FOR INFORMATION ONLY.
WHEN PERFORMING
THE ASSAY ALWAYS REFER
TO PACKAGE INSERT
SUPPLIED
WITH THE KIT

HE4 EIA

REF 404-10

IVD

CE

Instructions for use. 2019-07

Read highlighted changes

EN	**EXPLANATION OF SYMBOLS**
BG	**ОБЯСНЕНИЕ НА СИМВОЛИТЕ**
CS	**VÝZNAM SYMBOLŮ**
DA	**SYMBOLFORKLARING**
DE	**ERKLÄRUNG DER SYMBOLE**
EL	ΕΠΕΞΗΓΗΣΗ ΤΩΝ ΣΥΜΒΟΛΩΝ
ES	**SIGNIFICADO DE LOS SÍMBOLOS**
ET	**SÜMBOLITE SELGITUS**
FR	**EXPLICATION DES SYMBOLES**
HR	**OBJAŠNJENJE SIMBOLA**
HU	**JELMAGYARÁZAT**
IT	**SPIEGAZIONE DEI SIMBOLI**
LT	SIMBOLIŲ PAAIŠKINIMAI
LV	**SIMBOLU SKAIDROJUMS**
NL	**VERKLARING DER SYMBOLEN**
NO	**SYMBOLFORKLARING**
PL	OBJAŚNIENIE SYMBOLI
PT	**EXPLICAÇÃO DOS SÍMBOLOS**
RO	SEMNIFICAŢIA SIMBOLURILOR
RU	ОБОНАЧЕНИЯ
SV	**SYMBOLFÖRKLARING**
SK	**VÝZNAM SYMBOLOV**
SL	**RAZLAGA SIMBOLOV**
SR	**OBJAŠNJENJE SIMBOLA**
TR	SEMBOLLERİN AÇIKLAMALARI

Use By/Годно до/Použitelné do/ Holdbar til/Verwendbar bis/ Ημερομηνία λήξης/Fecha de caducidad/Kõlblik kuni/ Utiliser jusque/Rok valjanosti/ Felhasználható/Utilizare entro/ Sunaudoti iki/Izlietot līdz/Houdbaar tot/Brukes innen/Użyć przed/ Prazo de validade/Expiră la/ Использовать до/Använd före/ Použite´né do/ Uporabno do/ Upotrebljivo do/Son Kullanma Tarihi

LOT

Batch code/Номер на партида/ Číslo šarže/Lotnummer/ Chargenbezeichnung/Αριθμός Παρτίδας/Código de lote/Partii kood/Code du lot/Kod serije/ Sarzsszám/Codice del lotto/ Partijos kodas/Partijas kods/Lot nummer/Partikode/Kod partii/ Código do lote/Număr de lot/ Номер лота/Lotnummer/Číslo šarže/Številka serije/Kod partije/ Parti Kodu

Date of manufacture/Дата на производство/Datum výroby/ Produktionsdato/Herstellungsdatum/ Ημερομηνία παραγωγής/Fecha de fabricación/Valmistamise kuupäev/ Date de fabrication/Datum proizvodnje/ Gyártási idő/Data di produzione/ Pagaminimo data/Ražošanas datums/ Productiedatum/Fremstillingsdato/ Data produkcji/Data de fabrico/Data fabricaţiei/Дата производства/ Tillverkningsdatum/Dátum výroby/Datum izdelave/Datum proizvodnje/Üretim tarihi

Temperature limitation/ Температурни граници/ Teplotní omezení/ Temperaturbegrænsning/ Temperaturbegrenzung/ Περιορισμοί θερμοκρασίας/ Límites de temperatura/ Temperatuuri piirang/ Limite de température/ Temperaturno ograničenje/ Hőmérsékletre vonatkozó korlátozás/ Limiti di temperatura/ Temperatūriniai apribojimai/ Temperatūras ierobežojums/ Temperatuurbeperking/ Temperaturbegrensninger/ Temperatury graniczne/ Limite de temperatura/ Limite de temperatură/ Температурный режим/ Temperaturbegränsning/ Teplotné obmedzenie Omejitev temperature/ Temperaturno ograničenje/ Sıcaklık sınırlaması/

IVD

In Vitro Diagnostic Medical Device/ Медицински уред за диагностика ин витро/Diagnostický zdravotnický prostředek in vitro/Medicinsk udstyr til in vitro-diagnostik/In-vitro-Diagnostikum/ Ιατροτεχνολογικό προϊόν για διάγνωση In Vitro/Dispositivo médico para diagnóstico in vitro/In vitro diagnostiline meditsiiniseade/Dispositif médical de diagnostic in vitro/Diagnostički medicinski uređaj In Vitro/In vitro orvosdiagnosztikai eszköz/Dispositivo medico per test diagnostici in vitro/In Vitro Diagnostinė Medicinos Priemonė/Medicīniska ierīce in vitro diagnostikai/In vitro-diagnostisch medisch instrument/In vitro diagnostisk medisinsk utstyr/Wyrób medyczny do diagnostyki in vitro/Dispositivo Médico de Diagnóstico In Vitro/Dispozitiv medical pentru diagnostic in vitro/Только для диагностики In Vitro/Endast för in vitro-diagnostik/ Zdravotnícka pomôcka na diagnostiku in vitro/In vitro diagnostični pripomoček/Diagnostički medicinski uređaj In Vitro/<96> testleri için yeterlilik içerir

Contains sufficient for <96> tests/Съдържа достатъчно количество за тестове <96>/Lze použít pro <96> testů/Indeholder tilstrækkeligt/Inhalt ausreichend für <96> Prüfungen/Περιεχόμενο επαρκές για «96» εξετάσεις/Contenido suficiente para <96> ensayos/Kogusest piisab <96> testi läbiviimiseks/Contenu suffisant pour "96" tests/Sadrži dovoljno za <96> testova/A doboz tartalma <96> vizsgálat elvégzéséhez elegendő/Contenuto sufficiente per "96" saggi/Turinys skirtas atlikti <96> tyrimus/ Saturs pietiekams <96> testiem/Inhoud voldoende voor "96" testen/til "96" test/ Tilstrekkelig innhold for <96> prøver/ Wystarczy na wykonanie <96> testów/ Conteúdo suficiente para "96" ensaios/ Conţinut suficient pentru 96 de teste/ Содержит достаточные количества для «96» определений/Innehåller tillräckligt till "96" antal tester/Obsah postačuje na tento počet testov: <96>/Vsebina zadostuje za <96> testov/Sadržina dovoljna za <96> testova/<96> testleri için yeterlilik içerir

REF

Catalogue number/Каталожен номер/ Katalogové číslo/Katalognummer/ Bestellnummer/Αριθμός καταλόγου/ Número de catálogo/Kataloogi number/ Numéro de catalogue/Kataloški broj/ Katalógusszám/Numero di catalogo/ Katalogo numeris/Numurs katalogā/ Katalogusnummer/Katalognummer/ Numer katalogowy/Número do catálogo/ Număr de catalog/Номер по каталогу/ Produktnummer/Katalógové číslo/ Kataloška številka/Kataloški broj/ Katalog numarası

Consult Instructions for Use/ Прочетете инструкцията за употреба/Konzultujte s návodem k použití/Se brugsanvisning/Siehe Gebrauchsanweisung/Συμβουλευτείτε τις Οδηγίες σχετικά με τη χρήση/ Consulte las instrucciones de uso/ Vt kasutusjuhendit/Consulter le mode d'emploi/Pročitajte upute za uporabu/ Olvassa el a használati utasítást/ Consultare le istruzioni per l'uso/Dėl naudojimo žiūrėkite instrukcijas/Izlasiet lietošanas instrukciju/Raadpleeg de instructies voor gebruik/Les instruksene før bruk/Sprawdzić w instrukcji użycia/ Consulte as Instruções de Utilização/ Consultaţi instrucţiunile de utilizare/ Обратитесь к инструкции по применению/Se bruksanvisning/ Prečítajte si návod na používanie/ Pročitajte uputstvo za upotrebu/ Kullanım Talimatlarına Bakınız

CONT

Contents of kit/Съдържание на набора/ Obsah soupravy/Kittets indhold/Inhalt des Kits/Περιεχόμενα του κιτ/Contenido del kit/Komplekt sisaldab/Contenu du kit/Sadržaj opreme/A készlet tartalma/ Contenuto del kit/Rinkinio turinys/ Komplekta saturs/Inhoud van de set/ Settets innhold/Zawartość zestawu/ Conteúdo do kit/Conţinutul setului/ Компоненты набора/Kit innehåll/ Obsah súpravy/Vsebina kompleta/Sadržaj opreme/Kitin içindekiler

Biological risks/Биологическа опасност/Biologická rizika/Biologisk fare/Biologische Gefahren/Βιολογικοί κίνδυνοι/Riesgos biológicos/ Bioloogilised ohud/Risques biologiques/ Biološki rizici/Biológiai kockázatok/Rischi biologici/Biologinis pavojus/Bioloģiskais risks/Biologische risico's/Biologiske risikoer/Zagrożenie biologiczne/Riscos biológicos/ Biologisk risk/Pericole biologice/Биологическая опасность/ Biologicky rizikové/Biologické riziká/ Biološki rizici/Biyolojik riskler

ORIG | HUM

Human/С човешки произход/Lidské/ Humant/Human/Δείγματα αναφοράς/ Humano/Inimpäritolu/Humaine/Ljudskog porjekla/Humán/Origine Umana/ Žmogaus kilmės/Cilvēku izcelsmes/ Human/Menneske/Ludzka/Humano/ Origine umană/Человеческого происхождения/Human/Ľudské/ Humanega izvora/Ljudskog porekla/İnsan

ORIG | MOU

From mouse/С миши произход/Myší/ Fra mus/Maus/από ποντίκι/de ratón/ Hiirtelt/De souris/Mišijeg porjekla/ Egérből/Murino/Pelės kilmės/No peles/ Van muizen/Fra mus/Mysia/Do rato/De la şoareci/Мышиного происхождения/ Från mus/Myšie/Mišjega izvora/Mišijeg porekla/Fareden

