MEDICINES AND MEDICAL DEVICES AGENCY

GOVERNMENT OF THE REPUBLIC OF MOLDOVA

21-05-2025 Nr. Rg02-002453

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The Medicines and Medical Devices Agency, following the unannounced inspection of the clinical study Mife50 carried out at the medical facility *Centrul de Medicină Intervențională Cardiomed SRL* (Novamed Polyvalent Hospital) and the Contract Research Organisation 'Bona Artis CRO', which took place on 13-14 May 2025, hereby submits the GCP Inspection Report.

Annex: 15 pages

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Medicines and Medical Devices Agency

GOVERNMENT OF THE REPUBLIC OF MOLDOVA

Report

Unannounced inspection of the Mife50 clinical study
of the medical facility *Centrul de Medicină Intervențională Cardiomed SRL*
(Novamed Polyvalent Hospital)
and the Contract Research Organisation 'Bona Artis CRO'

PART I
Unannounced inspection of the clinical study Mife50 of the medical facility Centrul de Medicină Intervențională Cardiomed SRL (Novamed Polyvalent Hospital), Principal Investigator Dr. Irina Tripac

Purpose of the inspection:
Verification of the conduct of the clinical study 'Prospective, multicentre, single-arm open study of the long-term efficacy, safety and acceptability of orally administered Mifepriston, weekly 50 mg, for contraceptive purposes' at the medical facility *Centrul de Medicină Intervențională Cardiomed SRL* (Novamed Polyvalent Hospital), Principal Investigator Dr. Irina Tripac.

Reason for the inspection:
Referral to the Medicines and Medical Devices Agency (AMDM) by the Contract Research Organisation (OCC) and the sponsor of the clinical study regarding a suspicion of fraud (falsification of clinical study data), on 06 May 2025, by email (Annex 1).

General information on the inspection	
Name and address of the medical facility	*Centrul de Medicină Intervențională Cardiomed SRL* (Novamed Polyvalent Hospital)
Date of inspection	13 May 2025
Inspection criteria	• Guidelines for good clinical practice • Approved protocol for clinical study
Inspection team	
Delegated Inspector	Lina Gudima, Deputy General Manager AMDM,
Coordinating Inspector	Ecaterina Guzinschi, Head of Service GCP, GVP, GLP, GRP
Principal Inspector	Eugeniu Deminet, pharmacist, service GCP, GVP, GLP, GRP
Principal Inspector	Roxana Dimitriu, service GCP, GVP, GLP, GRP
Delegated Inspector	Marcelina Cebanovschi, Head of Service clinical studies
Delegated Inspector	Daniela Cocu, pharmacist, AMDM

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General information about the clinical study	
Protocol code# EUCT number	Mife50// 2020-002355-38
Sponsor	Women on Waves, The Netherlands
Contract Research Organisation	Bona Artis CRO, Republic of Moldova
Protocol title of clinical study	Prospective, multicentre, single-arm open study of the long-term efficacy, safety and acceptability of orally administered Mifepriston, weekly 50 mg, for contraceptive purposes.
Phase of clinical study	III - therapeutic confirmation

Field of application	Gynaecology (contraception)
Participants of study	Women aged between 18 and 35 years, who do not intend to become pregnant during the 12-month duration of the study, have a normal menstrual cycle of 21-35 days unless using hormonal contraceptives (except Depo-Provera), and are willing to use the study medicine as their sole method of method of contraception during the study. At the time of inspection, 476 subjects were screened and 364 subjects were enrolled at the site of the clinical study.
Investigational Medicinal Product (IMP)	• trade name: Ginestryl • active substance: *mifepristonum* • pharmaceutical form: tablets • dose: 50 mg • division: N10*3 • manufacturer: SA 'Nijfarm', Russia • method of administration: per os, one tablet per week for one year

Conduct of the inspection

The inspection was conducted in 3 stages, in accordance with the Plan of Inspection:
• opening meeting;

• review of documentation and interviews with study team members;
• closing meeting.

