ethical approval (CEP/CONEP)
> 8.1.3. Contracts/Agreements
> 8.2. ORGANIZATION AND TEAM
> CLINICAL TRIAL CENTER
> 8.3. INFRASTRUCTURE
> 8.3.1. Study archive
> 8.3.2. Pharmacy or place of
> storage of products under
> investigation
> 8.3.3. Consultancies
> 8.3.4. Inpatient ward or room
> infusion
> 8.3.5. Collection and handling room
> biological samples
> 8.3.6. Clinical laboratory
> 8.3.7. Equipment
> 8.3.8. Waste management
> 8.3.9. Computerized systems
> 8.4. QUALITY SYSTEM
> 8.4.1. Written procedures and
> study controls
> 8.5. SOURCE DOCUMENTATION AND
> CASE REPORT FORM
> 8.5.1. Free and Consent Form
> Enlightened
> 8.5.2. Data collected of the
> clinical trial participants
> 8.5.3. Case Report Form
> (CRF)
> 8.6. PRODUCT UNDER INVESTIGATION
> 8.7. INVESTIGATOR'S FILE

Despite the limitations of the
number of COPEC employees, in
2023 9 inspections were carried out
BPC in clinical trial centers,
with the support of inspectors from other
areas of the Second Directorate (DIRE2), and
205 observations were noted
considered as critical and major,
as presented below
(Figure 17), according to the items
correspondents verified in
centers:

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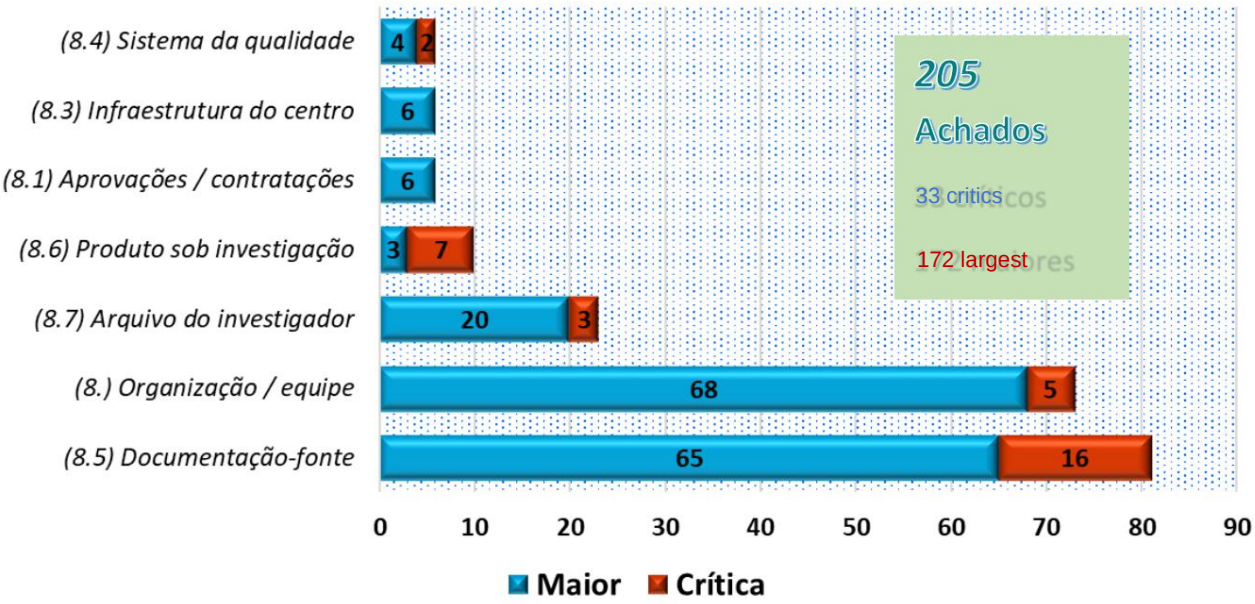