ORIG | BOV

Bovine/С говежди произход/ Hovězí/Bovin/Rind/από βοοειδή/ Bovino/Veistelt/Bovine/Rogate stoke/ Szarvasmarha/Bovino/Jaučio/No liellopa/Bovien/Bovin/Wołowy/Bovino/ Origine bovină/крупного рогатого скота/Från ko/Hovädzie/Govejega izvora/Rogate krupne stoke/Bovin

Reconstitute with/Разтваряне с/ Rozřeďte pomocí/Rekonstitueres med/ Rekonstituieren mit/Ανασύσταση με/ Reconstituir con/Lahjendamine/ Reconstituer avec/Rekonstituirajte s/ Feloldáshoz/Ricostituire con/Atkurti, ištirpdant su/Atšķaidīt ar/Reconstitutie met/Rekonstitueres med/Odtworzyć za pomocą/Reconstituir com/A se reconstitui cu/Растворить в/ Rekonstituera med/Rozrieďte pomocou/ Rekonstituirajte z/s/Ponovno formiranje sa/Yeniden oluşturulur

Manufacturer/Производител/Výrobce/ Producent/Hersteller/Κατασκευαστής/ Fabricante/Tootja/Fabricant/Proizvođač/ Gyártó/Fabbricante/Gamintojas/ Ražotājs/Fabrikant/Produsent/ Producent/Fabricante/Producător/ Производитель/Tillverkare/ Výrobca/ Izdelovalec/Proizvođač/Üretici

INSTRUCTIONS FOR USE

EN

INSTRUCTIONS FOR USE

Please visit our website **www.fdi.com/ifu** to obtain the Instructions For Use (IFU) in additional languages.

To ensure that you download the correct IFU for your kit lot, please select the revision corresponding to the issue date printed on the front page of the IFU provided with this kit.

Please follow the IFU carefully. Instructions for safe handling are found in the WARNINGS AND PRECAUTIONS section. Material Safety Data Sheets (MSDS) are available on our website **www.fdi.com**. If you do not have access to the internet, please contact you local distributor, or Fujirebio Diagnostics AB for assistance.

CS

NÁVOD K POUŽITÍ

Návod k použití v dalších jazycích najdete na našich webových stránkách **www.fdi.com/ifu.**

Abyste se ujistili, že jste si stáhli správný návod k použití pro vaši šarži sady, vyberte revizi odpovídající datu vydání vytištěnému na přední straně návodu k použití dodanému s touto sadou.

Návod k použití pøesnì dodržujte. Pokyny pro bezpeènou manipulaci najdete v èásti VAROVÁNÍ A UPOZORNÌNÍ. Tabulky údajù o bezpeènosti materiálu (MSDS) najdete na stránkách **www.fdi.com**. Nemáte-li pøístup k Internetu, požádejte o pomoc místního distributora nebo spoleènost Fujirebio Diagnostics AB.

DA

BRUGSANVISNINGER

Gå ind på vores hjemmeside **www.fdi.com/ifu** for at hente brugsanvisninger på andre sprog.

For at sikre at du henter den rette brugsanvisning til det pågældende kitlot, skal du vælge det revisionsnummer, der svarer til den udgivelsesdato, der er trykt på forsiden af den brugsanvisning, der følger med kittet.

Følg brugsanvisningen omhyggeligt. Vejledning i sikker håndtering findes i afsnittet ADVARSLER OG FORSIGTIGHEDSREGLER. Sikkerhedsdataark (MSDS) kan hentes på vores hjemmeside **www.fdi.com/ifu**. Hvis du ikke har adgang til internettet, kan du kontakte den lokale distributør eller Fujirebio Diagnostics AB for assistance.

DE

GEBRAUCHSANWEISUNG

Auf unserer Website **www.fdi.com/ifu** finden Sie die Gebrauchsanweisung in weiteren Sprachen.

Um sicherzustellen, dass Sie die richtige Gebrauchsanweisung für Ihre Kit-Charge herunterladen, wählen Sie bitte die Version, die mit dem Veröffentlichungsdatum auf der Titelseite der mit diesem Kit mitgelieferten Gebrauchsanweisung übereinstimmt.

Halten Sie sich bitte genau an die Gebrauchsanweisung. Anweisungen für den sicheren Umgang finden Sie im Abschnitt „SICHERHEITSHINWEISE UND VORSICHTSMASSNAHMEN“. Die Materialsicherheitsdatenblätter (MSDS) finden Sie auf unserer Website **www.fdi.com**. Sollten Sie keinen Zugang zum Internet haben, so wenden Sie sich bitte an Ihren örtlichen Vertriebshändler oder an Fujirebio Diagnostics AB.

EL

ΟΔΗΓΙΕΣ ΧΡΗΣΗΣ

Για να λάβετε τις Οδηγίες χρήσης και σε άλλες γλώσσες, επισκεφθείτε την τοποθεσία μας στο web **www.fdi.com/ifu**.

Για να διασφαλίσετε ότι κάνετε λήψη των σωστών Οδηγιών χρήσης για την παρτίδα του κιτ σας, επιλέξτε την αναθεώρηση που αντιστοιχεί στην ημερομηνία έκδοσης που αναγράφεται στην μπροστινή σελίδα των Οδηγιών χρήσης αυτού του κιτ.

Ακολουθήστε τις Οδηγίες χρήσης με προσοχή. Μπορείτε να βρείτε οδηγίες για ασφαλή χειρισμό στην ενότητα ΠΡΟΕΙΔΟΠΟΙΗΣΕΙΣ ΚΑΙ ΠΡΟΦΥΛΑΞΕΙΣ. Στην τοποθεσία μας στο web **www.fdi.com** διατίθενται Φύλλα δεδομένων ασφαλείας υλικών (MSDS). Εάν δεν έχετε πρόσβαση στο internet, επικοινωνήστε με το διανομέα της περιοχής σας ή με την Fujirebio Diagnostics AB για βοήθεια.

ES

INSTRUCCIONES DE USO

Visite nuestro sitio web **www.fdi.com/ifu** para obtener instrucciones de uso (IFU) en otros idiomas.

Para asegurarse de que descarga las instrucciones de uso adecuadas a su lote de kits, seleccione el número de revisión que corresponda a la fecha de emisión impresa en la primera página de las instrucciones de uso suministradas con este kit.

Por favor, siga las instrucciones atentamente. Las instrucciones relativas a la seguridad en la manipulación figuran en el apartado ADVERTENCIAS Y PRECAUCIONES. Las fichas de seguridad de los materiales (MSDS) también están disponibles en nuestro sitio web: **www.fdi.com**. Si no tiene acceso a Internet, póngase en contacto con su distribuidor local o con Fujirebio Diagnostics AB para obtener ayuda.

ET

KASUTUSJUHEND

Erinevates keeltes kasutusjuhend on kättesaadav meie veebilehel **www.fdi.com/ifu**.

Komplekti partiile vastava kasutusjuhendi allalaadimise tagamiseks valige versioon, mis vastab komplektile lisatud kasutusjuhendi esilehel toodud väljaandmise kuupäevale.

Palun järgige kasutusjuhendit hoolikalt. Ohutusjuhised on toodud HOIATUSTE JA ETTEVAATUSABINÕUDE osas. Materjali ohutuskaardid on kättesaadavad meie veebilehel **www.fdi.com**. Kui Teil ei ole võimalik Internetti kasutada, pöörduge abi saamiseks kohaliku esindaja või Fujirebio Diagnostics AB poole.

FR

MODE D'EMPLOI

Visitez notre site Web, **www.fdi.com/ifu**, pour obtenir le mode d'emploi dans d'autres langues.

Pour être sûr que vous téléchargez le mode d'emploi correspondant à votre lot de kit, sélectionnez la version correspondant à la date de publication imprimée sur la première page du mode d'emploi joint à ce kit.

Veuillez suivre soigneusement les indications du mode d'emploi. Les instructions de manipulation sans risque se trouvent dans la section AVERTISSEMENTS ET PRÉCAUTIONS. Des fiches de données de sécurité (MSDS) sont disponibles sur notre site Web, **www.fdi.com**. Si vous n'avez pas accès à Internet, veuillez contacter votre distributeur local ou Fujirebio Diagnostics AB pour obtenir de l'aide.

HR

UPUTA ZA UPORABU

Molimo posjetite naše stranice **www.fdi.com/ifu** radi preuzimanja Upute za uporabu (IFU) na ostalim jezicima.

Da biste osigurali preuzimanje ispravnih IFU za vaš komplet, molimo odaberite reviziju koja odgovara datumu izdavanja otisnutim na prednjoj stranici IFU koje ste dobili s kompletom.

Molimo slijedite IFU pažljivo. Uputstva za sigurno rukovanje nalaze se u odjeljku UPOZORENJA I MJERE OPREZA. Sigurnosno-tehnički listovi (MSDS) su dostupni na našim stranicama **www.fdi.com**. Ako nemate pristup ineternetu, molimo da se obratite lokalnom distributeru ili Fujirebio Diagnostics AB za pomoć.

HU

HASZNÁLATI UTASÍTÁS

További nyelveken készült Használati utasítások találhat a **www.fdi.com/ifu** honlapon.

Annak biztosítása érdekében, hogy az Ön kit tételének megfelelő Használati utasítást töltse le, válassza a kithez mellékelt Használati utasítás első oldalán lévő kibocsátási dátumnak megfelelő módosítást.

Kérjük, tartsa be a Használati utasítás előírásait. A biztonságos kezelésre vonatkozó utasítások a FIGYELMEZTETÉSEK ÉS ÓVINTÉZKEDÉSEK című fejezetben találhatók. A Biztonsági adatlapok (MSDS) honlapunkon **(www.fdi.com)** elérhetőek. Amennyiben Ön nem rendelkezik internet hozzáféréssel, forduljon segítségért helyi értékesítőjéhez vagy a Fujirebio Diagnostics AB-hez.