Opening meeting	
Action points Principal Investigator	The Principal Investigator (PI), Irina Tripac, was informed at 09:25 by the Coordinating Inspector, in her office (nr. 122) that an unannounced GCP inspection was to be conducted by the team of inspectors, by order of the General Manager of AMDM. At the same time, she was introduced to the inspection team, informed of the purpose and reason of the inspection and asked to provide a room for the evaluation of the documentation at the site of the study. Arguing that she did not have the time or space to conduct the inspection, the PI left the office stating that she would bring the study documentation for evaluation and did not return. The PI was contacted by telephone by the Coordinating Inspector to be informed that the inspection team was waiting for her, but she did not answer the phone. In addition, the PI was contacted by sub-investigators present at the inspection, who were told that the PI was in surgery and did not have time to participate in the inspection, but that after completing her work for the day, she would return to the inspected location in office 122. The video recordings from the first floor of the clinic were checked and it was established that the PI left the medical facility at 11:42 hrs without notifying the inspection team or the study team. Thus, two members of the study team, who were appointed by the PI to bring the study documentation to her office for inspection, attended the opening meeting: 1. Cristina Noroc, gynaecologist; 2. Cristiana Nichitovici, resident oncologist.
Conduct of opening meeting	During the opening meeting, the legal framework of the inspection was explained and, the methods and procedures to be used by the inspectors during the inspection were outlined. The responsibilities and roles of the study team members were identified and general discussions were held about the activities of the investigators, which found that: 1. The study team declared to the AMDM to consist of the following members: - PI: Irina Tripac; - sub-investigator: Cristina Noroc

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	- sub-investigator: Oxana Podolean - sub-investigator: Irina Bratan - sub-investigator: Ainura Abdulraghimov - sub-investigator: Cristina Nichitovici - sub-investigator: Eugeniu Valic - sub-investigator: Diana Gavriluță Oxana Podolean is no longer involved in this clinical study and according to Cristina Noroc and Cristina Nichitovici, they sometimes meet Eugeniu Valic and Diana Gavriluță during study activities, but have never met the other sub-investigators. 2. Cristina Noroc reported that within the study (which she referred to as a 'project' throughout the inspection) she was responsible for consulting volunteers during study visits, taking blood samples and completing the Castor electronic system with information about the study visits and the results of clinical and paraclinical investigations. Cristina Noroc explained the study information to the volunteers and participated in the signing of the Informed Consent Forms (ICF) at the beginning of the study, after which these processes were handled exclusively by the PI. Cristina Noroc stated that she was involved in the study processes since the beginning of the study at the inspected medical facility (May 2024). 3. Cristiana Nichitovici reported that she has been involved in the conduct of the study since November 2024, when she started working with Irina Tripac, who was appointed as scientific supervisor for her

	bachelor's thesis (onco-gynaecology). Cristiana Nichitovici declared that her responsibility in the study was to enter information into the Castor electronic system. The sub-investigators were informed by the PI in the morning of the inspection that the clinical study was being stopped because one of the volunteers of the study was pregnant.

Review of documentation and interviews with study team members

GCP training in study processes and procedures for study team members	Cristina Noroc stated that she had not received any training on study processes and procedures, nor had she been trained on how to enter information into the Castor electronic system; she mentioned that she had received training at the Alfa Diagnostic laboratory on taking blood samples, but that she did not have a certificate for this training. She does not know any details or have any information about the clinical study protocol. Cristiana Nichitovici stated that she had not received any training on study processes and procedures, nor had she been trained on how to enter information into the Castor electronic system; however, she mentioned that she is aware of the existence of a clinical study protocol and the investigator's brochure – these documents were sent to her by email but she did not read them and could not describe their purpose and content.
Legal relationship between the study team and the inspected medical facility	Following discussions with the two sub-investigators, it was found that neither of them had an employment contract with the *Centrul de Medicină Intervențională Cardiomed SRL* (Novamed Polyvalent Hospital); Cristina Noroc is employed by SRL Primamed Expert – a company managed by the PI Irina Tripac, which has a collaboration agreement with Novamed Polyvalent Hospital, and Cristiana Nichitovici is not employed by Novamed Polyvalent Hospital or SRL Primamed Expert.
Legal relationship between the study team and the sponsor	Neither Cristina Noroc nor Cristiana Nichitovici have established obligations and responsibilities in the Mife50 clinical study, have not signed contracts with the sponsor or the PI, and have never been remunerated for their participation in the study.
Documentation of clinical study:	
Individual patient files	Individual patient files were made available to the study team by these 2 sub-investigators – they were brought from another office (nr. 121) – file cabinets containing 10 individual subject files each. A total of 6 file cabinets were brought in. The office from which the volunteer files were brought, was assessed and it was found that all file cabinets were kept on the window sills in that office, with access to the office by medical staff not involved in the study and clinic patients. Not all individual patient files were evaluated. However, the sample checked revealed that: - all files contained the outdated signed version of the ICF (Version of 4 of 08 March 2023), and not the updated version (Version of 5 of 28 November 2024);

