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SFHK ILE RUHSAT SAHIPLERINCE YÜRÜTÜLEN FV ÇALIŞMALARININ USUL VE ESASLARI HK. KILAVUZ 15.11.2023_EN

Telephone:(0312)2183000Fax:(0312)2183460 E-mail:tufam@titck.gov.tr Web:https://www.titck.gov.tr/ TurkishMinistryofHealth TurkishMedicinesandMedicalDevicesAgency GUIDELINEONPRINCIPLESANDPROCEDURESFOR PHARMACOVIGILANCEACTIVITIESBYCONTRACT PHARMACOVIGILANCESERVICEPROVIDERSANDMARKETING AUTHORIZATIONHOLDERS FVK-KLVZ-17 InitialVersionEffectiveDate 11.05.2023 1 st RevisionEffectiveDate 15.11.2023

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Purpose

ARTICLE1–(1)ThisGuidelinesetsforththeoperatingprinciplesandproceduresand responsibilitiesofContractPharmacovigilanceServiceProviders(CPSPs)andmarketing authorizationholderstoensurethatpharmacovigilanceservicesareconductedinlinewiththe applicableregulations.

Scope

ARTICLE2–(1)UndertheRegulationonSafetyofMedicinalProducts,marketingauthorization holdersmaydelegateallorsomeoftheirpharmacovigilanceresponsibilitiestoaCPSP,withthe marketingauthorizationholderretainingultimateresponsibilityforfullandaccuratefunctioningofthe pharmacovigilancesystem.Thisguidelineappliestomarketingauthorizationholdersand CPSPs. Marketingauthorizationholderswhofilltheirpharmacovigilanceobligationsinternallyarealso expectedtomeettheminimumcriteriarequiredofCPSPs.

Basis

ARTICLE3–(1)ThisGuidelineisissuedbasedontheRegulationonSafetyofMedicinalProducts, publishedinOfficialGazette#28973ofApril15,2014,Law#6698onProtectionofPersonalData, publishedinOfficialGazette#29677ofApril07,2016,andtheRegulationonPersonalHealthData, publishedinOfficialGazette#30808ofJune21,2019.

Definitions

ARTICLE4–(1)ForthepurposesofthisGuideline:
a)AdverseReactionorAdverseDrugReactionmeansaresponsetoamedicinalproductwhich isnoxiousandunintended;
b)QualifiedPersonforPharmacovigilancemeansaphysicianorpharmacistemployedbythe marketingauthorizationholderoraCPSPtofulfillrequirementsoftheRegulationonSafety ofMedicinalProducts;
c)ControlledAccessProgrammeansaprogramconducted,conditionalonfulfillmentofasetof

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patientaccesscriteria,toallowaccesstomedicinalproducts,whichhaveprovenbenefitsbut whichcarrysignificantrisks,priortobeingprescribedorplacedonthemarkettoensuretheir safeuseandthattherisksinvolvedareminimized;
ç)AgencymeansTurkishMedicinesandMedicalDevicesAgency;
d)MedDRAmeansamedicaldictionaryforregulatoryactivities,createdbytheInternational CouncilforHarmonization;
e)MedDRAMaintenanceandSupportServicesOrganization(MSSO)meansaservice organizationestablishedtomaintain,distributeandsupportMedDRAforusersunder supervisionoftheICHMedDRAManagementCommittee;
f)Periodicbenefit/riskassessmentreport(PBRAR)meansareportcompiledbymarketing authorizationholdersatdefinedpost-authorizationtimepointsinaspecificformattoevaluate thebalanceofbenefitsvsrisksofamedicinalproduct;
g)RiskManagementPlan(RMP)meansadetaileddescriptionoftheriskmanagementsystem;
ğ)MarketingAuthorizationHoldermeansanaturalorlegalpersonwhoholdsmarketing authorizationforahumanmedicinalproduct;
h)ContractPharmacovigilanceServiceProvidermeansanorganizationmeetingthecriterialaid downinthisguidelineandauditedandaccreditedbytheAgency,whichemploysatleastone personincapacityofQualifiedPersonforPharmacovigilanceandatleastonepersonastheir deputy,andtowhichamarketingauthorizationholderhasdelegatedallorsomeofits pharmacovigilanceobligationsonawrittencontract;and
ı)Auditmeansasystematic,disciplined,independentanddocumentedprocessforobtaining auditevidenceandevaluatingitobjectivelytodeterminetheextenttowhichtheauditcriteria arefulfilled.