IT

ISTRUZIONI PER L'USO

Istruzioni per l'uso in altre lingue sono disponibili sul nostro sito web **www.fdi.com/ifu.**

Per scaricare le Istruzioni per l'uso corrispondenti al lotto del proprio kit, selezionare la revisione corrispondente alla data di emissione stampata sulla prima pagina delle Istruzioni per l'uso fornite insieme al kit.

Seguire attentamente le Istruzioni per l'uso. Le istruzioni per una gestione sicura sono contenute nella sezione AVVERTENZE E PRECAUZIONI. Sul nostro sito web **www.fdi.com** sono disponibili le schede tecniche relative alla sicurezza dei materiali. Qualora fosse impossibile accedere a Internet, contattare il proprio distributore locale oppure rivolgersi a Fujirebio Diagnostics AB.

LT

NAUDOJIMO INSTRUKCIJOS

Kad gautumėte naudojimo instrukcijas kitomis kalbomis, apsilankykite mūsų tinklalapyje: **www.fdi.com/ifu.**

Kad atsisiųstumėte instrukcijas, kurios tikrai tinka Jūsų komplektui, pasirinkite peržiūros datą, kuri atitinka pagaminimo datą, atspausdintą su šiuo komplektu pateiktų instrukcijų viršelyje.

Atidžiai laikykitės instrukcijų. Saugaus naudojimo instrukcijos yra skyriuje PERSPĖJIMAI IR ATSARGUMO PRIEMONĖS. Medžiagų saugos duomenų lapus (MSDS) rasite mūsų tinklalapyje **www.fdi.com**. Jeigu neprieinate prie interneto, kreipkitės pagalvos į savo vietinį distribiutorių arba į„Fujirebio Diagnostics AB“.

LV

LIETOŠANAS INSTRUKCIJA

Lai iegūtu lietošanas instrukciju (LI) citās valodās, lūdzu, apmeklējiet mūsu vietni www.**fdi.com/ifu**.

Lai lejupielādētu pareizo LI savam komplektam, lūdzu, izvēlieties versiju, kas atbilst šim komplektam pievienotās LI pirmajā lappusē iespiestajam izdošanas datumam.

Lūdzu, rūpīgi iepazīstieties ar LI un ievērojiet to. Norādījumi drošai lietošanai sniegti sadaļā BRĪDINĀJUMI UN PIESARDZĪBAS PASĀKUMI. Materiālu drošības datu lapas (MDDL) ir pieejamas mūsu vietnē **www.fdi.com**. Ja jums nav pieejams internets, lūdzu, sazinieties ar vietējo izplatītāju vai Fujirebio Diagnostics AB, lai iegūtu palīdzību.

NL

INSTRUCTIES VOOR GEBRUIK

Ga naar onze website **www.fdi.com/ifu** voor de Instructies voor gebruik in andere talen.

Om ervoor te zorgen dat u de juiste Instructie voor gebruik downloadt voor uw setpartij, selecteert u de revisie die overeenkomt met de uitgavedatum die afgedrukt staat op de voorpagina van de Instructies voor gebruik die bij deze kit bijgeleverd zijn.

Volg de Instructie voor gebruik zorgvuldig op. U vindt de instructies voor een veilig hanteren in het gedeelte WAARSCHUWINGEN EN VOORZORGS-MAATREGELEN. Op onze website **www.fdi.com** zijn ook Veiligheidsinformatiebladen (MSDS) beschikbaar. Als u geen toegang hebt tot het internet, neemt u dan contact op met uw plaatselijke distributeur of met Fujirebio Diagnostics AB voor assistentie.

NO

BRUKSINSTRUKSER

Bruksinstrukser (IFU) på andre språk kan lastes ned fra vår hjemmeside **www.fdi.com/ifu**.

For å sikre at du laster ned den riktige IFU-en for ditt settparti, vennligst velg oppdateringen som svarer til utstedelsesdatoen på forsiden av IFU-en levert med settet ditt.

Vennligst følg IFU-instruksene nøye. Instrukser for sikker håndtering fins i avsnittet ADVARSLER OG FORHOLDSREGLER. Materialesikkerhetsdatasider (MSDS) kan lastes ned fra vår hjemmeside **www.fdi.com**. Dersom du ikke har adgang til internettet, vennligst kontakt din lokalforhandler eller Fujirebio Diagnostics AB for å få hjelp.

PL

INSTRUKCJA UŻYCIA

Instrukcje użycia (IFU) w innych językach znaleźć można na naszej stronie internetowej **www.fdi.com/ifu**.

Aby mieć pewność, że pobierasz instrukcję użycia właściwą dla partii zestawu, wybierz wersję odpowiadającą dacie wydania nadrukowanej na okładce IFU dostarczonej z zestawem.

Należy ściśle przestrzegać zaleceń zawartych w instrukcji użycia. Instrukcje dotyczące bezpiecznej pracy znaleźć można w części OSTRZEŻENIA I ŚRODKI OSTROŻNOŚCI. Karty charakterystyki substancji (MSDS) dostępne są na naszej stronie internetowej **www.fdi.com**. W przypadku braku dostępu do Internetu, pomoc można uzyskać u lokalnego dystrybutora lub w firmie Fujirebio Diagnostics AB.

PT

INSTRUÇÕES DE UTILIZAÇÃO

Visite o nosso sítio da Internet **www.fdi.com/ifu** para obter Instruções de Utilização (IDU) em idiomas adicionais.

Para assegurar que descarrega as IDU correctas para o lote do seu kit, seleccione a revisão correspondente à data de emissão impressa na capa das IDU fornecida com este kit.

Siga as IDU cuidadosamente. É possível encontrar instruções para um manuseamento seguro na secção ADVERTÊNCIAS E PRECAUÇÕES. As Fichas de Dados de Segurança do Material (FDSM) estão disponíveis em **www.fdi.com**. Se não tiver acesso à Internet, contacte o seu distribuidor local ou a Fujirebio Diagnostics AB para obter ajuda.

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INSTRUCŢIUNI DE UTILIZARE

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Urmaţi cu atenţie instrucţiunile de utilizare. Instrucţiunile pentru o manevrare în siguranţă se regăsesc în secţiunea AVERTISMENTE ŞI PRECAUŢII. Fişele de date despre siguranţa materialelor (Material Safety Data Sheets - MSDS) sunt disponibile pe site-ul nostru Web **www.fdi.com**. Dacă nu aveţi acces la Internet, contactaţi pentru asistenţă distribuitorul dvs. local sau Fujirebio Diagnostics AB.

SK

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Aby ste sa uistili, že ste prevzali správny návod na použitie pre danú šaržu súpravy, vyberte revíziu zodpovedajúcu dátumu vydania vytlačenému na prednej strane návodu na použitie dodanému s touto súpravou.

Návod na použitie presne dodržujte. Pokyny na bezpečnú manipuláciu nájdete v časti VÝSTRAHY A UPOZORNENIA. Tabuľky údajov o bezpečnosti materiálu (MSDS) nájdete na stránkach **www.fdi.com**. Ak nemáte prístup na internet, požiadajte o pomoc miestneho distribútora alebo spoločnosť Fujirebio Diagnostics AB.

SL

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Če želite zagotoviti, da ste prenesli ustrezna navodila za uporabo za vašo serijo kompleta, izberite različico, ki ustreza datumu izdaje, natisnjenemu na sprednji strani navodil za uporabo, priloženih temu kompletu.

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SR

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Da biste bili sigurni da ste skinuli odgovarajuće Uputstvo za upotrebu za Vaš set proizvoda, molimo Vas da odaberete odeljak koji odgovara datumu odštampanom na prednjoj strani Uputstva za upotrebu koje ste dobili uz proizvod.

Molimo Vas da pažljivo sledite uputstva data u Uputstvu za upotrebu. Uputstva za bezbedno korišćenje su data u odeljku pod naslovom UPOZORENJE I OPREZ. Informacije vezane za bezbedno korišćenje materijala su dostupne na sajtu **www.fdi.com**. Ako nemate pristup Internetu, molimo Vas da stupite u kontakt sa lokalnim distributerom ili se telefonom obratite Fujirebio Diagnostics službi za davanje informacija.

SV

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Säkerställ att du laddar ner rätt bruksanvisning för din kit lot genom att välja samma revisionsdatum som anges på framsidan av den bruksanvisning som medföljer denna förpackning.

Vänligen följ noga anvisningarna i bruksanvisningen. Instruktioner för säker användning finns i stycket VARNINGAR OCH FÖRSIKTIGHETSÅTGÄRDER. Säkerhetsdatablad (MSDS) finns att ladda ner från vår hemsida, **www.fdi.com**. Om du inte har tillgång till internet, vänligen kontakta din lokala distributör eller Fujirebio Diagnostics AB för att få hjälp.

KULLANIM TALIMATLARI

İlave dillerde Kullanım Talimatlarını (KT) almak için lütfen **www.fdi.com/ifu** adresindeki web sitemizi ziyaret edin.

Kit partiniz için doğru KT'nı indirdiğinizden emin olmak için lütfen bu kitle birlikte verilen KT'ının ön sayfasında yazılı düzenlenme tarihiyle eşleşen gözden geçirmeyi seçin.

Lütfen KT'nı dikkatli bir şekilde izleyin. Güvenli kullanımla ilgili talimatlar UYARILAR VE ÖNLEMLER bölümünde bulunmaktadır. Malzeme Güvenliği Veri Sayfaları (MGVS) **www.fdi.com** adresindeki web sitemizde bulunmaktadır. Internet erişiminiz bulunmuyorsa, destek için lütfen yerel distribütörünüz veya Fujirebio Diagnostics AB ile temasa geçin.

EN

HE4 EIA

Instructions for use

Enzyme immunometric assay kit
For 96 determinations

INTENDED USE

The HE4 EIA is an enzyme immunometric assay for the quantitative determination of HE4 in human serum. The assay is to be used as an aid in monitoring response to therapy for patients with invasive epithelial ovarian cancer. Serial testing for patient HE4 assay values should be used in conjunction with other clinical methods used for monitoring ovarian cancer.
It is further intended to be used in conjunction with either ARCHITECT CA 125 II or CanAg CA125 EIA or Lumipulse ***G*** CA125II as an aid in estimating the risk of epithelial ovarian cancer in premenopausal and postmenopausal women presenting with pelvic mass. The results must be interpreted in conjunction with other methods in accordance with standard clinical management guidelines.