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	- the file of subject MD010.22: did not contain ICF; - the file of subject MD010.31: visit 2 was not documented; for visit 3 no electrocardiogram (ECG) was performed during visit 3 (ECG); - the file of subject MD010.33: ultrasound performed on 24.10.2024 was performed at 05:06 hrs; - the file of subject MD010.34: the description of the ultrasound (USG) performed on 10.06.2024 did not correspond to the information in the USG image (size of the uterus). Several individual files were also identified in which the time of the ultrasound was 04:00 and 05:00 hrs. In some Informed Consent Forms the handwritten signatures and surnames of the volunteers raised suspicion of forgery, as they were identical to those of the PI. Another issue identified during the evaluation of the documentation was that the signature of the PI Irina Tripac appeared differently in various documents, with 5 identified variations (Annex 2). When checking the results blood tests for the quantitative determination of progesterone and estradiol, conducted by the Alfa Diagnostica laboratory, it was established that the statement 'Moldac non-accredited tests' appeared on the test results.
Individual notes of sub-investigator Cristina Noroc	It was identified that sub-investigator Cristina Noroc had drawn up working lists of the subjects examined indicating the surnames, first names and contact telephone numbers of the volunteers and investigations conducted, which list were periodically presented to the reception desk of *Centrul de Medicină Intervențională Cardiomed SRL* (Novamed Polyvalent Hospital) so that the hospital could keep a record of the number of subjects involved in the study. According to Cristina Noroc, the information presented to the NovaMed reception desk did not begin with initiation of the study, but later (October-November 2024). These lists were presented to the reception desk, without any access control. These lists are not part of the approved documentation of clinical study.
Investigator Site File (ISF)	The ISF (Investigator Site File) was identified in a cabinet indicated by the sub-investigators. The evaluation established the absence of: - the study subject identification log; - the study subject screening and enrolment log; - the IMP monitoring logs;

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	- certificates of the study team training in study processes and procedures. The study task delegation log was assessed and it was found that not all study team members had signed the delegated responsibilities, and in the case of other members – the same signature appeared for different employees.
Investigational Medicinal Product (IMP)	The IMP was identified by the inspectors in the same cabinet in which the ISF was found. 6 boxes of Ginestryl with serial number 51122 and expiry date 11.2027 were found on a shelf, with primary and secondary packaging and the Patient Information Leaflet in Russian. On another shelf, 1,315 tablets of Ginestryl were found, with serial number 20719 and expiry date 31.08.2024, with primary and secondary packaging and the Patient Information Leaflet in Russian, and stickers on the secondary packaging in what appeared to be Georgian. The shelves for the study of medicines were not labelled or marked. A thermometer was found inside the cabinet, but no temperature monitoring logbook (recording and verification) was found.
The ultrasound device and its general results	Since the evaluation the subjects' individual files, it was established that the first and last names of the subjects were not indicated on any of the ultrasound images. A discussion was initiated with the sub-investigators on this issue, who stated that due to lack of time to set individual identifiers, it was decided that this data should not be included in the investigation results. So there is no correlation between the imaging and the participant of the clinical study.
Castor EDC Electronic Data Capture	

Although both Cristina Noroc and Cristiana Nichitovici enter information about the study in Castor, neither of them had been trained on how to use the program.
Cristina Noroc her individual Castor account from the PI's office computer to demonstrate its structure and functionality. At the time of the inspection, 476 subjects were registered in the program.
Cristiana Nichitovici stated that she also has an individual profile in the electronic system, which was created jointly with clinical study monitor Maria Macari, and which she accesses from home.

	Thus, the information in the Castor system was evaluated against the source documents for subject MD010.51 and discrepancies were identified between the data in the source documents and the Castor system.
Quality Management System	
Monitoring of the clinical study site	The initial visit took place on 31 May 2024, by Maria Macari and Tatiana Bacalu (Bona Artis CRO employees); subsequent visits were carried out by Maria Macari. The last monitoring visit took place on 16 April 2025, carried out by a team of monitors: Maria Macari, Dumitru Bădiceanu and Tatiana Bacalu.

Closing meeting	
The closing meeting was attended by 2 sub-investigators and the director of the *Centrul de Medicină Intervențională Cardiomed SRL* (Novamed Polyvalent Hospital) - Dr. Ion Popovici. The contribution, openness and professional attitude of the two sub-investigators participating in the inspection were noted, after which the list of deficiencies identified during the inspection was presented.	
Critical deficiencies	
Deficiency	*Legal provision violated*
Reference to the study team	
The Principal Investigator did not show her willingness and openness for the unannounced inspection, leaving the inspection site without permission.	Pct. 108 of Annex 1, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: "108. During the inspection of the clinical study site, the Principal Investigator/investigator (or persons to whom the duties of investigator have been delegated) must be present. Representatives of the sponsor may also be present." Pct. 30 of Annex 2, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: "30. The investigator must have enough time to conduct and complete the study within the time period deemed necessary for the purpose."