MinimumcriteriathatmustbemetbyMarketingAuthorizationHoldersandCPSPs
ARTICLE5–(1)MarketingauthorizationholdersandCPSPsdelegatedmustmeetthefollowing criteria:
a)ProperEquipmentandaSufficientNumberofPersonnel:
MarketingAuthorizationHoldersandCPSPsareobligatedtohaveasufficientnumberof employees,proportionaltotheirworkload,andtoexpanditsstaffandequipmenttoreflectgrowing workloadwhichmayresultfromincreasednumberofclientsormedicinalproductsforwhichtheyare responsible. Thekeypersonnelinpharmacovigilancearethequalifiedpersonforpharmacovigilanceand theirdeputy.Itmustbeensuredthatthepersonnelemployedinthoserolesreceiveappropriatetraining andhavesufficientexperience,andtheyaremaintainedinthoseroles.
i)Mandatorytrainingforqualifiedpersonforpharmacovigilanceandtheirdeputy:
Aftertheirappointmentintheseroles,thequalifiedpersonforpharmacovigilanceand theirdeputymustundergoandsuccessfullycompleteaninitialtrainingprogram providedbytheAgency.Participantswhofailtoattendthetrainingsessionswithout anexcuseacceptabletotheAgencymaynotcontinueintheirroleuntiltheycomplete thetraining. TheymustcompletethebasicMedDRAcodingtrainingofferedbyMedDRAMSSO (CodingwithMedDRa,SafetyDataAnalysisandStandardMedDRAQueries[SMQs]) withinsixmonthsafterstartingintheirrole.Theymustattend,receiveanddocument thattheyhavereceivedalltheotherface-to-faceoronlinesessionsorganizedby MedDRAMSSO(e.g.Let'sCodeTogether,AdvancedMedDRACoding).
Theymustattend,receiveanddocumentthattheyhavereceivedsuchotherface-to-faceoronlinetrainingrelevanttotheirotherroles(e.g.reportingadversereactions, preparingPBRARsandRMPs).
Intheeventofsignificantamendmentstopharmacovigilanceregulations(e.g.a regulationmodifyingthecurrentpractices,guidelineupdates,newGVPguidelines), theymustattendsubsequenttrainingsessionsorganizedbytheAgencytoupdatetheir trainingcertificate. ii)Experience
Theymusthavenotlessthanoneyearofdocumentedexperienceworkingina pharmacovigilanceroletobeeligiblefortheroleofqualifiedpersonfor pharmacovigilance. iii)Workload

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Aqualifiedpersonforpharmacovigilancemayassumeresponsibilityof pharmacovigilanceactivitiesfornotmorethan150activesubstances,ifworkingwithina marketingauthorizationholder'sorganization,ornotmorethan100activesubstancesif workingwithintheorganizationofaCPSP.Thecaponnumberofactivesubstancesfor whichtheymayberesponsiblecanbeincreasedbyupto10%.Theactivesubstancesfor whichaqualifiedpersonforpharmacovigilancewouldberesponsibleshouldbe designated;up-to-daterecordsthereofmustbemaintainedfromthebeginningdateof responsibilityandmadeavailabletotheAgencyforimmediatereviewuponrequest.Itis recommendedtodesignateactivesubstancesbasedontheirrespectivetherapyareas. WhereaCPSPservesmultiplemarketingauthorizationholdersforthesameactive substance,theseshouldberegardedasdifferentactivesubstancesandaccounttowardthe quotaof100activesubstances.
Apersonwhoactsasqualifiedpersonforpharmacovigilanceata CPSPmaynotdeputize forthequalifiedpersonforpharmacovigilanceatanothercompany.However,wherea commonpharmacovigilancesystemisoperatedbydifferentmarketingauthorization holdersbelongingtothesameparentorganization,apersonactingincapacityofqualified personforpharmacovigilanceforoneofsuchmarketingauthorizationholdersmay deputizeforthequalifiedpersonforpharmacovigilanceofanothercompanybelongingto thesameparentorganization.