SUMMARY AND EXPLANATION OF THE ASSAY

Human epididymis protein 4 (HE4) belongs to the family of whey acidic four-disulfide core (WFDC) proteins with suspected trypsin inhibitor properties. Other proteins in this family include SLPI, Elafin, and PS20 (WFDC1) (1, 2). The HE4 gene codes for a 13kD protein, although in its mature glycosylated form the protein is approximately 20-25 kD, and consists of a single peptide containing two WFDC domains (3). HE4 was first identified in the epithelium of the distal epididymis and originally predicted to be a protease inhibitor involved in sperm maturation (4, 5). HE4 has since been reported to be expressed in several normal tissues including epithelia of respiratory and reproductive tissues and also in ovarian cancer tissue (6-10). In addition to expression on a cellular level, secreted HE4 has been detected in high levels in the serum of ovarian cancer patients. In a case/control study comparing patients with ovarian cancer to healthy and benign conditions, Hellström et al. found that HE4 detected ovarian cancer with 67% sensitivity at a specificity level of 96% (11). In a subsequent study evaluating numerous known biomarkers for ovarian cancer, HE4 showed the highest sensitivity for the detection of ovarian cancer, particularly in early stage disease. In this study, the combination of HE4 and CA 125 was a more accurate predictor of malignancy than either marker alone, with a sensitivity of 76% and a specificity of 95% (12).
Ovarian cancer is the fourth most common cause of cancer-related death in women worldwide. In Europe, the mortality rate range is from 3.6 to 9.3 per 100.000 women

(13). The symptoms of ovarian cancer are related to the presence of adenxal masses and are often vague and unspecific. The primary goal of diagnostic evaluation of an adnexal mass is to determine whether it is benign or malignant. It is estimated that 5 to 10 percent of women in the United States will undergo a surgical procedure for a suspected ovarian neoplasm during their lifetime, and 13 to 21 percent of these women will be found to have an ovarian malignancy (14). The American College of Obstetricians and Gynecologists Practice Bulletin published in 2007 states the following "Women with ovarian cancer whose care is managed by physicians who have advanced training and expertise in the treatment of women with ovarian cancer, such as gynecologic oncologists, have improved overall survival rates compared with those treated without such collaboration." (15). Since the majority of adnexal masses are benign, it is important to determine preoperatively whether a patient is at high risk for ovarian malignancy, in order to ensure proper management (15). Since the initial report in 1988, clinical impression, serum CA125 and ultrasound along with CT scan, MRI and CT/PET have been the standards in the determination of whether an adnexal mass is suspicious for malignancy (16). Although the literature is replete with papers describing which modality is the more accurate, the combination of physical examination, CA125 and imaging affords the highest positive predictive value (17-19). To improve the triage of patients presenting with pelvic mass, the HE4 EIA may be used in conjunction with either the ARCHITECT CA 125 II or CanAg CA125 EIA or Lumipulse ***G*** CA125II assay as an aid in estimating the risk that the patient is harboring epithelial ovarian cancer. The results must be interpreted in conjunction with other methods in accordance with standard clinical management guidelines. An additional use of the HE4 EIA is as an aid in monitoring response to therapy for patients with invasive epithelial ovarian cancer. The results should be used in conjunction with other clinical methods used for monitoring ovarian cancer.

PRINCIPLE OF THE TEST

The HE4 EIA is a solid-phase, non-competitive immunoassay based upon the direct sandwich technique using two mouse monoclonal antibodies, 2H5 and 3D8, directed against two epitopes in the C-WFDC domain of HE4. Calibrators, controls and patient samples are incubated together with biotinylated Anti-HE4 monoclonal antibody (MAb) 2H5 in streptavidin coated microstrips. HE4 present in calibrators or samples is adsorbed to the streptavidin coated microstrips by the biotinylated Anti-HE4 MAb during the incubation. The strips are then washed and incubated with HRP labeled Anti-HE4 MAb 3D8. After washing, buffered Substrate/Chromogen reagent (hydrogen peroxide and 3, 3', 5, 5' tetra-methyl-benzidine) is added to each well and the enzyme reaction is allowed to proceed. During the enzyme reaction a blue color will develop if antigen is present. The intensity of the color is proportionate to the amount of HE4 present in the samples.

The color intensity is determined in a microplate spectrophotometer at 620 nm (or optionally at 405 nm after addition of Stop Solution). Calibration curves are constructed for each assay by plotting absorbance value versus the concentration for each calibrator. The HE4 concentrations of patient samples are then read from the calibration curve.

REAGENTS

- Each HE4 EIA kit contains reagents for 96 tests.
- The expiry date of the kit is stated on the label on the outside of the kit box.
- Do not use the kit beyond the expiry date.
- Do not mix reagents from different kit lots.
- Store the kit at 2–8° C. Do not freeze.
- Opened reagents are stable according to the table below provided they are not contaminated, stored in resealed original containers and handled as prescribed. Return to 2–8° C immediately after use.

Component	Quantity	Storage and stability after first use
MICROPLA		
Microplate	1 Plate	2–8° C until expiry date stated on the plate
12 x 8 breakable wells coated with streptavidin. After opening, immediately return unused strips to the aluminium pouch, containing desiccant. Reseal carefully to keep dry.		
CAL | HE4 | A		
HE4 Calibrator A	1 x 8 mL	2–8° C until expiry date stated on the vial
Phosphate buffered salt solution containing bovine serum albumin, an inert yellow dye, and a non-azide antimicrobial preservative. Ready for use. Should also be used for dilution of samples.		

Component	Quantity	Storage and stability after first use
HE4 Calibrators B-F	5 vials, lyophilized	Stability after reconstitution 4 weeks at 2-8° C 4 months at -20° C or below
CAL HE4 B	1 x 1 mL	
CAL HE4 C	1 x 1 mL	
CAL HE4 D	1 x 1 mL	
CAL HE4 E	1 x 1 mL	
CAL HE4 F	1 x 1 mL	

The lyophilized calibrators contain HE4 antigen in a phosphate buffered salt solution containing bovine serum albumin, an inert yellow dye, and a non-azide antimicrobial preservative. To be reconstituted with distilled or deionized water before use.
NOTE: The exact HE4 concentration is lot specific and is indicated on the label of each vial.

HE4 Controls	2 vials, lyophilized	Stability after reconstitution 4 weeks at 2-8° C 4 months at -20° C or below
CONTROL HE4 1	1 x 1 mL	
CONTROL HE4 2	1 x 1 mL	

The lyophilized controls contain HE4 antigen in a human serum matrix and a non-azide antimicrobial preservative. To be reconstituted with distilled or deionized water before use.

BIOTIN Anti-HE4		
Biotin Anti-HE4	1 x 15 mL	2–8° C until expiry date stated on the vial

Biotin Anti-HE4 monoclonal antibody from mouse, approximately 1 µg/mL. Contains phosphate buffered saline (pH 7.2), bovine serum albumin, blocking agents, detergent, an inert red dye, and a non-azide antimicrobial preservative. Ready for use.

Component	Quantity	Storage and stability after first use
CONJ | Anti-HE4		
Tracer, HRP Anti-HE4	1 x 0.75 mL	2–8° C until expiry date stated on the vial

Stock Solution of HRP Anti-HE4 monoclonal antibody from mouse, approximately 40 µg/mL. Contains non-azide antimicrobial preservatives. To be diluted with Tracer Diluent prior to use.

DIL | CONJ		
Tracer Diluent	1 x 15 mL	2–8° C until expiry date stated on the vial

Phosphate buffered saline (pH 7.2) with bovine serum albumin, blocking agents, detergents, an inert blue dye, and a non-azide antimicrobial preservative. Ready for use.

SUBS | TMB		
TMB HRP-Substrate	1 x 12 mL	2–8° C until expiry date stated on the vial

Contains buffered hydrogen peroxide and 3, 3', 5, 5' tetra-methylbenzidine (TMB). Ready for use.

STOP		
Stop Solution	1 x 15 mL	2–8° C until expiry date stated on the vial

Contains 0.12 M hydrochloric acid. Ready for use.

Component	Quantity	Storage and stability after first use
WASHBUF | **25X**		
Wash Concentrate	1 x 50 mL	2–8° C until expiry date stated on the bottle

A Tris-HCl buffered salt solution with Tween 20. Contains Germall II as preservative. To be diluted with distilled or deionized water 25 times before use.

Indications of instability

The TMB HRP-Substrate should be colorless or slightly bluish. A blue color indicates that the reagent has been contaminated and should be discarded.

WARNINGS AND PRECAUTIONS

For In Vitro Diagnostic Use:

- Follow the instructions in the Package insert. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.
- Handle all patient specimens as potentially infectious. It is recommended that human source reagent and human specimens be handled in accorance with the OSHA Standard on Bloodborne pathogens (20). Biosafety level 2 (21) or other appropriate biosafety practices should be used for material that contain or are suspected of containing infectious agents.
- Follow local guidelines for disposal of all waste material.

Caution

Material used in the preparation of human source reagent has been tested and found to be Non-Reactive for HIV 1 and 2 Antibody, HCV Antibody and Hepatitis B Surface Antigen (HBsAg). Since no method can completely rule out the presence of blood borne diseases, the handling and disposal of human source reagents from this product should be made as if they were potentially infectious.

SPECIMEN COLLECTION AND HANDLING

The HE4 EIA is intended for use with serum (including serum collected in separator tubes (SST)). Plasma and other body fluids have not been validated for use with the HE4 EIA. Collect blood by venipuncture and follow the tube manufacturer's processing instructions for collection tubes. When serial specimens are being evaluated, the same type of specimen should be used throughout the study.