The difference between the number of subjects screened and enrolled at this medical facility (476 subjects screened and 364 subjects enrolled), in a relatively short period of time, compared to other medical facilities participating in the clinical study. No serious adverse events reported, although 364 subjects received the medicine.	Pct. 55 and 56 of Annex 1, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: "55. The sponsor of a clinical study and the investigator must ensure that the clinical study is conducted in accordance with the protocol and the principles of good practices in clinical study. 56. In order to verify that rights, safety and well-being of subjects are protected, that the reported data are reliable and robust and that the clinical study is conducted in accordance with the requirements in this Regulation, the sponsor must adequately supervise the conduct of clinical study.

	The extent and nature the monitoring shall be determined by the sponsor on the basis of an evaluation that takes into account all the characteristics of the clinical study, including the following characteristics: 1) whether the clinical study is a low-intervention clinical study; 2) the objective and methodology of the clinical study; and 3) the degree of deviation of the intervention from common clinical practice."
The study team members notified to the Medicines and Medical Devices Agency (AMDM), are not employees of the *Centrul de Medicină Intervențională Cardiomed SRL*.	Pct. 57 e) of Annex 1, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: "57. e) The investigator must work in the medical facility where the clinical study is planned to be conducted."
The sub-investigators Cristiana Nichitovici and Cristina Noroc; the only sub-investigators available during the inspection, did not sign any legal document assigning them activities in the study and were not remunerated for the work performed in the study.	Article 7^1 of the Labour Code of the Republic of Moldova: Prohibition of undeclared work (1) undeclared work is prohibited. (2) undeclared work means: Any work performed by a natural person for and under the authority of an employer without complying with the provisions of this code relating to the conclusion of an individual employment contract.
The sub-investigators Cristiana Nichitovici and Cristina Noroc are not aware of any details.	Pct. 13 of Annex 2, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova:

relating to the clinical study protocol and the investigator's brochure.	"13. Each person involved in the conduct of a clinical study must be qualified by education, training and experience in order to perform their respective tasks.' Pct. 32 of Annex 2, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: '32. The investigator must ensure that all persons participating in the study are adequately informed about the protocol, the Investigational Medicinal Product as well as their tasks and functions in the study."
The sub-investigators Cristiana Nichitovici and Cristina Noroc were misinformed by the PI about the reason of stopping the study (the pregnancy of a volunteer) with a false reason being given by the PI.	Pct. 15 of Annex 2, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: '15. All information relating to the clinical study must be recorded, handled and stored in such a way as to ensure the accuracy of the reporting, interpretation and verification.' Pct. 55 of Annex 1, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: "55. The sponsor of a clinical study and investigator must ensure that the clinical study is conducted in accordance with the protocol and of principles good practices in clinical study." Pct. 89 of Annex 1, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: "89. A Principal Investigator must ensure the compliance of a clinical study at a clinical site with the requirements in this Regulation. The Principal Investigator must distribute tasks among the members of the team of investigators in such a way as not to compromise the safety of the subjects and the reliability and robustness of the data generated in the clinical study at that clinical study site."
Reference to the study documentation	

The subjects' individual files are kept on a shelf in a patient consultation office (No. 121), to which employees and patients who are not involved in the study have access.	Pct. 16 of Annex 2, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: "16. The confidentiality of records that can identify subjects must be protected in accordance with the legal regulations in force on confidentiality and secrecy."
Personal data of the volunteers participating in the study were sent to NovaMed.	Pct. 97 of Annex 1, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: "97. The processing of personal data conducted within the study must be carried out in accordance with the national data protection legislation and international agreements."
The ISF lacks documents ensuring the identity of the subjects enrolled and their randomisation.	Pct. 15 of Annex 2, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova:

	"15. All information relating to the clinical study must be recorded, handled and stored in such a way as to ensure the accuracy of the reporting, interpretation and verification."
The ISF lacks records for monitoring the traceability of the IMP: receipt, distribution to volunteers, receipt from the volunteers.	Pct. 46 of Annex 2, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: "46. The investigator/institution and/or a pharmacist or other appropriate person, appointed by the investigator/institution, must keep records relating to the distribution of the medicines at the study site, the inventory at that site, the use of the medicines by each subject and the return of the medicines to the sponsor or to another assigned destination, if specified: these records must include dates, quantities, serial numbers, expiry dates (if applicable) and unique code numbers assigned to medicines/medicinal products for clinical investigation and subjects of the study. The investigators must keep records that adequately demonstrate that the doses specified in the protocol were