 Adeputyqualifiedpersonforpharmacovigilancemaydeputizeforuptotwoqualified personsforpharmacovigilance. iv)Recognitionandreachability Toraiseawarenessforimprovingreportingofadversereactionsandensurereportsare submittedappropriatelyandwithintheprescribedtimelines,thequalifiedpersonfor pharmacovigilanceandtheirdeputyshouldbeknownto,andrecognizedandreachableby everyoneatthecompanyforwhichtheyassumeresponsibilityofpharmacovigilance obligations,includingcallcenterstaff,securitypersonnelandmanufacturingteams.
b)Suitableworkingenvironment
Itisessentialthatasuitablelocation,andsufficienttechnicalmeansandequipment(e.g. informationtechnology(IT)systems,(electronic)archives)areavailabletocarryout pharmacovigilanceactivities.
TheCPSPshouldhaveaphysicalarchivefacility,sufficientlylargetoaccommodatethe numberofpharmacovigilanceclientsservedbyit.Thearchiveshouldbeequippedwithstainlesssteel cabinetskeptunderlockandkey,assignedtoeachclient.Accesstothearchiveshouldberestrictedto authorizedpersonnel.Accesstothearchivefacilityshouldbeloggedtoensureeffectivemonitoring. Thetemperatureandhumidityofthephysicalarchivefacilityshouldbeloggedandcompatiblewith onlinetransmission.
Documentsmaybestoredinanelectronicformat,providedthattheelectronicsystemis properlyvalidatedandappropriateprecautionsareinplacetoensuresystemsecurity,accessand backup.Wherethedocumentsareconvertedtoanelectronicformatfromhardcopy,theconversion processusedshouldensurethatallinformationfromtheoriginaldocumentarelegiblypreservedand themediumusedforstorageremainsreadableovertime. c)Safetydatabase ThesafetydatabaseshouldbeE2B(R3)-compatibleandfullyvalidated.Itmustbeensuredthat datamaintainedatCPSPsbelongingtoindividualclientsarestoredinfullysegregateddatabasesand privacyofthedatastoredthereinisensured.
ThedatabaseshouldincorporatethelatestversionofMedDRAandtheWHODrugDictionary. ThedatabasesthatmaybeusedincludeArgusSafety(Oracly),ARISg/LifeSphereSafety,ArisGlobal IRT,PVWorks(EnnovGroup,PvEdge(Sarjen),SafetyEasy(ABCube),VaultSafety(Veeva), SafetyBaseInterchangeand,ifproperlyvalidatedandequippedwithappropriatesystemsecurity, accessandbackupfeatures,anin-housedatabasedevelopedbythecompany.
ç)InformationSecurityandCyberSecurity

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Informationsecurityencompassesabroadspectrumoftopics,rangingfromphysicaland peripheralsecuritytohumanresourcessecurity,securityofcommunicationsandcorrespondence security,andinformationsystemssecurity.
Allinformationstoredinhardcopyandelectronicdevicesmustbemanagedinlinewiththe principlesofconfidentiality(ensuringdataispreventedfromaccessbyunauthorizedpersonneland protectedagainstunauthorizedaccess),integrity(preventingmodificationofdatabyunauthorized personnel)andaccessibility(ensuringdataremainsavailableandaccessibletoauthorizedpersonnel whenneeded). Toensuretheforegoingrequirementismet,companiesmustmeetinformationsecurity standards,complywithallapplicableregulatoryrequirements,identifyandmanagerisksto informationassets,undertakecontinualreviewoftheinformationsecuritysystemandtakeactionas appropriate,andinformusers(i.e.everyonewhohasaccesstoinformation,includingpersonnelof marketingauthorizationholders,CPSPsandthirdpartiesconductingcontrolledaccessprograms, employeesofbusinesspartners,andcompanysupportpersonnel).
Toensurethesecurityofinformationsystems,documentationshouldbeinplaceaccordingto TSISO/IEC27001InformationSecurityManagementSystemStandardandTSISO/TEC20000 InformationTechnologyServiceStandard,andtherequirementsandprocedureslaiddowntherein shouldbecompliedwith.Someparticularlysignificantaspectsoftheiso27001standardare specificallyhighlightedbelow: InformationSecurityObligationsoftheOrganization: Anumberofproceduresandcontrolsmustbeperformedpriortohiring,duringemployment, atrolechangeandseveranceofallpersonnel(e.g.full-timeandpart-timecontractedemployees,