Serum can be stored at 2–8° C for 3 days before being tested. For longer periods store samples at -40° C or colder.
Bring frozen samples to room temperature and mix THOROUGHLY by gently inverting multiple times before analysis. Samples that contain gross particulates should be centrifuged at 10.000 x g for 10 minutes prior to use to eliminate any particulate matter that may have developed from the thawing process.

PROCEDURE

Materials required but not supplied with the kit

1. **Microplate shaker**
   Shaking should be medium to vigorous, approximately 700-1100 oscillations/min.
2. **Microplate washer**
   Automatic plate washer capable of performing 1, 3 and 6 washing cycles, and with a minimal fill volume of 350 µL/well/washcycle.
   An 8-channel pipette with disposable plastic tips for delivery of 350 µL is recommended if an automatic microplate washer is not used.
3. **Microplate spectrophotometer**
   With a wavelength of 620 nm and/or 405 nm, and an absorbance range of 0 to 3.0.
4. **Precision pipettes**
   With disposable plastic tips for dispensing microliter volumes. An 8-channel pipette or dispenser pipette with disposable plastic tips for delivery of 100 µL is recommended but not required. Pipettes for dispensing milliliter volumes.
5. **Distilled or deionized water**
   For reconstitution of HE4 Calibrators, HE4 Controls and for preparation of diluted Wash Solution.

Procedural notes

1. A thorough understanding of this package insert is necessary to ensure proper use of the HE4 EIA kit. The reagents supplied with the kit are intended for use as an integral unit. Do not mix identical reagents from kits having different lot numbers. Do not use the kit reagents after the expiry date printed on the outside of the kit box.
2. Reagents should be allowed to reach room temperature (20–25° C) prior to use. Frozen specimens must be gently but thoroughly mixed after thawing. **The assay should only be performed at temperatures between 20–25° C to obtain accurate results.**

3. Before starting to pipette calibrators and patient specimens it is advisable to mark the strips to be able to clearly identify the samples during and after the assay.
4. The requirement for efficient and thorough washing for separation of bound and unbound antigen and reagents from the solid-phase bound antibody-antigen complexes is one of the most important steps in an EIA. **In order to ensure efficient washing make sure that <u>all</u> wells are completely filled to the top edge with wash solution during each wash cycle, that wash solution is dispensed at a good flow rate, that the aspiration of the wells between and after the wash cycles is complete and that the wells are empty. If there is liquid left, invert the plate and tap it carefully against absorbent paper.**

- Automatic strip washer: Follow the manufacturer's instructions for cleaning and maintenance diligently and wash the required number of wash cycles prior to and after each incubation step. The aspiration/wash device should not be left standing with the Wash Solution for long periods, as the needles may get clogged resulting in poor liquid delivery and aspiration.

5. The TMB HRP-Substrate is very sensitive to contamination. For optimal stability of the TMB HRP-Substrate, pour the required amount from the vial into a carefully cleaned reservoir or preferably a disposable plastic tray to avoid contamination of the reagent. Be sure to use clean disposable plastic pipette tips (or dispenser pipette tip).
6. Be sure to use clean disposable plastic pipette tips and a proper precision pipetting technique when handling samples and reagents. Do not allow the pipette tip to touch the surface of the liquid in order to avoid carry-over. A diligent pipetting technique is of particular importance when handling the samples and the TMB HRP-Substrate solution.

Preparation of reagents	Stability of prepared reagent
HE4 Calibrators B-F	4 weeks at 2–8° C 4 months at -20° C or below

Add exactly 1.0 mL of distilled or deionized water to each vial. Allow to stand for at least 15 minutes to reconstitute and mix gently before use. NOTE: The concentration of the calibrators is stated on the labels and should be used for calculation of results.

Preparation of reagents	Stability of prepared reagent
HE4 Controls 1 and 2	4 weeks at 2–8° C 4 months at -20° C or below

Add exactly 1.0 mL of distilled or deionized water to each vial and mix gently. Allow to stand for at least 15 minutes to reconstitute and mix gently before use. NOTE: The ranges of the controls are stated on the labels.

Wash Solution	2 weeks at 2–25° C in a sealed container

Pour the 50 mL Wash Concentrate into a clean container and dilute 25-fold by adding 1200 mL of distilled or deionized water to give a buffered Wash Solution.

Tracer Working Solution	4 weeks at 2–8° C in a sealed container

Prepare the required quantity of Tracer working solution by mixing 50 µL of Tracer, HRP Anti-HE4 with 1 mL of Tracer Diluent per strip (see table below):

No. of Strips	Tracer, HRP Anti-HE4 (µL)	Tracer Diluent (mL)
1	50	1
2	100	2
3	150	3
4	200	4
5	250	5
6	300	6
7	350	7
8	400	8
9	450	9
10	500	10
11	550	11
12	600	12

Be sure to use a clean plastic or glass tube for preparation of Tracer working solution.

Alternative: Pour the contents of the Tracer, HRP Anti-HE4 into the vial of Tracer Diluent and mix gently. Make sure that the entire content of the Tracer, HRP Anti-

Protocol Sheet

HE4 EIA REF 404-10

Prepare the components directly before use. Use wash and incubation conditions according to the Instructions.
Note. The assay should only be performed at temperatures between 20–25°C to obtain accurate results.

Step		Vial/Plate	Procedure
1.	Prepare HE4 Calibrators	CAL | HE4 B, C, D, E, F	Add 1 mL of distilled or deionised water to each vial and mix gently. Allow to stand for at least 15 minutes. NOTE: The exact concentration of each calibrator is stated on the label. Reconstituted stability: 4 weeks at 2-8°C.
	Prepare HE4 Controls	CONTROL | HE4 1, 2	
	Prepare Wash Solution	WASHBUF | 25X	Dilute 50 mL of Wash Concentrate with 1200 mL of distilled or deionised water.
	Prepare Tracer working solution	CONJ | Anti-HE4 DIL | CONJ	Mix 50 µL of Tracer, HRP Anti-HE4 with 1mL of Tracer Diluent per strip:

No. of Strips	Tracer, HRP Anti-HE4 (µL)	Tracer Diluent (mL)
1	50	1
2	100	2
3	150	3
4	200	4
5	250	5
6	300	6
7	350	7
8	400	8
9	450	9
10	500	10
11	550	11
12	600	12

			11 550 11 12 600 12
2.	Wash	MICROPLA	Wash each well once with Wash Solution. Use manual or automatic washer.
3.	Add calibrators, controls and samples	CAL HE4 A, B, C, D, E, F CONTROL HE4 1, 2	25 µL in each well
4.	Add Biotin Anti-HE4	BIOTIN Anti-HE4	100 µL in each well
5.	Incubate	MICROPLA	1 hour shaking at 20–25°C
6.	Wash	MICROPLA	Wash each well three times with Wash Solution Use manual or automatic washer.
7.	Add Tracer working solution	TRACER WORKING SOLUTION	100 µL in each well
8.	Incubate	MICROPLA	1 hour shaking at 20–25°C
9.	Wash	MICROPLA	Wash each well six times with Wash Solution. Use manual or automatic washer.
10.	Add TMB HRP-Substrate	SUBS TMB	100 µL in each well
11.	Incubate	MICROPLA	30 min shaking at 20–25°C
12.	Read absorbance	MICROPLA	620 nm
Alt.12	Add Stop Solution	STOP	100 µL in each well
Alt.13	Mix	MICROPLA	Allow to mix at 20–25°C
Alt.14	Read absorbance	MICROPLA	Read at 405 nm within 15 min

HE4 vial is transferred to the vial of Tracer Diluent.
NOTE: The Tracer working solution is stable for 4 weeks at 2–8° C. Do not prepare more Tracer working solution than will be used within this period and make sure that it is stored properly.

ASSAY PROCEDURE

Perform each determination in duplicate for both calibrators, controls and unknown specimens. A calibration curve should be run with each assay. All reagents and specimens must be brought to room temperature (20–25° C) before use.

1. Start preparing Calibrators B-F, Controls 1 and 2, Wash Solution and Tracer working solution. It is important to use clean containers. Follow the instructions carefully.
2. Transfer the required number of microplate strips to a strip frame. (Immediately return the remaining strips to the aluminum pouch containing desiccant and reseal carefully). Wash each strip once with the Wash Solution. Do not wash more strips than can be handled within 30 min.
3. Pipette 25 µL of each of the HE4 Calibrators (CAL A, B, C, D, E and F), HE4 Controls (C1, C2) and unknown specimens (Unk) into the strip wells according to the following scheme:

	1	2	3	4	5	6	7 etc
A	Cal A	Cal E	1 st Unk				
B	Cal A	Cal E	1 st Unk				
C	Cal B	Cal F	2nd Unk				
D	Cal B	Cal F	2nd Unk				
E	Cal C	C1					
F	Cal C	C1					
G	Cal D	C2					
H	Cal D	C2					

4. Add 100 µL of Biotin Anti-HE4 to each well using a 100 µL precision pipette (or an 8-channel 100 µL precision pipette). Do not allow the pipette tip to touch the surface of the liquid in order to avoid carry-over.

5. Incubate the plate for 1 hour (± 10 min) at room temperature (20-25° C), constantly shaking the plate using a microplate shaker.
6. After the first incubation aspirate and wash each strip 3 times using the wash procedure described in Procedural notes, item 4.
7. Add 100 µL of Tracer working solution to each well. Use the same pipetting procedure as in item 4 above.
8. Incubate the frame for 1 hour (± 5 min) at room temperature (20–25° C) with constant shaking.
9. After the second incubation aspirate and wash each strip 6 times, using the wash procedure described in Procedural notes, item 4.
10. Add 100 µL of TMB HRP-Substrate to each well using the same pipetting technique as described in item 4 above.
    The TMB HRP-Substrate should be added to the wells as quickly as possible and the time between addition to the first and last well should not exceed 5 min.
11. Incubate for 30 min (± 5 min) at room temperature (20–25° C) with constant shaking. Avoid exposure to direct sunlight.
12. Immediately read the absorbance at 620 nm in a microplate spectrophotometer.