	administered to the subjects and that the data justify the entire quantity of the Investigational Medicinal Product received from the sponsor.'
The ISF lacks training certificates in study procedures for the study team.	Pct. 32 of Annex 2, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: "32. The investigator must ensure that all persons participating in the study are adequately informed about the protocol, medicine for the clinical investigation, as well as about the tasks and functions in the study."
The Principal Investigator's signature appears differently in various documents.	5 variants of the signature were identified – suspicion of forgery.
In some Informed Consent Forms, the handwritten signatures and surnames of the volunteers raised suspicion of forgery, as they were identical to those of the PI.	Pct. 58 of Annex 2, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: "58. Before the subject participates in the study, the written Informed Consent Form must be signed and dated personally by the subject or his/her legal representative by the person who provided the information during the discussion with the subject/his/her legal representative."
The Informed Consent Form is lacking from the individual file of subject MD010.22.	Pct. 14 of Annex 2, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: "14. Informed consent must be obtained freely from each subject before their participation la clinical study."
All individual files of subjects in the sample evaluated contained the outdated version of the Informed Consent Form.	Pct. 52 of Annex 2, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: "52. The Informed Consent Form and other written information for subjects must be updated whenever new information becomes available that may be important for the subject's informed consent."

Reference to the study of medicines	
Inadequate storage of IMP: Although a thermometer was found in a storage cabinet, no documentation of the temperature regime and its verification was identified. The shelves for storing medicinal products not are labelled properly.	Pct. 59 1) of Annex 2, Order No. 648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: "59. Traceability, storage, the return and the destruction of medicinal products for clinical investigation: 1) Medicinal products for clinical investigation must be traceable. They must be stored, returned and/or destroyed in an appropriate and proportionate manner to ensure the safety of the subjects and the reliability and robustness of the data generated in the clinical study, taking into account in particular whether the Investigational Medicinal Product was an authorised Investigational Medicinal Product and whether the clinical study was a low-intervention clinical study. The first paragraph also applies to unauthorised ancillary medicinal products."
Reference to the study facilities	
An additional office (No. 121) was involved in the conduct of the study other than that approved by the CCP inspection of 17.05.2024 following a request by the applicant Bona Artis CRO, Republic of Moldova.	Pct. 118 of Annex 1, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: "118. The authorisation was issued by AMDM at the request of the interested entity in accordance with the regulatory acts in force."
There are no training certificates of the study team in the use of the Castor EDC system.	Pct. 32 of Annex 2, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova:

	"32. The investigator must ensure that all persons participating in the study are adequately informed about the protocol, the Investigational Medicinal Product, as well as about the tasks and functions in the study."
Access to the Castor electronic platform can be gained from any electronic device, including outside the medical facility.	Pct. 64 of Annex 2, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: '64. Recording, processing, handling and storing information:

	1) All information relating to the clinical study must be recorded, processed, handled and stored by the sponsor or the investigator, as appropriate, in such a way that it can be accurately, interpreted and verified while at the same time protecting the confidentiality of the records and personal data of the subjects in accordance with applicable law on the protection of personal data; 2) Appropriate technical and organisational measures must be implemented to protect information and personal data against access, disclosure, dissemination, unauthorised alteration or accidental destruction or loss, in particular if the processing involves transmission via a network."
Reference to the paraclinical investigations	
Progesterone and estradiol testing conducted by the Alfa Diagnostica laboratory are not Moldac-accredited tests.	Pct. 4 e) of Annex 1, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: "4. e) A clinical study may only be conducted if it is designed to generate reliable and robust data." Pct. 55 of the Annex. 1, Order No.648 of 12.08.2016: "The sponsor of a clinical study and the investigator must ensure that the clinical study is conducted in accordance with the protocol and the principles of good practices in clinical study. Without prejudice to other provisions of Moldovan law or AMDM guidelines, when drafting the protocol and applying this regulation and the protocol, the sponsor and the investigator, must also take due account of the quality standards and ICH guidelines on good practices in clinical study."
Ultrasound images cannot be linked to the identity of the subjects, as this information is lacking.	Pct. 66 of Annex 2, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: "66. The investigator must ensure that the data submitted to the sponsor in the Case Report Form