employeesofcontractors,businesspartnersandsupportcompanies)whohaveaccesstothe informationprocessingfacilities.
Allpartiesshouldbemadeawarethatapersonaland/orcorporateconfidentialityagreement willbeexecutedwithallpersonnelandcontractorspriortohiring.Thecontentoftheagreementand theobligationsofparteslaiddownthereinshouldbeexplainedindetail.Theagreementsshould clearlyspecifyinformationsecurityresponsibilitiesofindividualsandthemanagement.
Individualswillbeobligatedtomaintainconfidentialityofdatalearnedbythemduringtheir employmentandrefrainfromdisclosingthesamewithoutauthorizationinanymannerwhatsoever evenafterchangeofroleorseverance.Theconfidentialityobligationremainsinforceindefinitely.It mustbeensuredthattheseveranceprocedureofpersonnelwholeavetheorganizationorareassigned toadifferentrolearecconductedimpeccablyfromaninformationsecurityviewpoint.
Datatransferisacriticalprocess,whichmayhavelegalramificationsandgiveriseto administrativeorcriminalpenaltiesifperformedincorrectlyorwithoutauthorization.Theprecautions laiddowninKVKKDecree#2018/10mustbeinplaceforanytransmissionofspecialpersonaldata (healthdata).
Wherethedataaretobetransferredtoanother CPSP,theformercontractserviceproviderof themarketingauthorizationholderwillperform“secureerasure”ofallpharmacovigilancedataafter thetransferhasbeencompleted,andemployanappropriateproceduretodestroytheharddrivesthat wereusedforstoringthedata.Alldocumentsinhardcopymustbedeliveredtothemarketing authorizationholderonaformalreport,withoutmodificationorduplication.
Ifacloudserviceisused,theCPSPmustnotifythemarketingauthorizationholderandobtain theirconsent.Ifthemarketingauthorizationholderconsentstotheirdatabeingstoredoncloud,the pharmacovigilancedatamustbeencryptedusingcryptographictechniques.
Ariskmanagementapproachshouldbeemployedforsecuringinformationassetsonthebasis ofISO/IEC27005andTSISO31000standards.
Logsofalltransactionswithdatashouldbesecurelymaintainedonaseparatemediumfornot lessthantwoyearsandremainavailableduringaudits,andremoteaccesstodata,ifapplicable,should bebasedonnotlessthantwo-factorauthenticationandarrangementsfordatabackupmustbeinplace.
FortransfersofpersonalhealthdatawithinTürkiyeandabroad,therequirementsofLaw

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#6698mustbesatisfied. InformationSecurityObligationsofPersonnel:
a)IfCPSPpersonnelpersonallybreachesinformationsecurity,theywillbeliableforany resultingdamagetotheiremployer,themarketingauthorizationholderorthirdparties.
b)Personnelwillusethedataentrustedtothemortowhichtheyhavebeengrantedaccessby theiremployersolelyinconnectionwiththeirassignedtasks.Theywillprotectthedataas theirownandnotshareitwithanyunauthorizedparties,andeventhenonaneed-to-know basis.
c)Personnelmaynotsharedatawithanyunauthorizedparties,includingofficersofclients, unlessspecificallyauthorizedtodoso.
ç)Personnelmaynotusetheinformationtheyhaveacquiredtoservetheinterestsofany individual,group,institutionororganization.
d)Personnelisunderobligationtomaintainconfidentialityofandrefrainfromdisclosingto thirdpartiesanyconfidentialinformationlearnedbythem,whetherornotrelatedtotheir assignment.Thisobligationsremainsinforceafterthepersonnelleavestheiremployer.
e)Personnelmaynotunlawfullyacquire,alter,attempttoerase,transferorduplicatethe softwareapplications,dataorotheritemsstored/usedininformationsystems.
f)Personnelmaynotengageinanybehaviorthatmayresultindestruction,alteration, erasureoftheinformationprocessingsystemsusedbythemandthedatastoredtherein, partiallyorcompletely,normaytheyattempttoobstructsystemfunctionalityorcause systemmalfunction,whethertoharmothersortoderiveabenefitforthemselvesorothers, orfornospecificreason.

 g)Personnelmaynotwithoutdueauthorizationandforanypurposewhatsoeveruse, duplicate,moveortransferdataacquiredbytheminthecontextoftheirroleorarestored ininformationprocessingsystemsinanyform(e.g.printed,magneticmedium).

