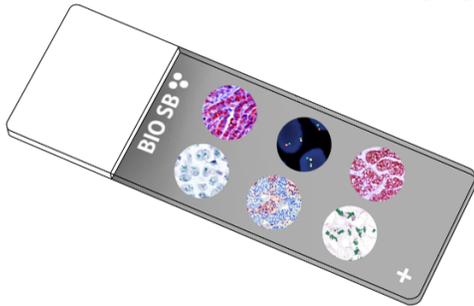


## ROS-1 Control Slides



### Intended Use

For In Vitro Diagnostic Use.

### Summary and Explanation

ROS1 (ROS Proto-Oncogene 1, Receptor Tyrosine Kinase) is a receptor tyrosine kinase that undergoes genetic rearrangements in various human cancers and in humans is encoded by the ROS1 gene. The protein encoded by this gene is a type I integral membrane protein with tyrosine kinase activity with structural similarity to the anaplastic lymphoma kinase protein. The protein may function as a growth or differentiation factor receptor. ROS1 expression is limited in normal tissues to occasional staining cerebellum, stomach, small intestine, colon and kidney.

Gene rearrangements involving the ROS1 gene were first detected in glioblastoma tumors and cell lines. ROS1 fusion partners include CD74, SLC34A2 and SDC4, leading to oncogenic transformation. ROS1 rearrangement was identified in a cell line derived from a lung adenocarcinoma patient and multiple studies have demonstrated its incidence in lung cancers. While ROS1 is undetectable in the normal lung, studies have described ROS1 rearrangements in 1-2% of NSCLC by FISH. Recent reports have demonstrated strong correlation between ROS1 IHC with FISH positivity. ROS1 fusions have been detected in multiple other tumors, including glioblastoma, non-small cell lung cancer, cholangiocarcinoma, ovarian cancer, gastric adenocarcinoma, colorectal cancer, inflammatory myofibroblastic tumor, angiosarcoma, and epithelioid hemangioendothelioma.

### Presentation

Five slides of ROS-1 positive tissues, each mounted on Hydrophilic Plus Slides, provided in a plastic mailer.

<i>Catalog No.</i>	<i>Quantity</i>
BSB-9365-CS	5 slides
BSB 3629	5 slides

**Storage** Store at 20-25°C

### Precautions

1. For professional users only. Results should be interpreted by a qualified medical professional.
2. Ensure proper handling procedures are used with this reagent.
3. Always wear personal protective equipment such as a laboratory coat, goggles, and gloves when handling reagents.
4. Dispose of unused solution with copious amounts of water.
5. Follow safety precautions of the heating device used for epitope retrieval (TintoRetriever Pressure Cooker or similar).
8. For additional safety information, refer to the Safety Data Sheet for this product.
9. For complete recommendations for handling biological specimens, please refer to the CDC document, "Guidelines for Safe Work Practices in Human and Animal Medical Diagnostic Laboratories" (see References in this document).

### Stability

**This product is stable up to the expiration date on the product label.**

Do not use the after expiration date listed on the package label.

### IHC Protocol

1. Subject tissues to heat induced epitope retrieval (HIER) using a suitable retrieval solution such as ImmunoDNA Retriever with Citrate (BSB 0020-BSB 0023) or EDTA (BSB 0030-BSB 0033).

2. Any of three heating methods may be used:

#### a. TintoRetriever Pressure Cooker or Equivalent

Place tissues/slides in a staining dish or coplin jar containing the ImmunoDNA Retriever with Citrate or EDTA and place on trivet in the pressure cooker. Add 1-2 inches of distilled water to the pressure cooker and turn heat to high. Incubate for 15 minutes. Open and immediately transfer slides to room temperature.

#### b. TintoRetriever PT Module or Water Bath Method

Place tissues/slides in a pre-warmed staining dish or coplin jar containing the ImmunoDNA Retriever with Citrate or EDTA at 95°-99° C. Incubate for 30-60 minutes.

#### c. Conventional Steamer Method

Place tissues/slides in a pre-warmed staining dish or coplin jar containing the ImmunoDNA Retriever with Citrate or EDTA in a steamer, cover and steam for 30-60 minutes.