Figure 17 – *Major and Critical Findings from the 9 BPC inspections (2023).*

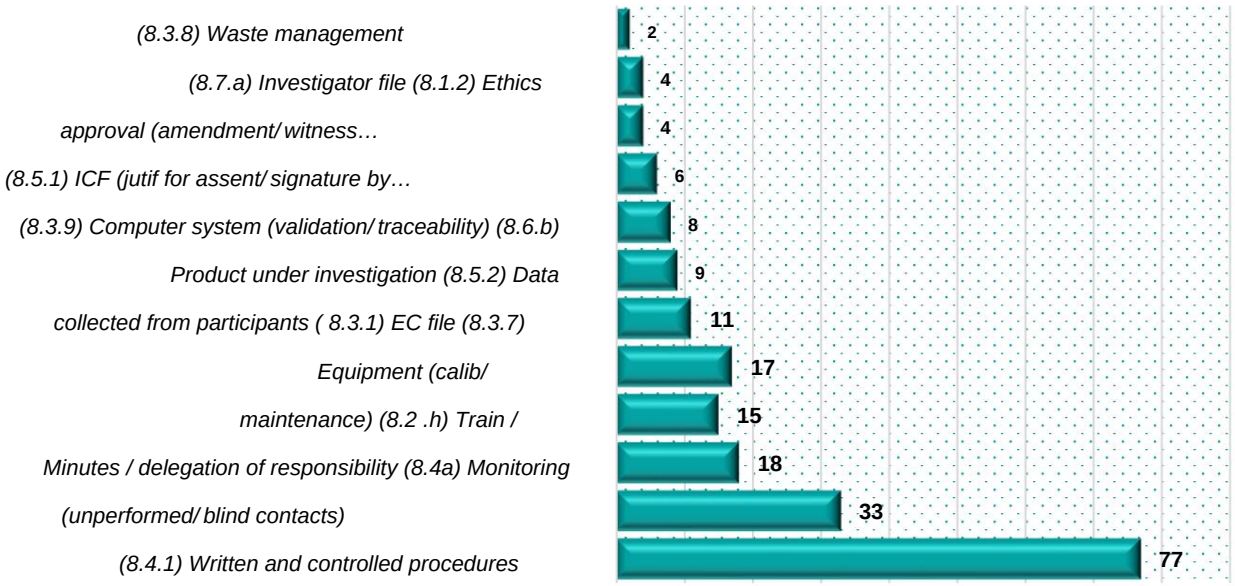

Figure 17a – *Detail of the 205 major and critical findings (2023)*

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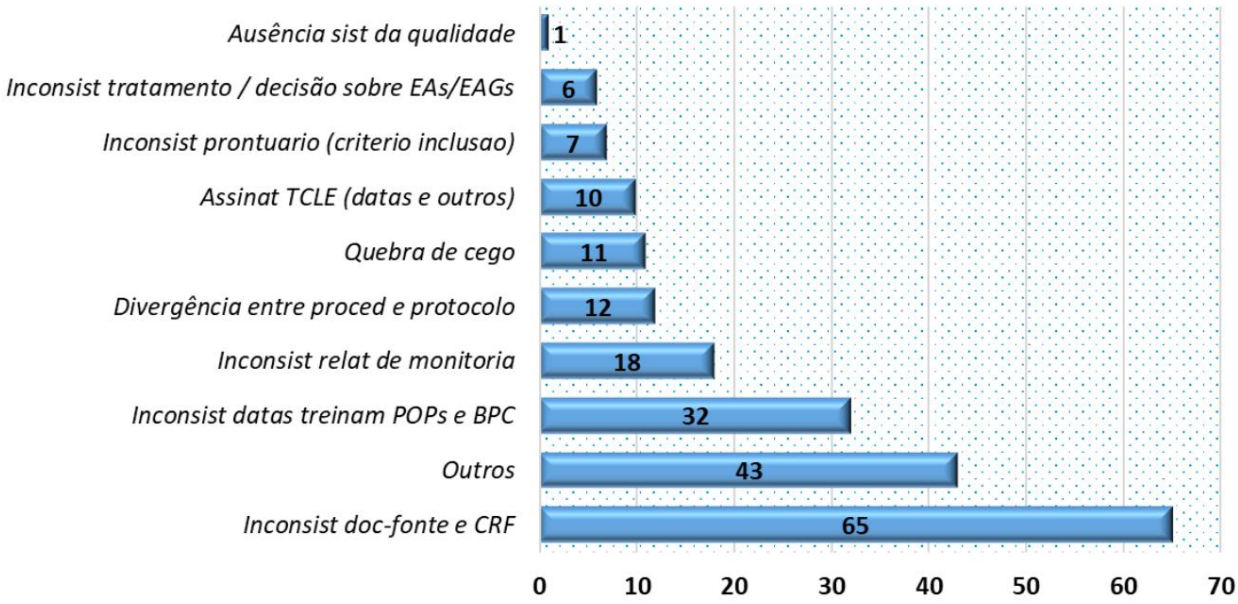

Figure 17b – *Detail of the 77 findings referring to item 8.4.1 (Guide nº 35/2022) of 205 major and critical finds (2023)*

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12. OTHER ACTIVITIES

Matters related to DDCMs and DEECs represent the largest volume among all matters dealt with by the technical area and is the main activity in the area (COPEC). However, there are other activities performed by the area that make up the workload and the sometimes requires significant time of the technical team.