	and in all required reports are correct, complete, intelligible and sent on time." Pct. 15 of Annex 2, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: "15. All information relating to the clinical study must be recorded, handled and stored in such a way as to ensure the accuracy of the reporting, interpretation and verification."
Some USG images show the time of the investigation as 04:00 hrs, 05:00 hrs, 05:06 hrs, etc.	Pct. 15 of Annex 2, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: "15. All information relating to the clinical study must be recorded, handled and stored in such a way as to ensure the accuracy of the reporting, interpretation and verification."
Reference to the AMDM notification regarding changes made to the clinical study protocol	
The AMDM was not notified of the change in the blood sample management process compared to other sites previously involved in the study - which facilitated the possibility of inclusion of subjects in the study contrary to the protocol and approved procedures.	Pct. 55 of Annex 1, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: The sponsor of a clinical study and the investigator must ensure that the clinical study is conducted in accordance with the protocol and of principles good practices in clinical study."
Major deficiencies	
Deficiency	*Legal provision violated*
The file of subject MD010.31 does not document visit 2; no electrocardiogram (ECG) was performed during visit 3.	Pct. 40 of Annex 2, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: "40. The investigator/institution must conduct the study in accordance with the protocol approved by the sponsor and the competent authorities and for which the approval/favourable opinion of the CNEESC has been obtained."

The file of subject MD010.34: The description of the ultrasound performed on 10.06.2024 did not correspond to the information in the USG image (size of the uterus).	Pct. 67 of Annex 2, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: "67. The data reported in the Case Report Form, derived from the source documents, must

	be consistent with the source documents, and any differences must be explained."
Discrepancies between the information in the source documents and the Castor system for subject MD010.51	Pct. 67 of Annex 2, Order No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: "67. The data reported in the Case Report Form, derived from the source documents, must be consistent with the source documents, and any differences must be explained."

Based on the above, in order to remove the identified objections, the following documents are requested to be presented to the AMDM:
1. Employment contracts of all study team members:
- PI: Irina Tripac
- sub-investigator: Cristina Noroc
- sub-investigator: Oxana Podolean
- sub-investigator: Irina Bratan
- sub-investigator: Ainura Abdulraghimov
- sub-investigator: Cristina Nichitovici
- sub-investigator: Eugeniu Valic
- sub-investigator: Diana Gavriluță

2. Contract between *Centrul de Medicină Intervențională Cardiomed SRL* (Novamed Polyvalent Hospital) and SRL Primamed Expert.

3. Specimen of the signature of the PI Irina Tripac.

Annex 1: 1 page
Annex 2: 3 pages

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PART II

Unannounced inspection of the Contract Research Organisation 'Bona Artis CRO'.

Purpose of the inspection:
Verification of the activities carried out with regard to Contract Research Organisation Bona Artis CRO, Republic of Moldova.

Reason for the inspection:
Results identified in part 1 of the unannounced inspection of the medical facility, *Centrul de Medicină Intervențională Cardiomed SRL* (Novamed Polyvalent Hospital) for the Clinical study Mife50, Principal Investigator Dr. Irina Tripac.

General information on the inspection	
Contract Research Organisation	SRL Bona Artis CRO Legal address: str. Dimineții 22, oficiu (ap). 40, MD-2002, Chișinău, Republic of Moldova
Date of inspection	14 May 2025
Inspection site	Or. Chișinău, str. Korolenko 2/1 – Medicines and Medical Devices Agency. Since the legal address of Bona Artis is located at the domicile of the administrator of Bona Artis, it was decided that the CRO representatives would come to the AMDM headquarters with all the documentation and information in electronic format at their disposal.
Inspection criteria	Guidelines for good clinical practice
Inspection team	
Coordinating Inspector	Ecaterina Guzinschi, Head of Service GCP, GVP, GLP, GRP
Principal Inspector	Roxana Dimitriu, service GCP, GVP, GLP, GRP
Delegated Inspector	Marcelina Cebanovschi, Head of Service clinical studies

Conduct of the inspection

The inspection was conducted in 3 stages, in accordance with the Plan of Inspection:
• opening meeting;
• review of documentation and interviews with study team members;
• closing meeting,

Opening meeting	
Time	14:45 hrs
Present	Tatiana Bacalu - administrator Boha Artis CRO- 55% shareholding

	Dumitru Bădiceanu asociat Bona Artis CRO - 45% shareholding

Introductory part on Bona Artis CRO	Bona Artis CRO was notified on 10 September 2020, with registration at the Public Service Agency. It did not carry out any activities until January 2022, when the Standard Operating Procedure (SOP) was developed, followed by the development of other standard operating procedures. The company currently has 3 employees: a clinical study monitor (Maria Macari), who also holds this role in other external collaborations whose services are subcontracted, an accountant and a Quality Assurance (QA) specialist – Cristina Gorbatovschi – also with subcontracted services. The administrator and partner also carry out clinical study monitoring activities. Since its establishment, the company has been managing the processes within a single clinical study at national level: Prospective, multicentre, single-arm open study of the long-term efficacy, safety and acceptability of orally administered Mifepriston, weekly 50 MG, for contraceptive purposes'.

