Annex 30
to the Procedure of registration materials examination of medicinal products,
submitted for state registration (re-registration),
as well as expert review of material for changes to registration materials
during the validity of the registration certificate
(art. 4, section IV)

Clinical research report № 1

1. Name of medicinal product (if available – number of registration certificate):	**Lenalidomide Krka Novo mesto 25 mg hard capsules**				
2. The applicant	Krka, d.d., Novo mesto, Smarjeska cesta 6, 8501 Novo mesto, Slovenia				
3. Manufacturer	Bulk manufacturer, quality control (chemical/physical and MKB), primary and secondary packaging and batch release site: KRKA-FARMA d.o.o., V.Holjevca 20/E, 10450 Jastrebarsko, Republic of Croatia Secondary packaging site: Krka, d.d., Novo mesto, Belokranjska cesta 26, 8000 Novo mesto Slovenia Quality control testing (Chemical/Physical and MKB) and batch release site: Krka, d.d., Novo mesto, Smarjeska cesta 6, 8501 Novo mesto, Slovenia				
4. the undertaken study:	**X**	yes	o	no	if not explain
1) the type of medicinal product for which the registration was made or planned	Generic medicinal product				
5. Full name of clinical research, coded number of clinical research	A Single-Dose, Bioequivalence Study of Two Formulations of Lenalidomide 25 mg Capsules, Hard under Fasting Conditions Protocol Number: 2019-4618 Version: 1.0 Date: 21.12.2018				
6. Phase of clinical research	Bioequivalence study				
7. Time frame of clinical research	23.02.2019 - 11.04.2019				

8. Countries where the clinical research was conducted	Canada
9. The number of persons under investigation:	planned: 70 subject actual: 67 subject
10. Purpose and secondary objectives of the clinical research	The primary objective of this study was to evaluate the bioequivalence between Lenalidomide 25 mg capsules, hard (Manufacturer: KRKA-FARMA d.o.o., Jastrebarsko, Republic of Croatia, EU) and Revlimid® 25 mg hard capsules (lenalidomide) (MAH and Manufacturer: Celgene Europe Limited, UK, EU) after a single dose in healthy subjects administered under fasted conditions. The secondary objective of this study was to evaluate the safety and tolerability of the study treatments.
11. Clinical research design	Open-label, single-dose, randomized, two-period, two-treatment, two-sequence, crossover, study, designed to evaluate the bioequivalence of lenalidomide in healthy, nonsmoking, male subjects under fasted conditions.
12. Main inclusion criteria	The study population included nonsmoking, male volunteers from 18 to 55 years of age, with a body mass index (BMI) ≥19.0 and ≤30.0 kg/m2 , who were deemed healthy based upon a medical history, 12-lead electrocardiogram (ECG), laboratory evaluation (biochemistry, hematology, serology, and urinalysis), physical examination, tuberculosis (TB) questionnaire, and vital signs measurements (blood pressure [BP], pulse rate [PR], respiration rate [RR], and temperature), and did not test positive for urine cotinine or urine drugs of abuse at screening.
13. Test medicinal product, method of administration, strength	Lenalidomide Krka 25 mg capsules, hard Method of Administration: Oral under fasted conditions Strength: 25 mg

14. Reference substance, dose, method of administration, strength	Revlimid® hard capsules Method of Administration: Oral under fasted conditions Strength: 25 mg INN: lenalidomide
15. Concomitant therapy	Not applicable
16. Efficacy evaluation criteria	Criteria for Evaluation: The 90% CIs of the relative mean plasma lenalidomide AUCt and Cmax of the test to reference products should be between 80.00 and 125.00%.
17. Safety assessment criteria	An assessment of safety was based primarily on the incidence, frequency, and severity of adverse events (AEs).
18. Statistical methods	Analysis of variance (ANOVA) (PROC GLM) was performed on log-transformed plasma lenalidomide AUCt, AUCinf, and Cmax. Based on log-transformed data, ratios of the geometric means for treatments and the corresponding 90% confidence intervals (CIs) were calculated for AUCt, AUCinf, and Cmax.
19. Demographic indicators of the population study (gender, age, race, etc.)	Healthy, nonsmoking, 70 male subjects, from 18 to 55 years of age.10 of those were Asian, 17 Black, 41 white and 2 other.
20. Efficiency results	The 90% CIs of the relative mean plasma lenalidomide AUCt and Cmax of the test to reference products were within the 80.00-125.00% bioequivalence range.
21. Safety results	The administration of the study drugs was generally well tolerated by the healthy subjects participating in this study. Overall, 15 AEs affecting 10 subjects (14.3% of subjects dosed) were reported in the study, with 9 AEs affecting 6 subjects (8.6%) judged to be possibly related to the IMP. The most prevalent treatment related AEs were headache (2 events affecting 2 subjects [2.9%]) and somnolence (2 events affecting 2 subjects [2.9%]). All AEs were mild in

	severity and resolved prior to the end of the study. No SAEs were reported during the conduct of this study. None of the AEs had a significant impact on the safety of the subjects or on the integrity of the study results.
22. Conclusion (evaluation)	The 90% CIs of the relative mean plasma lenalidomide AUCt and Cmax of the test to reference products were within the 80.00-125.00% bioequivalence range. The test product, Lenalidomide 25 mg capsules, hard (KRKA-FARMA d.o.o., Jastrebarsko, Republic of Croatia, EU), exhibited equivalent rate and extent of exposure compared to the reference product, Revlimid® 25 mg hard capsules (lenalidomide) (Celgene Europe Limited, UK, EU) after a single oral dose in healthy, nonsmoking male subjects under fasted conditions. Overall, the study medications were well tolerated by the healthy subjects that participated in this study.
Applicant (holder of registration certificate)	 (signature) Janja Recelj