d)QualityManagementSystem

Qualityoperationsmustbeconductedbyaunitproperlytrainedinqualityprocedures.CPSPs, aswithmarketingauthorizationholders,areobligatedtomeettherequirementslaiddowninthe GuidelineonGoodPharmacovigilancePractice(GVP),ModuleIV–PharmacovigilanceQuality System.Additionally,CPSPsmusthaveavalidISO9001QualityManagementCertificateissuedbya conformityassessmentorganizationauthorizedbyTURKAKforISO9001QualityManagement Accreditation. Thequalitymanagementsystememployedbymarketingauthorizationholdersand CPSPs mustmeetthefollowingminimumcriteria: Qualitypolicy Humanresourcesmanagement oMonitoringpersonnelrolesandcompetencies Roledefinitions Individualroleandcompetencycards Competencymonitoringandassessment Trainingrecordforms Informationsecuritymanagement oInformationsecuritydocuments oAccesscontrol/mobiledevicesandremoteworking oInformationclassification(andprocessing) oPhysicalandperipheralsecurity oAcceptableuseofassets/cleandeskandclearscreen oInformationtransfer,communicationsecurity oRestrictiononsoftwareinstallationanduse oBack-up oMalwareprotection oEmploymentofcryptographiccontrols oManagementoftechnicalgaps oPrivacyandprotectionofpersonallyidentifyinginformation oSupplierrelations oNewhireinitiationform(includingissuanceofpersonnelaccesscard,authorization toaccessbuildings/facilities,accountcreationforaccesstoinformationsystemsand authorizations,informationsecurityawarenesstraining,orientation,executionof confidentialityagreement). oSeveranceform. Procedures oStandardoperatingproceduredraftingandimplementationprocedure oAppointmentprocedureofqualifiedpersonforpharmacovigilance oAppointmentprocedureofdeputyqualifiedpersonforpharmacovigilance oManagementandreportingprocedureofadversedrugreactionreports oCausalityassessmentprocedureofadversereactions oLiteraturereportsmanagementprocedure oManagementprocedureofmedicinessubjecttoadditionalmonitoring oSafetyalertmanagementprocedure

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oSignalmanagementprocedure
oCPSPinternalandexternalcommunicationprocedure
oProcedurefordirecthealthcareprofessionalcommunications
oProcedureforpreparingperiodicbenefit/riskassessmentreports
oProcedureforpreparingriskmanagementplans
oProcedureforpreparinganddisseminatingtrainingmaterials
oProcedureforpreparingthePharmacovigilanceSystemMasterFile
oBenefit/riskassessmentprocedure oTrainingprocedure: CPSPpersonneltrainingprocedure Orientationprogram Annualon-the-jobtrainingplan Trainingassessmentform Newhireinitiationandroleadjustmentcontrolform Trainingneedanalysisform Trainingassessmentform Personneltrainingregistrationform Trainingassessmentreport Trainingprocedureforpharmacovigilanceserviceproviders Orientationprogram Trainingassessmentform Annualon-the-jobtrainingplan Trainingneedanalysisform Personneltrainingregistrationform Trainingassessmentreport
oCorrectiveandpreventiveactionsprocedure oPhysical/electronicarchiving Procedureforretrievingfilesfromthearchive Procedurefordeliveringfilesforarchiving Temperatureandhumiditytrackingdiagram oAuditprocedure oRiskmonitoringprocedure
oPharmacovigilancecrisismanagementprocedure oProcedureforcheckingconflictofinterest
oProcedureforpreparingandfollowinguponagreementswithcounterparties
oProcedureforprotectingpersonaldatainthecontextofpharmacovigilance Formsused Recordmanagement e)PerformanceCriteria
MarketingauthorizationholdersandCPSPsareobligatedtomeettheperformancecriteria designatedandannouncedbytheAgencyforreportingadversereactions.
Pharmacovigilanceresponsibilitiesofmarketingauthorizationholdersthatmaybedelegatedto CPSPs
ARTICLE6–(1)MarketingauthorizationholdersmaydelegatetoCPSPssomeoralloftheir followingpharmacovigilanceobligationsunderthe“RegulationonSafetyofMedicinalProducts”and otherapplicableguidelines.Inthatcase,anotarizedresponsibility-sharingagreement,describing whichpharmacovigilanceserviceswouldbecarriedoutbytheCPSP,mustbesubmittedtothe Agency.