Review of documentation and interviews with study team members	
OCC organisational chart	An outline of an organisational chart was introduced that does not reflect the current situation of Bona Artis CRO's positions and employees. There is no active organisational chart with employee positions.
SOPs	10 SOPs were presented relating to clinical study processes and 10 SOPs relating to quality management. All SOPs expired in January 2025. According to Tatiana Bacalu, a QA was contracted to update the company's SOPs. After evaluating the content of the SOPs, it was established that Bona Artis representatives do not follow the provisions of the SOPs in their daily activities. For example, SOP *CT-009 Version 01 Fraud and Misconduct* describes the steps to be taken by Bona Artis employees in case of suspicion of fraud, including its documentation (time of detection, type of fraud, records) – processes that were not implemented in the potential fraud identified in the case of the clinical study Mife50. The SOPs mention documents that must be implemented by employees but have not yet been developed by the company (e.g., *Bona Artis Code of Conduct)*.

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	In the *Responsibilities* section, these are assigned to roles that do not currently exist in the company's organisational chart (e.g. *compliance officer*, *senior management*) The SOPs do not include distribution lists. The SOPs are developed by Dumitru Bădicean and reviewed and approved by Tatiana Bacalu.
CVs and training certificates of the Bona Artis team	The updated CVs of Tatiana Bacalu, Dumitru Bădicean, Maria Macari and Cristina Gorbatovschi (QA) were presented. Training certificates were presented for Tatianei Bacalu (last training: January 2025), Dumitru Bădicean (last training: November 2024), Maria Macari (training: March 2024), Cristina Gorbatovschi (training: November 2024) in GCP. In December 2024, Cristina Gorbatovschi attended training on ISO 9001:2015.
Electronic platform	Bona Artis uses Microsoft 365 Drive electronic cloud storage in its daily work and for archiving purposes. This is an unsecured electronic platform and is not specific for use in clinical studies.
Quality assurance	The person appointed for the Quality Assurance process did not initiate any alert procedure when a suspicion of fraud was triggered.
Archiving	This OCC does not have a registered office. Therefore, the archiving of clinical study documentation cannot be justified/supported in the event of an inspection/audit in paper format or in electronic format.

Closing meeting	
Time	16:50 hrs
The deficiencies identified during the inspection were reported. All deficiencies are critical.	
Deficiency	*Legal provision violated*
The organisational chart presented does not reflect the structure and positions of the Bona Artis CRO employees	Pct. 87 (2) of Annex 2 No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: "The OCC must implement a Quality Assurance and Quality Management System."
The Quality Management System is not functional: The SOPs describe activities that are not	Pct. 87 (2) of Annex 2 No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: "The OCC must implement a Quality Assurance and Quality Management System."

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carried out and refer to internal documents that have not been developed	
The electronic platform used by the company is not specific for use in clinical studies and has unsecured access	Pct. 96 of Annex 2 No.648 of the Ministry of Health of 12.08.2016 on the regulation of the authorisation of clinical studies in the Republic of Moldova: "When using electronic systems for handling study data and/or external electronic data systems, the sponsor must meet the following requirements: a) ensure and demonstrate with documents that the

	electronic data processing systems meet the conditions established by the sponsor for the desired proper, complete, secure and accurate operation (e.g. validation); [...].”

Pct. 90 of Annex 2 Order No.648 of 12.08.2016:
‘All references to the sponsor in this document also apply to the OCC, in case the OCC has assumed duties and functions in the study that would have belonged to the sponsor,’

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Annex 1

From: Dumitru Badicean <dbadicean@yahoo.com>
Sent: Tuesday, May 6, 2025 12:10 PM
To: Marcelina Cebanovschi <marcelina.cebanovschi@amdm.gov.md>; svetlana.nichita <svetlana.nichita@yahoo.com>
Cc: Rebecca Gomperts <gompertsrebecca@gmail.com>; Waves Rebecca <gomperts@womenonwaves.org>; **Kristina Gemzell Danielsson** <kristina.gemzell@ki.se>; Office BonaArtis <office@bonaartis.md>; **Gunilla Kleiverda** <1<leiverd@xs4all.nl>., **Rodica Comendant** <comendantrodica73@gmail.com>
Subject: Mife50: suspicion for data manipulation and GCP violations at site MD010

Dear Marcelina Cebanovschi and Svetlana Nichita,

We have a strong suspicion of data manipulation and GCP violations at site MD-010 (PI Dr. Irina Tripac) within the Mife50 study.