Option

If the laboratory does not have access to a microplate reader capable of reading at 620 nm, the absorbance can be determined as described in the alternative item 12 below:

Alt. 12. Add 100 µL of Stop Solution, mix and read the absorbance at 405 nm in a microplate spectrophotometer within 15 min after addition of Stop Solution.

Measurement range

The HE4 EIA measures concentrations between 15 and 900 pM. If HE4 concentrations above the measuring range are expected, it is recommended that samples be diluted with HE4 Calibrator A prior to analysis (see “Calculation of results with diluted samples”).

Quality control

HE4 Control 1 and 2 should be used for validation of each assay series. Ranges of expected results are indicated on the vial labels.

The HE4 assay results should be considered valid if:

- The mean values of control duplicates are within the specified ranges.
- The duplicate replicates of calibrators B-F and controls do not exceed a CV of 15%.
- The duplicate replicates of calibrator A (zero) are not more than 0.06 OD units different from each other.

If an assay results in invalid calibrator or control results, a complete check of reagents, accuracy of pipettes, plate washer and reader performance should be made and the analysis repeated. Each laboratory may also prepare its own serum pools at different levels, which can be used as internal controls in order to assure the precision of the assay.

Reference material

Since no common reference material is available for HE4 antigen, HE4 EIA Calibrator values are assigned against a set of in-house reference standards.

CALCULATION OF RESULTS

If a microplate spectrophotometer with built-in data calculation program is used, refer to the manual for the spectrophotometer and create a program using the concentration stated on the label of each of the HE4 Calibrators.
For automatic calculation of HE4 results it is recommended to use either of the following methods:

- Cubic spline curve fit method. Calibrator A should be included in the curve with the value 0 pM.
- Interpolation with point-to-point evaluation. Calibrator A should be included in the curve with the value 0 pM.
- Quadratic curve fit method. Calibrator A should be included in the curve with the value 0 pM.

NOTE: 4-parametric or Linear regression evaluation methods should not be used.
For manual evaluation, a calibration curve is constructed by plotting the absorbance (A) values obtained for each HE4 Calibrator against the corresponding HE4 concentration (in pM).
The unknown HE4 concentrations can then be read from the calibration curve using the mean absorbance value of each patient specimen.

Calculation of results with diluted samples

If samples in an initial analysis give HE4 levels higher than 900 pM the samples should be diluted 1/10 and 1/100 with HE4 Calibrator A to obtain the accurate HE4 concentration of the samples.

- 1/10 dilution = 50 µL of specimen + 450 µL of HE4 Calibrator A
- 1/100 dilution = 50 µL of 1/10 dilution + 450 µL of HE4 Calibrator A

The HE4 concentration of the undiluted sample is then calculated as:

- Dilution 1/10: 10 x measured value
- Dilution 1/100: 100 x measured value

Calculation of ROMA value

The risk of Ovarian Malignancy Algorithm (ROMA) i a serum test that combines the results of HE4, CA125 and menopausal status into a ROMA value.

Calculation of Predictive Index

A Predictive Index (PI) is calculated for premenopausal and postmenopausal women separately using the equations (1) and (2) below. To calculate the PI, the assay values obtained from the HE4 EIA and either the ARCHITECT CA 125 II or CanAg CA125 EIA or Lumipulse ***G*** CA125II assays, respectively, are inserted into the applicable equation of the algorithm below, depending on the menopausal status of the woman.

(1) Premenopausal woman

Predictive Index (PI) = -12.0 + 2.38*LN[HE4] + 0.0626*LN[CA125]

(2) Postmenopausal woman

Predictive Index (PI) = -8.09 + 1.04*LN[HE4] + 0.732*LN[CA125]

Calculation of ROMA value

To calculate the ROMA value (i.e. Predictive Probability), insert the calculated value for Predictive Index into equation (3):

(3) ROMA value (%) = exp(PI) / [1 + exp(PI)] *100

The examples below can be used in order to validate calculations of PI and ROMA value:

Menopausal status	**HE4 (pM)**	**CA125 (U/ mL)**	**PI calculation**	**PI**	**ROMA (%)**
Pre-menopausal	37.5	74.9	-12.0+(2.38*3.624) +(0.0626*4.316)	-3.10388	4.29
Pre-menopausal	386.6	21.8	-12.0+(2.38*5.957) +(0.0626*3.082)	2.371517	91.5
Post-menopausal	66.7	11.3	-8.09+(1.04*4.200) +(0.732*2.425)	-1.94683	12.5
Post-menopausal	383.1	22.7	-8.09+(1.04*5.948) +(0.732*3.122)	0.381799	59.4

LIMITATIONS OF THE PROCEDURE

Patients with confirmed ovarian cancer may have HE4 assay values in the same range as healthy women. Certain histological types of ovarian cancer e.g. mucinous or germ cell tumors, rarely express HE4, therefore HE4 is not recommended for monitoring of patients with known mucinous or germ cell ovarian cancer (7). Conversely, elevated levels of HE4 antigen may be present in individuals with non-malignant disease. Therefore, the level of HE4 cannot be used as absolute evidence for the presence or absence of malignant disease and the HE4 test should not be used in cancer screening. The results of the test should be interpreted only in conjunction with other investigations and procedures in the diagnosis of disease and the management of patients, and the HE4 test should not replace any established clinical examination.

The risk of ovarian malignancy algorithm has not been validated for the following patient groups: patients previously treated for malignancy, patients currently being treated with chemotherapy and patients < 18 years of age. The form of the mathematical function referred to as the Risk of Ovarian Malignancy Algorithm (ROMA), depends on the premenopausal or postmenopausal status of a woman. The premenopausal or postmenopausal status must be based on ovarian function determined with information available from clinical evaluation and medical history. The ROMA value does not include age, family history, clinical findings, or imaging results and should be interpreted in conjunction with these parameters.

Failure of the HE4 EIA and/or the CA125 assay to perform as indicated, or error in the calculation of results could lead to inaccurate risk assessment and improper management of the patient. Specifically, a falsely low result of the assay(s) could result in a determination that the patient is at lower risk of having epithelial ovarian cancer, which could triage the patient to a less specialized level of care.

Use of the assay results without consideration of the other laboratory findings, imaging studies, and clinical assessment could therefore pose a risk.

Anti-reagent antibodies (human anti-mouse antibody (HAMA) or heterophilic antibodies) in the patient sample may occasionally interfere with the assay, even though specific blocking agents are included in the buffers.

Biotin may interfere with the assay giving false low results. This should be taken into consideration for patients taking dietary supplements or receiving therapy containing high (> 5mg/day) or extremely high (300 mg/day) biotin doses. Peak serum levels have been reported to occur 1-3h post ingestion and a physiological half-life of 8-16h depending on renal function (26,27). In a study by Grimsey et al. (26) a specimen concentration of 30 ng/mL was reached 8h following intake of 10 mg of biotin. For patients on very high doses of biotin it is recommended to stop taking biotin for at least 2 days before blood draw (28).

The assay must be performed in a temperature controlled environment since incubation at temperatures above the recommended temperature range 20 - 25° C may give false low results.

EXPECTED VALUES

The distribution of HE4 levels determined in 1983 specimens is shown in the tables below:

Distribution of HE4 Assay Values

	Number of subjects	0.0 - 150.0 pM	150.1 - 300.0 pM	300.1 - 500.0 pM	>= 500.1 pM
APPARENTLY HEALTHY					
Females (Premenopausal)	*423*	416 (98%)	4 (0.9%)	0 (0.0%)	3 (0.7%)
Females (Postmenopausal)	*443*	424 (96%)	16 (3.6%)	2 (0.5%)	1 (0.2%)
BENIGN CONDITIONS					
Pregnancy	*22*	21 (95%)	1 (4.5%)	0 (0.0%)	0 (0.0%)
Benign Gynecological Disease	*347*	324 (93%)	18 (5.2%)	1 (0.3%)	4 (1.2%)
Other Benign Disease	*107*	81 (76%)	8 (7.5%)	7 (6.5%)	11 (10%)
Hypertension/Cong. Heart Failure	*96*	75 (78%)	16 (17%)	2 (2.1%)	3 (3.1%)
CANCER					
Ovarian Cancer	*127*	27 (21%)	18 (14%)	21 (16%)	61 (48%)
Breast Cancer	*46*	40 (87%)	4 (8.7%)	2 (4.3%)	0 (0.0%)
Lung Cancer	*50*	28 (56%)	16 (32%)	6 (12%)	0 (0.0%)
Endometrial Cancer	*266*	203 (76%)	36 (14%)	11 (4.1%)	16 (6.0%)
Gastrointestinal Cancer	*56*	47 (84%)	8 (14%)	0 (0.0%)	1 (1.8%)

HE4 Assay levels distributed by age for apparently healthy subjects

Age (Years)	N	HE Result (pM)	
		Median	95th Percentile
< 40	316	47.6	81.6
40–49	110	48.2	110.6
50–59	179	52.5	104.4
60–69	208	60.7	113.0
≥70	53	91.1	233.3

In this study 98% of the premenopausal healthy women had a HE4 EIA value <150 pM and 96% of the postmenopausal healthy women had a HE4 EIA value <150 pM. It is recommended that each laboratory establish its own reference value for the population of interest.

Monitoring of Disease status in Patients Diagnosed with Ovarian Cancer

The effectiveness of the HE4 EIA as an aid in monitoring of disease status in ovarian cancer patients was determined by assessing changes in HE4 levels in serial serum samples from 80 patients compared to changes in disease status. A study involving a total of 354 pairs of observations was undertaken with an average number of 4.4 observations per patient. A positive change in HE4 was defined as an increase in the value that was at least 25% greater than the previous value of the test. This level of change takes into account the variability of the assay and the biological variability. Sixty percent (60%) or 76/126 of the patient samples with a positive change correlated with the disease progression while seventy-five percent (75%) or 171/228 of the patient serial samples with no significant change in HE4 value correlated with no progression. The total concordance was seventy percent (70% or 247/354). The following table presents the data in a 2 x 2 format.