In addition to subject codes specific to DDCMs and DEECs and secondary petitions for amendment of quality and amendments to the protocol clinic, in 2023 attention was drawn to the number of changes to the Presentation Form Clinical Trial (FAEC), code subject 10823.

The FAEC is a document that brings together summarized information and essential information about companies involved in the development clinician, centers and researchers and respective responsibilities and information about medicines experimental and clinical trials, the countries where the study will be or is being driven, among others.

FAEC is particularly important because it brings all information about inputs clinics, including medicines experiments and comparators that will be imported, when applicable, to conduct the clinical trial in Brazil.

Some the information present at FAEC may be changed, requiring only that a new updated FAEC be submitted. This is the case, for example, of change of the validity period of the experimental medicine, with rare exceptions, and that was the reason for most requests for change of FAEC in 2023. This fact stands out not only for its high number of applications submitted, but mainly because it points to the need for urgent changes to allow such changes be carried out more quickly and to reduce the workload for the technical area.

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A technological evolution in Datavisa system that would allow some FAEC fields could be changed automatically by the sponsoring company itself or designated company, could be a alternative to be implemented.

Currently, for each order change of FAEC, the technical area issues an approval letter from the change and forward the document, whether the Special Announcement or Import Document (DI) updated for the company requester.

12.1 Customer Service

A Lei nº 12,527, of 18 November 2011, known as Access to Information Law (LAI), establishes procedures, deadlines and obligations so that the administration public respond to requests for information required by any person, natural or legal, without it is necessary to present a reasons for the request. Like this therefore, Anvisa created mechanisms for serving the public and provision of information to citizen-users, such as the Central Customer Service and Customer Service Information to Citizens, as per Ordinance No. 52/Anvisa of January 27th of 2021.

The main channel for accessing information action is Contact Us (SAT) to clarification of doubts and requests information and Fala.BR - the Integrated Ombudsman Platform and Access to Information that allows the treatment of manifestations of ombudsman and requests for access to information from a single technological solution.

There is also the Scheduling Hearings Internet (Parliatory), for discussions development techniques clinician, whose guidelines are if not Decree nº 4.334, of 12 of August 2002.

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Figure 18 – *Number of hearings at the request of companies and number of responses to requests for information by the SAT and ombudsman, attended by COPEC in 2023.*

Based on *Ordinance No. 1,244, of July 25, 2017,* which provides for procedures for requesting and granting of in-person hearings or virtual, through the System Parlatório and the need to optimize technical assistance at meetings, COPEC published *NT nº 12/2021,* which provides information about the request for meetings with the area and can be consulted on the clinical research on the Anvisa portal.

12.2 Preparation and review of regulatory instruments

Technical Note (NT) No. 5 of May 16, 2023

Repeals NT 23/2020/SEI/COPEC/GGMED/DIRE2/ANVISA, NT 33/2021/SEI/COPEC/DDMED/DIRE2/ANVISA, NT 24/2022/SEI/COPEC/DDMED/DIRE2/ANVISA, NT 10/2022/SEI/COPEC/GGMED/DIRE2/ANVISA that bring guidance for sponsors, research centers and investigators involved in conducting trials and bioequivalence studies during the coronavirus pandemic Covid-19.

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DRC nº 790, May 15, 2023

Published in DOU No. 92, of February 16, 2023, changes the Resolution of Collegiate Board No. 573, of October 29, 2021, to extend its effective until May 23, 2021. RDC nº 573/2021 changes on an emergency basis and temporary the Resolution of the Collegiate Board - RDC nº 9, of February 20, 2015, which approves the regulation for carrying out clinical trials with medicines in Brazil.

DRC nº 791, May 15, 2023

Published in DOU No. 92, of February 17, 2023, changes the Resolution of Collegiate Board No. 601, of February 9, 202, to extend its validity until May 23, 2021. RDC nº 601/2022 provides for simplified analysis, on an exceptional and temporary basis, of petitions for Consent in the Process of Clinical Research, DDCM Modifications, Substantial Amendment to the Protocol Clinical and Consent in the Process of the Clinical Development Dossier of Medicine (DDCM) referring to the Experimental Medicine Dossier due to of the public health emergency of national importance arising from the outbreak of novel coronavirus (SARS-CoV-2).