At this site were enrolled (signed the ICF) 476 subjects, 362 of them received the IMP.

Based on the last Monitoring Visit and strange data patterns were investigated in more depth the lab results data for subjects who came to the visit same day: the lab results are very similar, it looks like from the same blood sample. At this site the blood sampling is performed on site and after that, the courier takes the samples to AlfaDiagnostica laboratory (local central laboratory) for analysis.

The TVUS photos contain only handwritten subject screening number or name, and not the preprinted number/name as usually must be done.

Due to all these suspicions and as agreed with the sponsor – we started to call the subjects (who received the IMP) to verify their participation în the study. We found that 47 out of 50 - participants already approached by us, are not aware of the Mife50 study, but confirmed that they signed a document for participation (most probably ICF), however they are not taking the IMP, are not doing the 3 monthly follow up visits and not getting ultrasounds or blood tests and are not filling in the eDiary. On the other side, the laboratory and ultrasound results are reported and eDiary is filled in regularly.

We plan to finish the call verification with the rest of the subjects from site MD010 and will submit to MMDA and NEC a Notification with more details on identified discrepancies.

For now, the Sponsor decided to stop all activities at site MD010 until the situation with potential data manipulation is clarified.

Best regards

Dumitru

Dr. Dumitru Badicean
mob: (+373)-790-12438

Connect with me on Linkedin: www.linkedin.com/in/Badicean

Participant number:

Annex 2

INFORMED CONSENT FORM

For participation in the clinical study:
Prospective, multicentre, single-arm open study of the long-term efficacy, safety and acceptability of orally administered Mifepriston, weekly 50 mg, for contraceptive purposes

By signing this form, I confirm that:
• I have received information about the objectives of the clinical study.
• I have had the opportunity to discuss the study, ask questions and receive satisfactory answers.
• I voluntarily agree to participate in the clinical study of the medicinal product mentioned above. I am informed that I have the right to refuse or withdraw from the study at any time.
• I agree to follow the instructions, cooperate responsibly with the Study Doctor and inform him/her immediately of any health problems or changes in my well-being.
• I know that I can discontinue my participation in the study at any time. In this case, I agree to inform the Study Doctor to give him/her the opportunity to assess my health and make appropriate recommendations.
• I give my consent for the use of information obtained during the study in accordance with the description provided in the Patient Information Sheet above.
• I am informed that I will receive timely medical care paid for by insurance in the event of damage to my health as a result of my participation in the study.
• I have signed and dated the “Informed Consent Form Version of 4.0 dated 03 March 2023” (10 pages) in duplicate. I have received a Patient Information Sheet with the Informed Consent Form, signed and dated, to take home with me.

Signature of participant
Date:

I, the undersigned, have provided a detailed and complete explanation of the study and ensure that, to the best of my knowledge, the above-mentioned participant/legal representative (cross out as appropriate) clearly understands the nature, risks and benefits of participating in this study.

___Tripac Irina_____

Surnames investigator (Study Doctor) (full name and surname, legibly handwritten by the by the investigator)

Signature of investigator (Study Doctor):
Date:

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Surnames investigator (Study Doctor) (full name and surname, legibly handwritten by the by the investigator

Signature of investigator (Study Doctor):
Date:

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Signature of participant (full name and surname, legibly handwritten by the by the participant)
Date:

I, the undersigned, have provided a detailed and complete explanation of the study and ensure that, to the best of my knowledge, the above-mentioned participant/legal representative (cross out as appropriate) clearly understands the nature, risks and benefits of participating in this study.

___Tripac Irina_____

Surnames investigator (Study Doctor) (full name and surname, legibly handwritten by the by the investigator

Signature of investigator (Study Doctor):
Date:

Signature page

Date	21-05-2025
Surname, first name	Lina Gudima
Position	Deputy General Manager AMDM

Signature	

Date	21-05-2025
Surname, first name	Guzinschi, Ecaterina
Position	Coordinating Inspector Head of Service GCP, GVP, GLP, GRP
Signature	

Date	21-05-2025
Surname, first name	Marcelina Cebanovschi
Position	Delegated Inspector, Head of Service clinical studies
Signature	

Date	21-05-2025
Surname, first name	Roxana Dimitriu
Position	Principal Inspector, service GCP, GVP, GLP, GRP
Signature	

Date	21-05-2025
Surname, first name	Eugeniu Demineț
Position	Principal Inspector, service GCP, GVP, GLP, GRP
Signature	

Date	21-05-2025
Surname, first name	Daniela Cocu
Position	Delegated Inspector, pharmacist, AMDM
Signature	

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