Change in Disease State per Sequential Pair			
Increase in HE-4 concentration	Progression	No Progression	Total
>25%	76	57	133
≤ 25%	50	171	221
Total	126	228	354

The following table shows the distribution per patient. Ninety-three percent (93%) or 54/58 of the per patient serum sets with a positive change correlated with the disease progression while Thirty-two percent (32%) or 7/22 of serum sets showing no significant change in HE4 value correlated with no progression. The total concordance in this study was seventy-six percent (76 %) or 61/80.

Change in Disease State per Patient			
Increase in HE-4 concentration	**Progression**	**No Progression**	**Total**
>25%	54	15	69
≤ 25%	4	7	11
Total	58	22	80

Risk estimation in patients presenting with pelvic mass

The effectiveness of HE4 EIA in combination with CA125 determined either with the ARCHITECT CA 125 II or CanAg CA125 EIA or Lumipulse ***G*** CA125II assay for risk estimation for epithelial ovarian cancer of patients presenting with pelvic mass was determined in a prospective, multi-center, double blind clinical trial. An algorithm (ROMA, see page 17) was developed for estimation of the risk of epithelial ovarian cancer. The algorithm takes into account the HE4 and CA125 values as well as the menopausal status of the patient. The algorithm calculates a predictive probability of finding epithelial ovarian cancer on surgery. In the prospective study a total of 502 patients were included and the predictive probability for ovarian cancer as well as the ability for separation into a low and a high risk group based on ROMA values was determined.

The cumulative frequency distribution of the ROMA values for benign and ovarian cancer cases including tumors of low malignant potential (LMP) respectively using the algorithm is shown in Figures 1 and 2 for the HE4 EIA + ARCHITECT CA125 II assay combination and in Figures 3 and 4 for the HE4 EIA + CanAg CA125 EIA combination. The HE4 EIA + Lumipulse ***G*** CA125II assay combination showed a very similar frequency distribution as the HE4 EIA + ARCHITECT CA125 II assay combination. The frequency distribution graphs illustrate the distribution of patients with benign disease and epithelial ovarian cancer (including LMP) respectively at different ROMA value cut-points.

Fig. 1 Cumulative frequency distribution of ROMA values for **premenopausal** women. HE4 EIA + **ARCHITECT CA125 II** assay combination

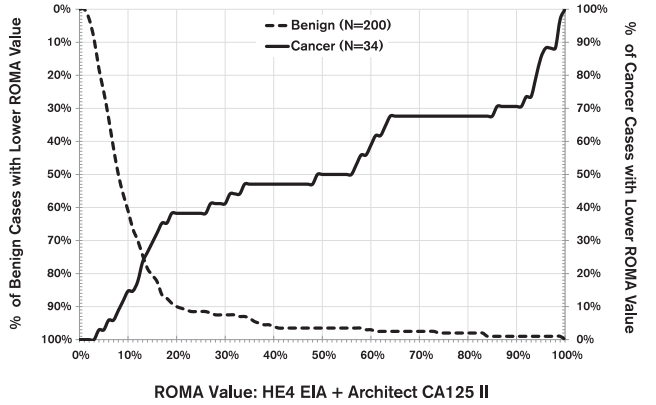


Fig. 2 Cumulative frequency distribution of ROMA values for **postmenopausal** women. HE4 EIA + **ARCHITECT CA125 II** assay combination

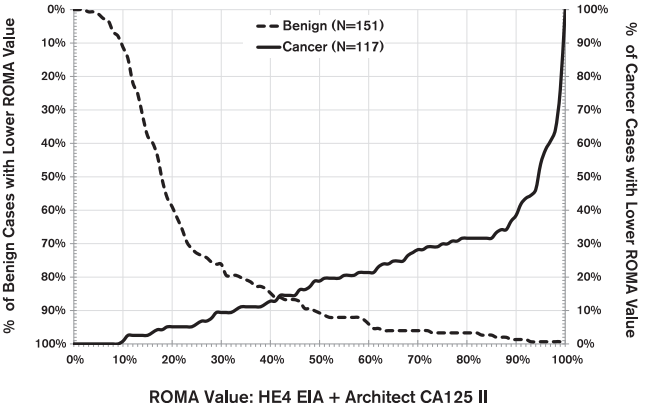


Fig. 3 Cumulative frequency distribution of ROMA values for **premenopausal** women. HE4 EIA + **CanAg CA125 EIA** combination

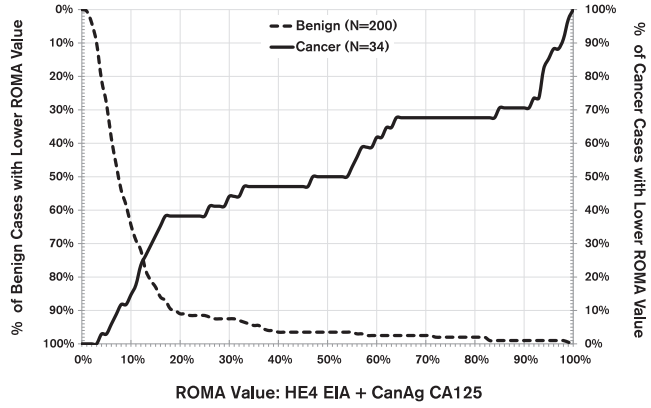
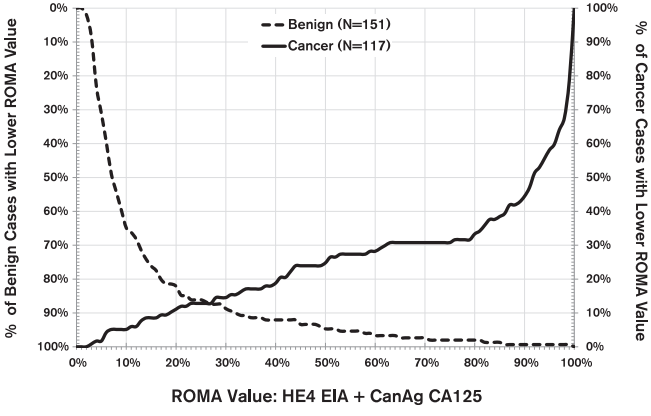


Fig. 4 Cumulative frequency distribution of ROMA values for **postmenopausal** women. HE4 EIA + **CanAg CA125 EIA** combination



Stratification into low risk and high risk groups

The risk of ovarian malignancy algorithm was used to stratify women into risk groups for finding epithelial ovarian cancer. The following cut-points were used in order to provide a specificity level of 75%.

It should be noted that different cut-points for risk stratification into high and low risk groups must be selected based upon which CA125 assay is used.

Cut-points to provide a specificity level of 75%, for the **HE4 EIA + ARCHITECT CA125II** assay combination:

Premenopausal women

ROMA value $\geq$ 13.1% = High risk of finding epithelial ovarian cancer
ROMA value $<$ 13.1% = Low risk of finding epithelial ovarian cancer

Postmenopausal women

ROMA value $\geq$ 27.7% = High risk of finding epithelial ovarian cancer
ROMA value $<$ 27.7% = Low risk of finding epithelial ovarian cancer

Cut-points to provide a specificity level of 75%, for the **HE4 EIA + CanAg CA125** assay combination:

Premenopausal women

ROMA value $\geq$ 12.5% = High risk of finding epithelial ovarian cancer
ROMA value $<$ 12.5% = Low risk of finding epithelial ovarian cancer

Postmenopausal women

ROMA value $\geq$ 14.4% = High risk of finding epithelial ovarian cancer
ROMA value $<$ 14.4% = Low risk of finding epithelial ovarian cancer

Cut-points to provide a specificity level of 75%, for the **HE4 EIA + Lumipulse *G* CA125II** assay combination:

Premenopausal women

ROMA value $\geq$ 13.1% = High risk of finding epithelial ovarian cancer
ROMA value $<$ 13.1% = Low risk of finding epithelial ovarian cancer

Postmenopausal women

ROMA value $\geq$ 27.7% = High risk of finding epithelial ovarian cancer
ROMA value $<$ 27.7% = Low risk of finding epithelial ovarian cancer

The risk stratification into high risk of harboring epithelial ovarian cancer of all patients presenting with adnexal mass using the ROMA values at 75% specificity level is shown in Table 1 including the risk stratification obtained for the separate premenopausal and postmenopausal patient groups respectively. The sensitivity for stratifying patients with epithelial ovarian cancer stage I-IV into the high risk group was 94% and the specificity was 75%, such that 75% of women with benign pelvic mass were classified into the low risk group. The positive and negative predictive values were 58 % and 97% respectively.

Table 1: Risk stratification into high risk of harboring Epithelial Ovarian Cancer (EOC) in patients presenting with adnexal mass using the HE4 EIA + **ARCHITECT CA125 II** assay combination to calculate ROMA value.
Premenopausal cut-point for stratification into high risk group at 75% specificity level $\geq$ 13.1%,
Postmenopausal cut-point for stratification into high risk group at 75% specificity level $\geq$ 27.7%.

	Premenopausal Women n = 234	**Postmenopausal Women n = 268**	**Pre- & Postmenopausal Women Combined n = 502**
Stage I – IV EOC & LMP combined	26/34 (76%)	108/117 (92%)	134/151 (89%)
Low Malignant Potential	10/16 (63%)	3/6 (50%)	13/22 (59%)
Stage I-II EOC	6/7 (86%)	24/28 (86%)	30/35 (86%)
Stage I – IIIC[a] EOC	7/8 (88%)	35/39 (90%)	42/47 (89%)
Stage I – IV EOC	16/18 (89%)	105/111 (95%)	121/129 (94%)

[a]Stage I – IIIb & Stage IIIC (Omentum negative, lymphnode positive) Epithelial Ovarian Cancer

The False Negative Rates and percentage of epithelial ovarian cancer stratified into low risk of harboring epithelial ovarian cancer in patients presenting with adnexal mass using the ROMA value at 75% specificity level is shown in Table 2. Stratification into low and high risk group of harboring epithelial ovarian cancer using the ROMA algorithm at 75% specificity level resulted in an overall False Negative Rate of 6.2%. Three (3) percent of all cases stratified into the low risk group represented epithelial ovarian cancer.