Clinical research report

Published 22nd Edition of the document "Location of Available Documents on the Anvisa (COPEC) portal", with several updates that have occurred since the edition previous. Check the changes in section 3 of the document.

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REFERENCES

RDC nº 9, of February 20, 2015: Provides for the Regulation for the carrying out clinical trials with medicines in Brazil.

Resolution No. 466 of December 12, 2012: Approves the guidelines and standards regulating research involving human beings.

RDC nº 172 of September 8, 2017: Provides for procedures for the import and export of goods and products intended for scientific research or technological and research involving human beings, and provides other measures

RDC nº 204, of July 6, 2005: Regulates the petitions procedure submitted for analysis by the technical sectors of ANVISA and revokes RDC nº 349, of December 3, 2003

RDC nº 573, of October 29, 2021: Changes on an emergency basis and the Resolution of the Collegiate Board of Directors - RDC nº 9, of February 20, 2015, is temporary. which approves the regulation for carrying out clinical trials with medicines in Brazil

RDC nº 204, of December 27, 2017: Provides for the framework in priority category, of registration petitions, post-registration and prior consent in clinical drug research.

RDC nº 205, of December 28, 2017: special procedure approved for approval of clinical trials, certification of good manufacturing practices, health registration of new medicines for rare diseases

CNS Resolution No. 563, of November 10, 2017: regulates the right of research participant to post-study access to clinical research protocols intended for patients diagnosed with ultra-rare diseases.

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RDC nº 23, of June 5, 2015: Amends Resolution RDC nº 204, of July 6 2005, which provides for the procedure for petitions submitted for analysis by technical sectors of ANVISA and revokes Resolution RDC nº 206, of July 14, 2005, which provides for rules that regulate the petition for temporary archiving and temporary custody and provides other measures.

RDC nº 55, of December 16, 2010: Provides for product registration new biologicals and biological products and provides other measures.

RDC nº 23/2015 of June 5, 2015: Amends Resolution RDC nº 204, of 6 of July 2005, which provides for the procedure for petitions submitted for analysis by the technical sectors of ANVISA and revokes Resolution RDC nº 206, of July 14, 2005, which provides for rules that regulate the petition for temporary archiving and temporary custody and other measures.

RDC nº 601, of February 16, 2022: Provides for simplified analysis, on an exceptional and temporary basis, of petitions for Consent in the Process of Clinical Research, DDCM Modifications, Substantial Amendment to the Protocol Clinical and Consent in the Process of the Clinical Development Dossier of Medicine (DDCM) referring to the Experimental Medicine Dossier due to of the public health emergency of national importance arising from the outbreak of novel coronavirus (SARS-CoV-2).

Ordinance No. 199 of January 30, 2014: Establishes the National Care Policy Comprehensive Care for People with Rare Diseases, approves the Guidelines for Comprehensive Care to People with Rare Diseases within the scope of the Unified Health System (SUS) and establishes financial funding incentives.

RDC nº 38, of August 12, 2013: Approves the regulations for the programs of expanded access, compassionate use, and post-study drug provision.

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Law No. 12,527, of November 18, 2011: Regulates access to information provided for in item XXXIII of art. 5th, in item II of § 3rd of art. 37 and in § 2 of art. 216 of the Federal Constitution.

Normative Instruction – IN nº 122, of March 9, 2022: Provides for inspection procedures in Good Clinical Practices for clinical trials with medicines.

Guides nº 35/2020 and nº 36/2020, version 2, of 01/26/2022: Inspection guide in Good Clinical Practices (GCP) regarding clinical trials with medicines and biological products – Inspection in Clinical Trial Centers

Ordinance No. 1,244, of July 25, 2017: Provides for procedures for requesting and granting in-person or virtual hearings, through the System Parliament, to individuals within the scope of the National Health Surveillance Agency – ANVISA

NT nº 12/2021: Guidance for scheduling hearings with the Coordination of Clinical Research in Medicines and Biological Products at Anvisa (COPEC)

Other information related to clinical research with medicines and products biological products are available at:
https://www.gov.br/anvisa/pt-br/assuntos/medicamentos/pesquisaclinica

To consult authorized clinical trials:
https://consultas.anvisa.gov.br/