3. After heat treatment, transfer slides in ImmunoDNA Retriever with Citrate or EDTA to room temperature and let stand for 15-20 minutes.
4. For manual staining, perform antibody incubation at ambient temperature. For automated staining methods, perform antibody incubation according to instrument manufacturer's instructions.
5. Wash slides with ImmunoDNA washer or DI water.
6. Continue IHC staining protocol. Wash slides between each step with ImmunoDNA washer solution.

### Abbreviated Immunohistochemical Protocol

Step	ImmunoDetector AP/HRP	PolyDetector AP/HRP	PolyDetector Plus HRP
Peroxidase/AP Blocker	5 min.	5 min.	5 min
Primary Antibody	30-60 min.	30-60 min.	30-60 min.
1st Step Detection	10 min.	30-45 min.	15 min.
2nd Step Detection	10 min.	Not Applicable	15 min.
Substrate- Chromogen	5-10 min.	5-10 min.	5-10 min.
Counterstain / Coverslip	Varies	Varies	Varies

### Abbreviated IF Protocol

Step	Incubation Time
Rinse slides in IF wash buffer	5 minutes
Drain and wipe excess IF wash buffer off slide	
Conduct remaining steps in the dark	
Apply Antibody	30-60 minutes
Rinse with 3 changes of IF wash buffer	3x15 minutes each
Coverslip with IF mounting medium	

### Mounting Protocols

For detailed instructions using biodegradable permanent mounting media such as XyGreen PermaMunter (BSB 0169-0174) or organic solvent based resin such as PermaMunter (BSB 0094-0097), refer to PI0174 or PI0097.

### Product Limitations

Due to inherent variability present in immunohistochemical procedures (including fixation time of tissues, dilution factor of antibody, retrieval method utilized, and incubation time), optimal performance should be established through the use of positive and negative controls. Results should be interpreted by a qualified medical professional.

### References

1. "Entrez Gene: ROS1 v-ros UR2 sarcoma virus oncogene homolog 1 (avian)".
2. Rabin M, Birnbaum D, Young D, Birchmeier C, Wigler M, Ruddle FH. "Human ros1 and mas1 oncogenes located in regions of chromosome 6 associated with tumor-specific rearrangements". *Oncogene Research*. 1987; 1 (2): 169-78.
3. Birchmeier C, Sharma S, Wigler M. "Expression and rearrangement of the ROS1 gene in human glioblastoma cells". *Proceedings of the National Academy of Sciences of the United States of America*. 1987; 84 (24): 9270-4.
4. Rikova K, et al. "Global survey of phosphotyrosine signaling identifies oncogenic kinases in lung cancer". *Cell*. 2007; 131 (6): 1190-203.
5. Davies KD, Doebele RC. "Molecular pathways: ROS1 fusion proteins in cancer". *Clinical Cancer Research*. 2013; 19 (15): 4040-5.
6. Sholl LM, et al. ROS1 immunohistochemistry for detection of ROS1-rearranged lung adenocarcinomas. *Am J Surg Pathol*. 2013 Sep;37(9):1441-9.
7. Luk P, et al. Biomarkers for ALK and ROS1 in Lung Cancer Immunohistochemistry and Fluorescent In Situ Hybridization. *Arch Pathol Lab Med*. 2018;142:922-928.
8. U.S. Department of Health and Human Services: Centers for Disease Control and Prevention. Guidelines for Safe Work Practices in Human and Animal Medical Diagnostic Laboratories. Supplement / Vol. 61, January 6, 2012. <https://www.cdc.gov/mmwr/pdf/other/su6101.pdf>

### Symbol Key / Légende des symboles/Erläuterung der Symbole

<b>EC REP</b>	QAdvis EAR AB Ideon Science Park Scheelevägen 17 SE-223 70 Lund, Sweden	 Storage Temperature Limites de température Zulässiger Temperaturbereich	 Manufacturer Fabricant Hersteller	<b>REF</b>	Catalog Number Référence du catalogue Bestellnummer
<b>IVD</b>	In Vitro Diagnostic Medical Device Dispositif médical de diagnostic in vitro In-Vitro-Diagnostikum	 Read Instructions for Use Consulter les instructions d'utilisation Gebrauchsanweisung beachten	 Expiration Date Utiliser jusque Verwendbar bis	<b>LOT</b>	Lot Number Code du lot Chargenbezeichnung