Table 2: False Negative Rate (FNR) and percentage of Epithelial Ovarian Cancers for all cases stratified into low risk group in patients presenting with adnexal mass using the ROMA value.
Premenopausal cut-point for stratification into low risk group at 75% specificity level < 13.1%, postmenopausal cut-point for stratification into low risk group at 75% specificity level < 27.7%.

Epithelial Ovarian Cancer[a]	False Negative Rate (FNR)			Percentage of cancers in Low Risk Group		
	False Negative Cancers	Total Cancers	FNR[b]	False Negative Cancers	True Positive Benign	% [c]
Premenopausal	2	18	11.1%	2	149	1.3%
Postmenopausal	6	111	5.4%	6	113	5.0%
All patients	8	129	6.2%	8	262	3.0%

[a] Tumors of Low Malignant Potential (LMP) not included; [b] FNR = False Negative/(True Positive + False Negative); [c] False Negative/(True Negative + False Negative)

There were no statistically significant differences in the sensitivity and specificity of the ROMA value using ARCHITECT CA125 II, CanAg CA125 EIA or Lumipulse ***G*** CA125II values to differentiate between benign diseases and epithelial ovarian cancer. Using the CanAg CA125 EIA + HE4 EIA assay combination, the sensitivity for stratifying patients with epithelial ovarian cancer stage I-IV into the high risk group was 93%. The positive and negative predictive values were 57 % and 97% respectively. Using the Lumipulse ***G*** 125II + HE4 EIA assay combination, the sensitivity for stratifying patients with epithelial ovarian cancer stage I-IV into the high risk group was 93%. The positive and negative predictive values were 58 % and 97% respectively.

PERFORMANCE CHARACTERISTICS

Precision

The HE4 assay precision is ≤ 15% total CV. A study was performed as described per the National Committee for Clinical Laboratory Standards NCCLS (CLSI) guideline EP5-A2 (22). A panel of four serum samples was assayed, using two lots of reagents, in replicates of two, at two separate times per day for 20 days. Data from this study is summarized below.*

Sample	Reagent lot	n	Mean conc. (pM)	Within-run SD (pM)	Within-run CV %	Total SD (pM)	Total CV %
1	1	80	50.3	0.81	1.6	2.34	4.7
	2	80	48.0	0.69	1.4	2.17	4.5
2	1	80	75.3	1.81	2.4	2.96	3.9
	2	80	72.4	1.73	2.4	4.70	6.5
3	1	80	255	5.68	2.2	12.0	4.7
	2	80	242	5.21	2.2	12.8	5.3
4	1	80	407	6.22	1.5	14.5	3.6
	2	80	385	8.71	2.3	21.6	5.6

*Representative data; results in individual laboratories may vary from these data.

Detection limit

The limit of detection of the HE4 EIA assay is $\leq$ 15 pM. The limit of detection (LoD) corresponds to the upper limit of the 95% confidence interval and represents the lowest concentration of HE4 antigen that can be distinguished from zero. The NCCLS guideline EP17-A (23) was used to design the LoD experiments. A study was conducted where HE4 Calibrator A (zero) and 4 samples from healthy subjects diluted to 5 pM with Sample Diluent was tested in replicates of 24 per run in 4 runs on two separate days. The LoD was calculated as follows:
LoD (pM) = 5.0 pM x (1.65 x SD_0 + 1.65 x SD_5) / (OD_5 - OD_0)
The Limit of Detection of the HE4 EIA Kit was calculated to be $<$ 2.5 pM.

Functional sensitivity

The functional sensitivity of the HE4 EIA assay is $\leq$ 25 pM. The functional sensitivity is expressed as the concentration of an analyte at which the CV is 20%. The NCCLS guideline EP5-A2 (22) was used to design the experiments for determination of functional sensitivity. A study was conducted where a five member sensitivity panel was tested in replicates of 4 in 2 runs on twenty separate days with two lots of reagents. The functional sensitivity determined for the HE4 EIA was found to be $<$ 5 pM.

Recovery

The HE4 EIA assay mean recovery is 100 ± 15%. A study was performed where dilutions of a patient sample with known concentrations of HE4 were added to normal human serum samples. The concentration of HE4 was determined using the HE4 EIA assay and the resulting percent recovery was calculated. Representative data from this study is summarized in the table below*.

Sample	Endogenous Assay Value (pM)	HE4 Antigen Added (pM)	Observed HE4 Assay Value (pM)	Percent Recovery** %
1	44.6	15	60.6	102
		75	96.0	89
		350	397	96
		650	686	96
2	41.1	15	55.7	99
		75	95.2	91
		350	400	98
		650	657	93
3	40.6	15	54.0	97
		75	95.1	91
		350	403	99
		650	680	96
4	46.6	15	63.3	103
		75	106	97
		350	410	99
		650	645	90
5	40.2	15	56.5	102
		75	102	98
		350	402	99
		650	676	96

The average recovery across the four separate spiked concentrations shown above was found to be 97%.

*Representative data; results in individual laboratories may vary from these data.

**% Recovery=Observed HE4 Concentration (pM)/Endogenous HE4 Conc. (pM) + HE4 Added (pM)

High Dose Hook

High dose hook is a phenomenon whereby very high level specimens may read within the dynamic range of the assay. For the HE4 EIA, no high dose hook effect was observed for samples containing up to 300 000 pM HE4 native antigen.

Dilution Linearity

The HE4 EIA assay mean dilution linearity is 100 ± 15%. A study was conducted for the HE4 EIA modeled after the NCCLS (CLSI) guideline EP6-A (24). Serum samples with elevated HE4 values were diluted with HE4 Calibrator A (zero). The HE4 concentration was determined for each dilution and the percent (%) recovery was calculated. Representative data from this study is summarized in the table below*.

Sample	Final Dilution Factor	Obtained Value (pM)	Expected Value (pM)	Percent Recovery** (%)
1	Undiluted	889.6	889.6	100
	1:1.25	720.0	711.7	101
	1:1.7	543.1	533.8	101
	1:2	450.6	444.8	101
	1:2.5	345.9	355.8	97.2
	1:5	183.6	177.9	103
	1:10	97.6	89.0	109
	1:20	49.1	44.5	110
	1:40	25.9	22.2	116
2	Undiluted	697.0	697.0	100
	1:1.25	544.9	557.6	97.7
	1:1.7	429.8	418.2	103
	1:2	361.1	348.5	104
	1:2.5	275.9	278.8	99.0
	1:5	134.5	139.4	96.5
	1:10	74.4	69.7	107
	1:20	39.1	34.9	112
	1:40	21.0	17.4	120
3	Undiluted	680.2	680.2	100
	1:1.25	499.7	544.2	91.8
	1:1.7	354.4	408.1	86.8
	1:2	296.7	340.1	87.2
	1:2.5	247.2	272.1	90.9
	1:5	124.9	136.0	91.8
	1:10	61.7	68.0	90.7
	1:20	34.6	34.0	102
	1:40	18.4	17.0	109

Average recovery across the three diluted samples shown above = 101%

*Representative data; results in individual laboratories may vary from these data.

**% Recovery= HE4 Concentration obtained x Dilution factor/Undiluted HE4 Concentration.

Analytical Specificity

The HE4 EIA assay mean assay specificity is 100 ± 15%. Recovery studies were performed to compare sera containing the following compounds at the indicated concentrations with control sera. The NCCLS guideline EP7-A (25) was used to design the interference experiments. The following substances and concentrations were tested and found not to interfere with the test.

Endogenous serum interferences	Test Concentration
Triglycerides	30 mg/mL
Billirubin	0.2 mg/mL
Hemoglobin	10 mg/mL
Total Protein	120 mg/mL

Chemotherapeutic drug interferences	Test Concentration
Carboplatin	500 µg/mL
Cisplatin	165 µg/mL
Clotrimazole	0.3 µg/mL
Cyclophosphamide	500 µg/mL
Dexamethasone	10 µg/mL
Doxorubicin	1.16 µg/mL
Leucovorin	2.68 µg/mL
Melphalan	2.8 µg/mL
Methotrexate	45 µg/mL
Paclitaxel	3.5 ng/mL

Biotin interference

A study was conducted to evaluate biotin interference. Low and high serum control samples were spiked to final biotin concentrations of 15, 30, 60, and 600 ng/mL. The mean HE4 concentration was determined for each sample and the percent recovery for each biotin concentration was calculated using the formula: Recovery (%) =100x (Mean HE4 concentration w. biotin added/Mean HE4 concentration w. diluent only added).

HE4 analyte level	Biotin test conc. (ng/mL)	Expected HE4 conc. (pM)	Observed HE4 conc. (pM)	Recovery (%)
Low	15	80,6	77,0	96
High	15	558	537	96
Low	30	81,5	77,3	95
High	30	554	514	93
Low	60	73,3	66,1	90
High	60	548	473	86
Low	600	73,0	7,30	10

Based on linear regression analysis, the lowest concentration of biotin found to influence test results (≥10%) was 53 ng/mL.

Potentially interfering clinical conditions

The HE4 EIA assay was evaluated using specimens with HAMA and Rheumatoid Factor (RF) to further assess the assay specificity. Five specimens positive for HAMA and five specimens positive for RF were evaluated for % recovery with HE4 antigen spiked into each specimen at approximately 50 and 450 pM. Mean recovery results are summarized in the following table.*

Clinical condition	Number of specimens	Mean % recovery
HAMA	5	101
RF	5	95

*Representative data; results in individual laboratories may vary from these data.

WARRANTY

The performance data presented here were obtained using the assay procedure indicated. Any change or modification of the procedure not recommended by Fujirebio Diagnostics may affect the results, in which event Fujirebio Diagnostics disclaims all warranties expressed, implied or statutory including the implied warranty of merchantability and fitness for use.

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