a)Managementofadversereactionreports
oGuidelineonGoodPharmacovigilancePractice(GVP)ModuleI– ManagementandReportingofAdverseDrugReactions
oGuidelineonProtectionofPersonalDatainPharmacovigilanceActivities
oGVPModuleIV–PharmacovigilanceQualitySystem oAnnexI–Definitions b)Literaturescreening
oGVPModuleI–ManagementandReportingofAdverseDrugReactions
oGVPModuleIV–PharmacovigilanceQualitySystem c)PreparingPBRARs
oGVPModuleIII–PeriodicBenefit/RiskAssessmentReport
oGVPModuleIV–PharmacovigilanceQualitySystem ç)PreparingPharmacovigilanceSystemMasterFile
oGVPModuleV–PharmacovigilanceSystemMasterFile
oGVPModuleIV–PharmacovigilanceQualitySystem d)PreparingRMPs
oGVPModuleVI–RiskManagementSystems
oGVPModuleVIAnnex1–BasicRequirementsforRiskManagementPlans forCOVID-19Vaccines
oGVPModuleIV–PharmacovigilanceQualitySystem
oGVPModuleIX–SelectionofRiskMinimizationMeasuresandTools
oGVPModuleIX–Annex1–TrainingMaterials e)Signaldetectionandassessment
oGVPModuleVII–SignalManagement oGVPModuleIV–PharmacovigilanceQualitySystem
f)Benefit/riskassessment oGVPModuleX–Pre-MarketingBenefit/RiskAssessment
oGVPModuleXI–Post-MarketingBenefit/RiskAssessment
oGVPModuleIV–PharmacovigilanceQualitySystem g)Pharmacovigilancetraining
CPSPsmustprovideappropriateperiodictrainingtopersonnelwhomayaffectthe

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pharmacovigilancesystemorconductofpharmacovigilanceactivities,includingpersonnelliaising betweentheCPSPandmarketingauthorizationholder.Thetrainingprovidedshouldcover,without limitation,productpromotionassociates,andpersonnelwhohavearoleinclinicaltrials,handling technicalproductcomplaints,medicalinquiries,salesandmarketing,regulatoryaffairs,public relations,legalandauditingprocedures.
Thetrainingsessionsshouldbeorganizedatleastonceayear.Thetrainingsessionsshould coverbasictrainingandasrefreshertraining,andutmostcaremustbetakentoensureclose monitoringofadversedrugreactions.Thetrainingprovidedshouldbelogged,andinitialandfinal testsshouldbeusedtoensuretraininghasbeensuccessful.
Considerationsfordelegationofpharmacovigilanceobligationsofmarketingauthorization holders
ARTICLE7–(1)Whereamarketingauthorizationholderhasdelegatedallofitsresponsibilitiestoa CPSP,theymaybeexemptedfromtherequirementtointernallyemployaqualifiedpersonfor pharmacovigilance.However,incaseswhereonlysomeofthepharmacovigilanceobligationshave beendelegatedtoaCPSP,aqualifiedpersonforpharmacovigilancewithadeputymustbeemployed onafull-timebasis.
(2)Beforedecidingonselectionofa CPSPtoworkwith,marketingauthorizationholders shouldtakeaccountofthefollowing:

Duediligencemustbeperformed. EvenifpharmacovigilanceobligationshavebeencompletelydelegatedtoaCPSP,the marketingauthorizationholderremainsultimatelyresponsibleandthereforeitis advisabletoconductanauditpriortodelegationofobligations.
Iftherearеanypost-auditobservations,asetofcorrectiveandpreventiveactions addressingthesameshouldbeidentified,andtheCPSPshouldbecontractedonly aftertheidentifiedactionshavebeencompleted.
Thecontractbetweenthemarketingauthorizationholderandthe CPSPshould unambiguouslyprovideeveryrelevantaspectoftheagreement,includingaclear descriptionofallrolesandresponsibilitiesthathavebeendelegated,leavingnogrey areas.Thecontractshouldbereviewedandapprovedbylegalcounselsofbothparties.
Anemployeeofthemarketingauthorizationholdershouldbeappointedaspointof contact.Thispersonnel: omustbeinformedabouteverycorrespondence,and othecontractmustlaydowntheresponsibilitiesofthecontactperson.
AftercontractingaCPSP,themarketingauthorizationholdershouldcommunicatethis, andthecontactdetailsofthepersonappointedaspointofcontact,totheAgencybya formalletter.
Themarketingauthorizationholdershouldmeetbeforehandwiththequalifiedperson forpharmacovigilanceandtheirdeputyattheCPSPwhowillcarryout pharmacovigilanceactivitiesonitsbehalf. Activitiesperformedshouldbedetailedinmonthlyreports.
TheCPSPshouldinformthemarketingauthorizationholderifandwhentheyundergo anexternalaudit.
Whenthemarketingauthorizationholderdecidestoterminatetheircontractwitha CPSP,theymusteitherplanforestablishingapharmacovigilancesystemwithintheir organizationorcontractanotherCPSP,preventinganyinterruptionof pharmacovigilancesystemcoverage.
Themarketingauthorizationholdermustimmediatelyinformthe Agencybyaformal noticeofterminationoftheircontractwiththeCPSP,andconcurrentlyappointanew qualifiedpersonforpharmacovigilanceandadeputytobearresponsibilityforthe pharmacovigilancesystem. RoleofCPSPinconductingcontrolledaccessprograms
ARTICLE8–(1)Theresponsibilityforconductingcontrolledaccessprogramsliewiththe marketingauthorizationholder,whoisalsoresponsibletoensureappropriatemeasuresareinplaceto assuresuccessfulconductoftheprogram.
(2)Inacontrolledaccessprogram,themarketingauthorizationholdercontractsa pharmaceuticalwholesalertowhichitshipstheproduct.Thecontractshouldcoverthefollowing aspects:

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a)Therisksofthemedicinalproductandanypotentialimplicationsifitisreceivedbypatients whohavenotbeenprescribedtheproduct.
b)Therulesforreceivingoftheproductbythepharmaceuticalwholesalerandreshipmentto thepharmacywhoreceivedtheoriginalorder. c)Penaltiesforbreachingtherules.
ç)Planning,executingandreportingjointactionstoimprovetheoperation.
Appropriatetrainingshouldbeprovidedtoensurethatthisinformationisknowntothe pharmaceuticalwholesaler'spersonnel,includingitsqualifiedperson,operationsmanagerandbranch manager. (3)Acontrolledaccessprogrammaybeconductedbya CPSP,orthroughathirdparty.Where thewholeofthepharmacovigilanceobligationshavebeendelegatedtoa CPSP,controlledaccess programactivitiesmaynotbeconductedbythesame CPSPoradifferentdepartmentofitdueto privacyofpersonaldata.

(4)Intheeventofterminationofcontractwiththemarketingauthorizationholderortransfer ofconductofthecontrolledaccessprogramtoanotherprovider,the CPSPorthethirdpartyconcerned mustdeliverallinformation,bothelectronicandinhardcopy,initspossessiontothenewservice providercontractedbythemarketingauthorizationholder,andgiveformalassurancethatnodata remainsinitspossession.Thisinformationmaynotunderanycircumstancesbedeliveredtothe marketingauthorizationholderorthirdparties.Anybreachoftheforegoingrequirementwillbe subjecttoapplicableprovisionsofLaw#6698onProtectionofPersonalData.
Transferofpharmacovigilanceactivitiesbetween CPSPs
ARTICLE9–(1)Afterterminationoftheircontractwitha CPSP,marketingauthorizationholders maycontractanother CPSP.Inthatcase,thepharmacovigilancedatamustbefullyandaccurately transferredtothenewly-contracted CPSP,andtheoriginal CPSPmustensurethatallofthedatahave beensecurelyerased. (2)Theterminated CPSPmustdeliveralldocumentsinhardcopytothemarketing authorizationholderwithaformalreceipt,withoutanymodificationorduplicationofthedocuments.
Effectiveness
ARTICLE10–(1)TheprovisionofArticle5,Paragraph1,Point(c)ofthisGuidelinewillenterinto forceon01.07.2025 (2)Theremainingprovisionsofthisguidelinewillenterintoforceon01.01.2024.
Enforcement ARTICLE11–(1)ThePresidentofTurkishMedicinesandMedicalDevicesAgencywillenforce thisGuideline.

REVISIONHISTORY NumberDescription Revision Number RevisionDate 1 RevisedtheGuidelinetitletoinclude"Marketing AuthorizationHolders." 01 15.11.2023 2 InArticle5.a,revisedthenumberofactive substancesto150formarketingauthorization holders,and100forCPSPs.Includedaprovision toallowincreasingthecapbynotmorethan 10%. 01 15.11.2023 3 InArticle5.a,revisedtheexperience requirementtooneyear. 01 15.11.2023 4 InArticle5.b,updatedthequalityrequirements andcriteriaforarchiveaccess. 01 15.11.2023 5 InArticle6.g,revisedtrainingrequirements. 01 15.11.2023 6 Revisedtheeffectivenessprovision. 01 15.11.2023

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